

Cerebellar Volume of Musicians

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There is evidence that the cerebellum is involved in motor learning and cognitive function in humans. Animal experiments have found structural changes in the cerebellum in response to long-term motor skill activity. We investigated whether professional keyboard players, who learn specialized motor skills early in life and practice them intensely throughout life, have larger cerebellar volumes than matched non-musicians by analyzing high-resolution T_1 -weighted MR images from a large prospectively acquired database ($n = 120$). Significantly greater absolute ($P = 0.018$) and relative ($P = 0.006$) cerebellar volume but not total brain volume was found in male musicians compared to male non-musicians. Lifelong intensity of practice correlated with relative cerebellar volume in the male musician group ($r = 0.595$, $P = 0.001$). In the female group, there was no significant difference noted in volume measurements between musicians and non-musicians. The significant main effect for gender on relative cerebellar volume ($F = 10.41$, $P < 0.01$), with females having a larger relative cerebellar volume, may mask the effect of musicianship in the female group. We propose that the significantly greater cerebellar volume in male musicians and the positive correlation between relative cerebellar volume and lifelong intensity of practice represents structural adaptation to long-term motor and cognitive functional demands in the human cerebellum.

Introduction

Structural differences exist in the human brain, that correlate with gender, handedness, degree of functional lateralization and special skills (Witelson, 1989; Peters, 1991; Schlaug *et al.*, 1995a,b; Steinmetz *et al.*, 1995; Amunts *et al.*, 1997, 2000; Maguire *et al.*, 2000; Schneider *et al.*, 2002). We, as others, have been particularly interested in the brain structure of musicians, whether it differs from that of non-musicians and whether training could account for these differences (Meyer, 1977; Schlaug *et al.*, 1995a,b; Amunts *et al.*, 1997; Zatorre *et al.*, 1998; Schneider *et al.*, 2002). Structural brain differences between musicians and non-musicians have been reported to exist in the posterior superior temporal lobe (Schlaug *et al.*, 1995a; Zatorre *et al.*, 1998), auditory cortex (Schneider *et al.*, 2002), corpus callosum (Schlaug *et al.*, 1995b) and motor cortex (Amunts *et al.*, 1997). Behavioral correlates are noted in these studies: increased left-ward asymmetry of the planum temporale is seen in musicians with absolute pitch; larger gray matter volume of the Heschl's gyrus was associated with an enhanced activation on listening to sinusoidal tones; larger non-dominant motor cortex is seen in key-board players correlating with higher non-dominant index finger tapping rates and earlier commencement of training and larger anterior corpus callosum in musicians who commence musical training before the age of seven. Although it appears a relationship exists between behavior and structure in musicians, the nature of this relationship has not been established.

Results from animal studies suggest a causal relationship exists between motor skill acquisition and practice and structural

changes in the cerebellum (Black *et al.*, 1990; Anderson *et al.*, 1994; Kleim *et al.*, 1997; Anderson *et al.*, 2002). The traditional view of cerebellar function has expanded from one of motor coordination to involve motor skill acquisition (Marr, 1969; Black *et al.*, 1990; Seitz *et al.*, 1994; Kleim *et al.*, 1997; Mauk *et al.*, 1998; Thach, 1998) and varied cognitive and sensory discrimination tasks (Kim *et al.*, 1994; Raichle *et al.*, 1994; Fiez *et al.*, 1996; Gao *et al.*, 1996; Allen *et al.*, 1997; Holcomb *et al.*, 1998; Schmahmann and Sherman, 1998; Timmann *et al.*, 2002).

Noting the previously reported correlations between certain brain structures and certain musical skills (Schlaug *et al.*, 1995a,b; Amunts *et al.*, 1997; Zatorre *et al.*, 1998; Schneider *et al.*, 2002) and the emerging evidence of the importance of the cerebellum to motor skill acquisition and many cognitive functions, we investigated whether the cerebellar volume of musicians is greater than that of non-musicians and whether there is a correlation between volume measurements and training intensity parameters.

Materials and Methods

Subjects

The data were derived from a prospectively acquired database of musicians and non-musicians. In a retrospective analysis we selected all right-handed keyboard players who had complete data sets of their biographical information including lifelong practice times. Sixty right-handed keyboard players were identified (30 male and 30 female). They were matched for handedness, gender, approximate height and age to non-musicians from our database. The subjects classified as musicians had to be professional, classically trained keyboard players and the subjects classified as non-musicians had never received formal musical training or played a musical instrument. Twenty-three of the 60 musicians played a string instrument in addition to the piano. Non-musicians were students or young professionals at local colleges and universities that responded to ads placed in colleges, hospitals and medical schools. All subjects, musicians and non-musicians, selected for this analysis were consistently right-handed according to hand preference questionnaires (Annett, 1970; Amunts *et al.*, 1997, 2000) and an index finger tapping test (Peters and Durning, 1978). All subjects filled out a musical background questionnaire to record the age of commencement of musical training, number of years of practice and intensity of lifelong practice (self estimates of the hours of practice per day for each five year interval from the age of commencement, averaged over the number of years of practice to give a lifetime average hours per day). This questionnaire included further questions addressing the acquisition and practice of other motor skills, which included sports, typing and hobby-related skills, and this data was recorded in a categorical format. In addition, all subjects had undergone a brief test to assess their verbal IQ using the Shipley-Hartford Vocabulary and Abstraction test. This variable correlates highly with the WAIS full scale IQ and therefore, was converted to this scale according to age level (Paulson and Lin, 1970).

Informed consent was obtained from each subject according to the declaration of Helsinki and the protocol and consent process was approved by the Institutional Review Board of Beth Israel Deaconess Medical Center, Boston.

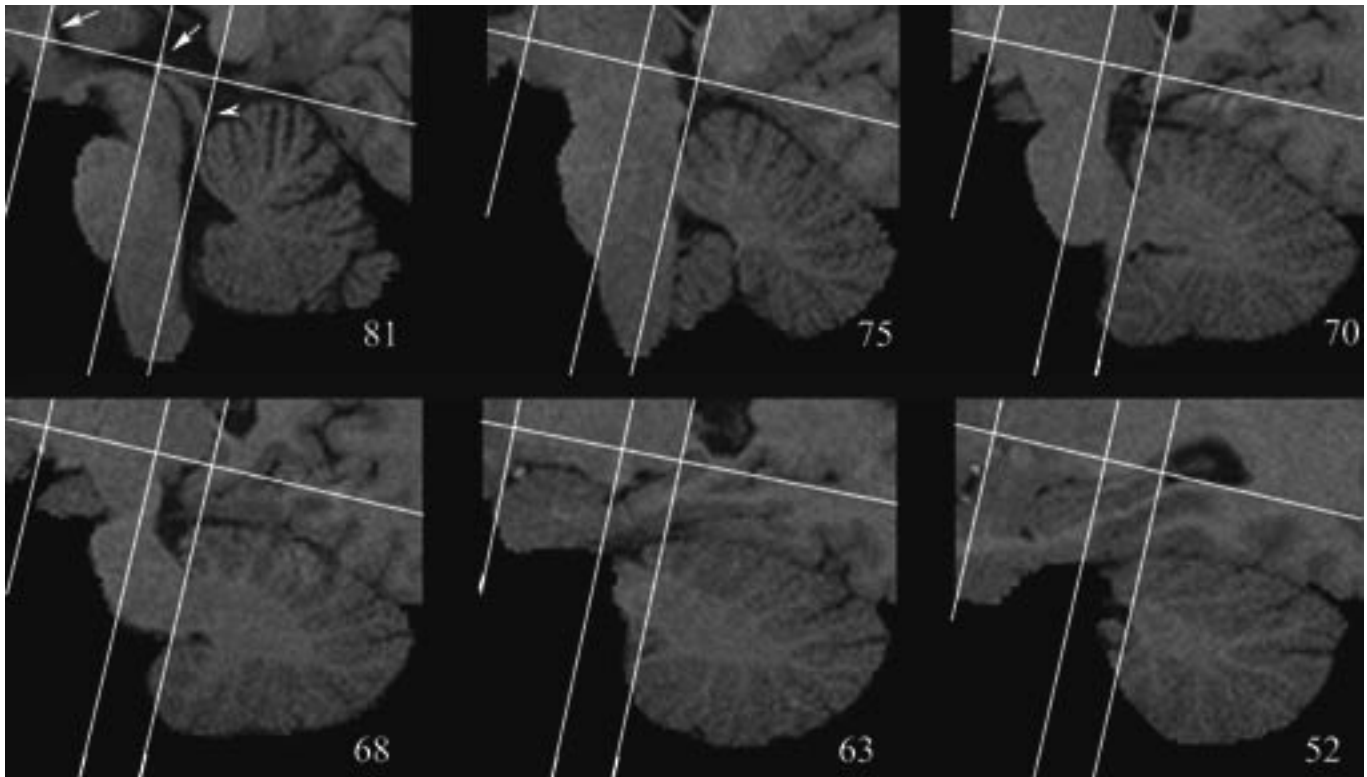


Figure 1. Landmark-based dissection of the cerebellar peduncles from the cerebellar white matter and the brainstem is shown. On the midsagittal slice (slice 81 of 160 in this subject) vertical lines are drawn perpendicular to the bi-commissural line at the AC and PC (arrows) and through the posterior border of the inferior colliculus (arrowhead). These lines are overlaid on all sagittal slices and the latter vertical line is used to dissect the cerebellar peduncles from the brainstem. A representative selection of slices is shown from one subject from medial to lateral (slice numbers are placed on bottom right corner of each slice).

Methods

All subjects underwent high resolution 'anatomical' imaging of the brain using a T_1 -weighted MR sequence (1 mm³ voxel size) with sagittal slice orientation (160 slices) on a 1.5 Tesla Siemens Vision MR scanner. Volumetric processing was performed in a method similar to that described by Luft *et al.* (Luft *et al.*, 1998).

Using custom-made software implemented in the Advanced Visualization Systems (AVS) software package on Hewlett Packard workstations, MR images were segmented into brain and non-brain tissue (skull and meninges) for whole brain and cerebellar volumetric measurement using a sobel-based detection and region-growing technique to create a new image, representing purely brain without any scalp and skull (Huang *et al.*, 1993; Peters *et al.*, 2000). Manual tracing was used to remove any remaining meninges. The cut-off between the brainstem and spinal cord was the last horizontal slice containing cerebellum. Although this is somewhat arbitrary, there are no clear and accepted gross anatomical landmarks to differentiate brainstem from spinal cord on MR images. Using the last horizontal slice that contained cerebellum, in brains that were AC-PC aligned, ensured that the cut-off was reliable and similar between brains. Regions of interest consisting of at least 30 voxels were drawn in the lateral ventricles and in the fourth ventricle. Regional means and standard deviations were determined from these regions of interest containing CSF. A mean plus two standard deviations was used as a threshold to separate brain from CSF. The final total segmented brain consisted of the forebrain, cerebellum and brainstem.

The cerebellum was segmented manually from the brainstem and cerebellar peduncles using established anatomical landmarks (Courchesne *et al.*, 1989; Press *et al.*, 1989) and criteria similar to those adopted in previous volumetric studies of the cerebellum (Filipek *et al.*, 1994; Luft *et al.*, 1998). On sagittal slices the cerebellum was separated from the tentorium and remaining meninges by manual tracing (the cerebellum was contained in ~80 sagittal slices). The cerebellar peduncles were removed from the cerebellar white matter on sagittal slices according to the following procedure (Fig. 1): on the mid-sagittal slice a vertical line

was drawn (perpendicular to a line connecting the anterior and posterior commissure) which touched the posterior border of the inferior colliculus. This vertical line was superimposed on all sagittal slices and was used as a guide to separate the cerebellar peduncles from the brainstem. Cerebellar cortex anterior to this line was not excluded and was manually traced as part of the cerebellum (note in Fig. 1 that this included parts of the anterior lobe, biventer and flocculus on more lateral slices and of the tonsils and anterior lobe of the vermis on more medial slices). The final segmented cerebellum consisted of the cerebellar hemispheres, deep nuclei and vermis.

Total brain and absolute cerebellar volume were the number of voxels (all voxel sizes were 1 mm³) above the CSF threshold.

Two raters, blinded to the identity of the subjects, selected 20 cases randomly from the total 120 cases to define and agree on the above landmarks. Following this process, the inter-rater reliability (Pearson correlation coefficient) for segmented cerebellar volumes on a further 15, previously unselected, brains was found to be 0.92 (two-sided $P < 0.01$). After this, one of the investigators, blinded to subject identity (gender and group), segmented all 120 cases.

Data Analysis

Cerebellar volume was normalized to reduce intersubject variability. Correlations (bivariate Pearson correlations with two-tailed tests of significance) were tabulated between (a) absolute cerebellar volume (aCV) and total brain volume (tBV) and (b) aCV and body height in order to determine whether tBV or body height should be selected to correct for inter-subject variability in cerebellar volume due to these factors. There was a higher correlation between aCV and tBV ($r = 0.677$, $P < 0.001$) than there was between aCV and body height ($r = 0.331$, $P < 0.001$) (two-tailed, Pearson Correlation). Therefore we chose to normalize aCV to tBV in order to partial out the inter-subject variability in tBV as a source of variance in aCV measurements, by calculating a relative cerebellar volume (rCV) in each subject as a percent ratio of their total brain volume, where $rCV (\%) = aCV/tBV \times 100$. There is precedence in

Table 1Mean values (\pm SD) for each measured variable in the groups that were studied^a

| | Height | Age | IQ | tBV | aCV | rCV |
|---------------------------|----------------------------|---------------|-------------|-------------------------------|-----------------|--------------------------|
| Males (60) | 181.04 [#] (6.33) | 26.13* (4.48) | 117.7 (5.4) | 1405.70 [#] (100.67) | 143.28* (12.70) | 1020 ⁺ (0.74) |
| Male non-musicians (30) | 180.67 (6.24) | 25.63 (4.68) | 118.4 (5.1) | 1402.77 (116.20) | 139.43† (14.05) | 9.95* (0.70) |
| Male musicians (30) | 181.43 (6.50) | 26.63† (4.29) | 116.7 (6.1) | 1408.63 (84.27) | 147.13† (10.01) | 10.46* (0.69) |
| Females (60) | 165.96 (6.68) | 24.06* (4.81) | 117.6 (6.6) | 1295.68 [#] (94.61) | 137.15* (11.28) | 10.60 (0.63) |
| Female non-musicians (30) | 167.33 (6.14) | 24.07 (4.81) | 117.0 (6.7) | 1285.23 (77.56) | 137.03 (11.40) | 10.67 (0.66) |
| Female musicians (30) | 164.59 (7.02) | 23.57† (5.24) | 118.7 (6.6) | 1306.13 (99.95) | 137.28 (10.50) | 10.53 (0.62) |

^aHeight (cm), Age at MRI scan (years), estimated WAIS full scale IQ (from Shipley–Hartford total raw score), tBV and aCV (in cc), rCV (% of total brain volume). Significant group differences are indicated: † $P < 0.05$, * $P < 0.01$, + $P < 0.005$, # $P < 0.001$.

Table 2

Pearson correlation coefficients for the relationship between brain volume measurements and measures of musical training in the musician groups

| | Female | | | Male | | | Total | | |
|-----------------------|--------|--------|--------|--------|--------|--------|--------|-------|--------|
| | tBV | aCV | rCV | tBV | aCV | rCV | tBV | aCV | rCV |
| Age of commencement | -0.127 | 0.153 | 0.376 | -0.087 | -0.262 | -0.176 | 0.109 | 0.124 | -0.038 |
| Total years | 0.042 | -0.125 | -0.197 | 0.122 | 0.193 | 0.064 | 0.102 | 0.051 | 0.104 |
| Intensity of practice | 0.003 | -0.226 | -0.283 | -0.299 | 0.318 | 0.595* | -0.038 | 0.104 | 0.167 |

*Significant, $P = 0.001$, two-tailed.

selecting brain volume or brain weight rather than body height to normalize brain morphometric data (Passingham, 1979; Witelson, 1989; Peters, 1991; Steinmetz *et al.*, 1995).

Three two-by-two (gender \times musicianship) factorials were performed to assess the effect of gender and musicianship on tBV, aCV and rCV. *Post hoc* testing employed Bonferroni adjusted comparisons for the planned comparisons, using adjusted Student's *t*-tests. The main effects were significant for gender in terms of tBV and aCV as has been previously described (Nopoulos *et al.*, 2000; Raz *et al.*, 2001). All P values reported are two-tailed. Similarly, Bonferroni-adjusted Student's *t*-tests were employed to assess whether the male and female musician groups differed in any of the measures of musicianship recorded from the questionnaire, namely, age of commencement of training, number of years of practice and lifelong intensity of practice or whether they differed in age. Furthermore we compared the data of body length, age and IQ between and within each gender group to determine whether there was a difference between genders or between musicians and non-musicians. This would indicate how well matched the groups were.

Bivariate Pearson correlations with two-tailed tests of significance were then performed within the male and female musician groups in order to assess the relationship between tBV, aCV and rCV and age of commencement of training, number of years of practice and intensity of lifelong practice. Amount of time spent per week on non-musical motor skills was categorical data, recording whether or not the subject performed sports or motor-skilled hobbies, including typing, the differences between the groups were analyzed with non-parametric significance testing.

Results

Volume Measurements: Analysis of Variance

All group means in tBV, aCV, rCV, height, age and estimated WAIS full scale IQ from Shipley–Hartford total raw scores are noted in Table 1. Within each gender, musicians and non-musicians did not differ significantly in height, age or IQ (all P s > 0.05). A series of two-way factorials were performed across tBV, aCV and rCV with musicianship and gender as factors. In terms of tBV, the interaction of the factors ($F = 0.176$, $P > 0.05$) and effect for musicianship ($F = 0.557$, $P > 0.05$) were not significant, but a significant effect for gender ($F = 37.647$, $P < 0.0005$) was found, with males having a greater tBV than females. Similarly, for aCV, there was no significant interaction ($F = 2.99$, $P > 0.05$) or main effect for musicianship ($F = 3.40$,

$P > 0.05$), but the main effect of gender was significant ($F = 8.09$, $P < 0.005$), with males having a greater aCV than females. An analysis of rCV did reveal a significant gender by musicianship interaction ($F = 7.169$, $P < 0.01$). Here also, there was no main effect for musicianship ($F = 2.429$, $P > 0.05$) but a significant main effect for gender ($F = 10.41$, $P < 0.01$), notably with females having a greater rCV than males.

Employing planned comparisons, the nature of the interaction was examined within each of the genders. In the female group, no significant difference was found between the musicians and non-musicians for height ($P = 0.113$), age ($P = 0.702$), tBV ($P = 0.397$), aCV ($P = 0.933$) and rCV ($P = 0.411$). In the male group there was a significant difference in rCV ($P = 0.006$) between musicians (10.46%, SD 0.69) and non-musicians (9.95%, SD 0.70), also a significant difference between the aCV ($P = 0.018$) of the male musicians (147.13 cc, SD 10.01) and non-musicians (139.43 cc, SD 14.05). Male musicians did not differ significantly from male non-musicians in tBV ($P = 0.824$), height ($P = 0.644$) or age ($P = 0.392$).

Parameters of Training Intensity: Analysis of Variance of Between Groups and of Correlation with Volume Measurements

Pearson correlation coefficients for the relationship between volume measurements for all musicians and the recorded measures of musicianship are reported in Table 2. A significant positive correlation ($r = 0.595$, $P = 0.001$, two-tailed) was found between intensity of practice and rCV in the male musician group (Fig. 2). Age of commencement of training and total years of musical training were not significantly associated with rCV in the male musician group and there was no significant correlation between the measures of musicianship and tBV or aCV. There was no significant correlation found in the female musician group or the whole musician group between the measures of musicianship and the variables of tBV, aCV and rCV.

There was no significant differences noted between the male and female musician group in total years of musical training and intensity of practice; significant differences were noted between the male and female musicians in age of commencement of musical training, with the female music group starting slightly

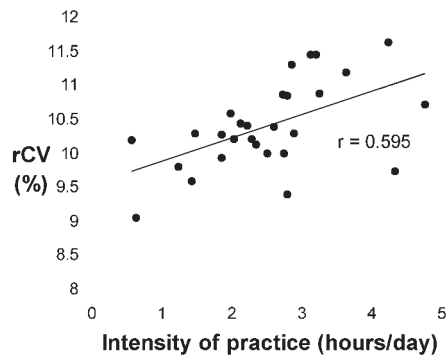


Figure 2. The relationship between relative cerebellar volume (rCV as a % of total brain volume) and lifelong intensity of practice (hours per day averaged over years of practice) for the male musician group. Bivariate Pearson correlation analysis revealed a significant positive correlation between the variables ($r = 0.595$, $P = 0.001$, two-tailed).

earlier than the male group (Table 3) and also in age at scanning with the female group being slightly younger than the male group (Table 1). There were no significant differences noted between the musician and non-musician groups of each gender for other examined variables including height, age and IQ. The distribution of those who spent time on non-musical motor skills was similar in all groups.

Discussion

Significantly Larger Cerebellar Volume in Male Musicians Correlates with Lifelong Intensity of Practice

Through morphometric analysis of total brain and cerebellar volume using high resolution MRI, we demonstrated that the male musician group had significantly larger aCV and rCV than the non-musician group. The difference amounts to a cerebellar volume difference between male musicians and non-musicians of ~5% (mean aCV of 147.13 cc and rCV of 10.46% in male musicians compared with an aCV of 139.43 cc and rCV of 9.95% in male non-musicians). There was no significant difference in mean tBV between these groups. Average brain size measurements vary greatly depending on the sample examined and methodology employed (Peters *et al.*, 1998). The mean tBV and aCV in the current study (excepting the female musicians, as discussed below) are equivalent to values obtained from MRI using similar (Luft *et al.*, 1998, 1999) and different (Giedd *et al.*, 1996; Nopoulos *et al.*, 2000) methodologies.

For the male musician group, there was a significantly positive correlation between the intensity of practice throughout life and rCV. There was no significant correlation between age of commencement of musical training or the total number of years of training and the cerebellar volume in the male musician group. Other studies have found correlations between the age of commencement of musical training and the degree of functional or structural difference that was found between musicians and non-musicians (Elbert *et al.*, 1995; Schlaug *et al.*, 1995b; Amunts *et al.*, 1997; Pantev *et al.*, 1998). From these correlations it has been speculated that if differences in brain structure and function associated with specific musical skills exist in professional musicians, it is because they commence tuition and practice intensely during a critical time point in brain development (Elbert *et al.*, 1995; Schlaug *et al.*, 1995a,b; Amunts *et al.*, 1997; Pantev *et al.*, 1998). Our study supports this speculation in that we found the more intensely a male musician practices, the larger his cerebellum. Most of the musicians examined in this study commenced tuition at an early age (mean of 6.4 ± 1.96

Table 3

Mean (\pm SD) for the measures of musicianship in each musician subgroup^a

| | Age of commencement | Intensity of practice | Years of practice |
|-----------------------|--------------------------|-----------------------|-------------------|
| Male musicians (30) | 6.40 (1.96) ⁺ | 2.62 (1.06) | 19.90 (4.35) |
| Female musicians (30) | 4.81 (1.83) ⁺ | 2.29 (1.06) | 19.25 (4.87) |

^aIn each subgroup ($n =$); Age of commencement of musical training (years of age); Intensity of practice (average hours per day over lifetime of practice); Years of practice (years of practice since commencement of musical training). ⁺Significant difference $P < 0.005$.

years for the male musician group) therefore the poor spread in this variable may have obscured a possible correlation between age of commencement of tuition and cerebellar volume in musicians. Although our findings support the hypothesis that structural change can occur in the brain in response to behavior, it remains possible that individuals with larger cerebellums have an affinity to the acquisition and practice of musical skill and therefore select it as a chosen behavior. A longitudinal study is required to definitively establish causal relationships between function and structural change.

The Importance of the Cerebellum to Musical Skill?

Although contested (Llinas and Welsh, 1993; Nixon and Passingham, 2000; Bischoff-Grethe *et al.*, 2002), investigators using varied methodologies have demonstrated cerebellar involvement in motor learning (Kleim *et al.*, 1997; Mauk *et al.*, 1998; Thach, 1998; Seitz *et al.*, 1994; Attwell *et al.*, 2002) and many cognitive functions (Leiner *et al.*, 1986; Courchesne *et al.*, 1988; Kim *et al.*, 1994; Middleton and Strick, 1994; Raichle *et al.*, 1994; Fiez *et al.*, 1996; Gao *et al.*, 1996; Allen *et al.*, 1997; Holcomb *et al.*, 1998; Schmahmann and Sherman, 1998; Timmann *et al.*, 2002). It has been proposed that the cerebellum processes motor, sensory and cognitive data in a similar manner, predicting information acquisition and coordinating responses (Leiner *et al.*, 1995; Allen *et al.*, 1997; Schmahmann and Sherman, 1998; Fiez, 1999). The cerebellum appears to be particularly important in the early error-driven adaptation phase of motor and cognitive skill learning and with increasing skill expertise the cerebellum is less active (Raichle *et al.*, 1994; Seitz *et al.*, 1994; Toni *et al.*, 1998). We would speculate that such adaptation to error in motor and non-motor skill acquisition is an important part of the intensity of practice variable that was recorded in the professional keyboard players we studied.

As expected, cerebellar activation is noted on functional imaging of musicians while playing (Sergent *et al.*, 1992), but also during motor sequence learning (Hund-Georgiadis and von Cramon, 1999) and the performance of many non-motor musical skills (Parsons, 2001). It is possible the cerebellar volume difference noted in musicians is associated with a specific motor or cognitive function, such as motor consolidation (Attwell *et al.*, 2002) or tone recognition (Holcomb *et al.*, 1998). Topographic specialization and lateralization of function has been noted in neuroimaging studies of the cerebellum (Allen *et al.*, 1997; Raichle *et al.*, 1994; Fink *et al.*, 2001). However, in the current study we did not sub-divide the cerebellum to determine if a specific anatomic or functional subregion dominated in the volume difference noted, as, no specific component of musical skill has been associated with the cerebellum, there were many possible candidate subregions that could be examined and to examine them all would significantly reduce the statistical power of our investigation.

The Relationship Between Function and Structure in the Cerebellum

Similar to other structure-to-function correlations (Witelson, 1989; Schlaug *et al.*, 1995a,b; Steinmetz *et al.*, 1995; Amunts *et al.*, 1997, 2000; Zatorre *et al.*, 1998; Maguire *et al.*, 2000), we are unable to determine whether the structural difference (cerebellar volume) exists as a result of the difference in function (intensity of practice) or whether the structural difference enabled the difference in function to arise. However, animal studies demonstrate that differences in behavior can lead to structural change in the cerebellum. Motor skill learning animals have quantifiable microstructural changes in Purkinje cells and the molecular layer when compared with motor exercise animals (Black *et al.*, 1990; Anderson *et al.*, 1994; Kleim *et al.*, 1997). Pysh and Weiss (Pysh and Weiss, 1979) quantified that the molecular layer was 10% larger in area and depth in active compared to inactive infant mice. The sum of such microstructural changes in these skill-learning animals may amount to a volume difference (Andersen *et al.*, 2002) which is similar to that found in the male musician group (approximately a 5% volume difference).

No Significant Effect of Musicianship on Cerebellar Volume in the Female Group but Significantly Larger Relative Cerebellar Volume in Females Compared to Males

The effect of musicianship on cerebellar volume was only significant in the male subgroup and was not seen in either the female subgroup or, therefore, the whole group. The absence of an effect in the female subgroup is not apparent. The male and female musician groups were well matched for number of years of practice and intensity of practice. The female musicians were significantly younger than the males at imaging (mean age of 23.57 compared with 26.53) and significantly younger at age of commencement of musical tuition (mean age of 4.81 compared with 6.40), however this difference would be expected to exaggerate effects of musicianship in the female group. The sample size employed was appropriate to find a 5% difference in aCV (effect size, $d = 0.60$; alpha, two-tailed = 0.05) in a Student's *t*-test with power calculated as 0.913, and this *post hoc* power calculation compares favorably to other morphometric studies in the cerebellum where it can be calculated [(Nopoulos *et al.*, 2000) have an effect size, $d = 0.60$; alpha, two-tailed = 0.05; power calculated as 0.773)].

It is of interest to note that the mean aCV of both female groups are equivalent and almost reach the mean aCV for male non-musicians, whereas the mean tBV of both female groups are significantly smaller than the mean tBV of both male groups. These results equate to the female groups, separately and as a whole, having significantly greater mean rCV than the male non-musician group and the whole male group. The effect of gender on total brain volume and weight is known (Dekaban, 1978; Giedd *et al.*, 1996). The differential effect of gender on tBV and aCV that is noted in this study has been observed before in studies where both tBV and aCV are measured but little commentary has been made about the relatively larger cerebellar, in relation to cerebral, volume in females (Luft *et al.*, 1998; Nopoulos *et al.*, 2000). Gender differences have been demonstrated in other brain structures (Witelson, 1989; Witelson and Kigar, 1992; Steinmetz *et al.*, 1995; Amunts *et al.*, 2000). It is not evident why the cerebellum is relatively larger in females. Although differences in various motor and cognitive measures have been associated with gender (Hantz *et al.*, 1996; Nicholson and Kimura, 1996; Sanders and Wenmoth, 1998; Kansaku *et al.*,

2000), gender effects on specific cerebellar associated functions have not been examined. Two studies of resting cerebellar metabolism have noted significant gender differences (Gur *et al.*, 1995; Volkow *et al.*, 1997) but have divergent results. Gender could influence brain function and structure through many mechanisms; sex difference affects animal models of cortical plasticity (Teskey *et al.*, 1999) and estrogen increases synaptic density in the hippocampus of rats (Woolley and McEwen, 1992).

We speculate that the strong gender effect that produces a relatively larger cerebellar volume in females may mask the effect of musicianship in this group. Caviness *et al.* (Caviness *et al.*, 1996) found that females, unlike males, reach adult cerebellar volume earlier in childhood, at this time both genders have equivalent relative cerebellar volumes. If both female musicians and non-musicians, under a stronger gender influence, reach cerebellar maturity at this earlier age, hitting a ceiling in structural development, the skill acquisition and long-term motor activity effects of professional musicianship subsequent to this time may be seen outside the cerebellum in other brain regions. It is of interest to note that there was a slight non-significant trend for larger total brain volume in female musicians that may support this speculation. It is also notable that the female non-musician group did not differ significantly from the other groups in verbal IQ or report of non-musical motor skills that might have accounted for the similarity in aCV between this group and female musicians.

Conclusion

In conclusion, this study finds a significant difference in absolute and relative cerebellar volume between male musicians and non-musicians. Relative cerebellar volume correlates positively with intensity of musical training throughout life in the male musician group. There is a strong effect of gender on relative cerebellar volume, with greater rCV in both female groups. These findings add to others (Elbert *et al.*, 1995; Schlaug *et al.*, 1995a,b; Steinmetz *et al.*, 1995; Amunts *et al.*, 1997; Pantev *et al.*, 1998; Zatorre *et al.*, 1998) that demonstrate structural and functional differences between the brains of musicians and non-musicians that positively correlate with early commencement of musical training. A correlation with lifelong training intensity has not been described in prior studies. Based on these correlations and inferences from animal studies, we would propose that the brain structural differences found in musicians are more the result of adaptation to the rigors of musical training, perhaps at a critical period of brain development, rather than the innate properties of a group of individuals who self-select themselves at an early age to become musicians. A longitudinal study is required to examine this hypothesis.

Notes

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References

- Allen G, Buxton RB, Wong EC, Courchesne E (1997) Attentional activation of the cerebellum independent of motor involvement. *Science* 275:1940–1942.
- Amunts K, Schlaug G, Jancke L, Steinmetz H, Schleicher A, Dabringhaus A, Zilles K (1997) Motor cortex and hand motor skills: structural compliance in the human brain. *Hum Brain Mapp* 5:206–215.
- Amunts K, Jancke L, Mohlberg H, Steinmetz H, Zilles K (2000) Interhemispheric asymmetry of the human motor cortex related to handedness and gender. *Neuropsychologia* 38:304–312.
- Annett M (1970) A classification of hand preference by association analysis. *Br J Psychol* 61:303–321.
- Anderson BJ, Li X, Alcantara A, Isaacs KR, Black JE, Greenough WT (1994) Glial hypertrophy is associated with synaptogenesis following motor-skill learning, but not with angiogenesis following exercise. *Glia* 11:73–80.
- Anderson BJ, Eckburg PB, Relucio KI (2002) Alterations in the thickness of motor cortical subregions after motor-skill learning and exercise. *Learn Mem* 9:1–9.
- Attwell PJ, Cooke SF, Yeo CH (2002) Cerebellar function in consolidation of a motor memory. *Neuron* 34:1011–1020.
- Bischoff-Grethe A, Ivry RB, Grafton ST (2002) Cerebellar involvement in response reassignment rather than attention. *J Neurosci* 22:546–553.
- Black JE, Isaacs KR, Anderson BJ, Alcantara AA, Greenough WT (1990) Learning causes synaptogenesis whereas motor activity cause angiogenesis, in cerebellar cortex of adult rats. *Proc Natl Acad Sci* 87:5568–5572.
- Caviness VS, Kennedy DN, Richelme C, Rademacher J, Filipek PA (1996) The human brain age 7–11 years: a volumetric analysis based on magnetic resonance images. *Cereb Cortex* 6:726–736.
- Courchesne E, Yeung-Courchesne R, Press GA, Hesselick JR, Jernigan TL (1988) Hypoplasia of the cerebellar vermal lobules VI and VII in autism. *N Engl J Med* 318:1349–1354.
- Courchesne E, Press GA, Murakami J, Berthoty D, Grafe M, Wiley CA, Hesselink JR (1989) The cerebellum in sagittal plane – anatomic-MR correlation: 1. The vermis. *Am J Radiol* 153: 829–835.
- Dekaban AS (1978) Changes in brain weights during the span of human life: relation of brain weights to body heights and body weights. *Ann Neurol* 4:345–356.
- Elbert T, Pantev C, Wienbruch C, Rockstroh B, Taub E (1995) Increased cortical representation of the fingers of the left hand in string players. *Science* 270:305–306.
- Fiez JA (1999) Cerebellar contributions to cognition. *Neuron* 16:13–15.
- Fiez JA, Raife EA, Balota DA, Schwarz JP, Raichle ME, Petersen SE (1996) A positron emission tomography study of the short-term maintenance of verbal information. *J Neurosci* 16:808–822.
- Filipek PA, Richelme C, Kennedy DN, Caviness VS Jr (1994) The young adult human brain: an MRI-based morphometric analysis. *Cereb Cortex* 4:344–360.
- Fink GR, Marshall JC, Weiss PH, Zilles K (2001) The neural basis of vertical and horizontal line bisection judgments: an fMRI study of normal volunteers. *Neuroimage* 14:S59–S67.
- Gao J-H, Parsons LM, Bower JM, Xiong J, Li J, Fox PT (1996) Cerebellum implicated in sensory acquisition and discrimination rather than motor control. *Science* 272:545–547.
- Giedd JN, Snell JW, Lange N, Rajapakse JC, Casey BJ, Kozuch PL, Vaituzis AC, Vauss YC, Hamburger SD, Kaysen D, Rapoport JL (1996) Quantitative magnetic resonance imaging of human brain development: ages 4–18. *Cereb Cortex* 6:551–560.
- Gur CR, Harper-Mozley L, Mozley PD, Resnick SM, Karp JS, Alavi A, Arnold SE, Gur RE (1995) Sex differences in regional cerebral glucose metabolism during a resting state. *Science* 267:528–531.
- Hantz EC, West Marvin E, Kreilick KG, Chapman RM (1996) Sex differences in memory for timbre: an event-related potential study. *Int J Neurosci* 87:17–40.
- Holcomb HH, Medoff DR, Caudill PJ, Zhao Z, Lahti AC, Dannals RF, Tamminga CA (1998) Cerebral blood flow relationships associated with a difficult tone recognition task in trained normal volunteers. *Cereb Cortex* 8:534–542.
- Huang Y, Knorr U, Schlaug G, Seitz RJ, Steinmetz H (1993) Segmentation of MR images for partial-volume-effect correction and individual integration with PET images of the human brain. *J Cereb Blood Flow Metab* 13:S315.
- Hund-Georgiadis M, von Cramon DY (1999) Motor-learning-related changes in piano players and non-musicians revealed by functional magnetic-resonance signals. *Exp Brain Res* 125:417–425.
- Kansaku K, Yamaura A, Kitazawa S (2000) Sex difference in lateralization revealed in the posterior language areas. *Cereb Cortex* 10:866–872.
- Kim S-G, Ugurbil K, Strick PL (1994) Activation of a cerebellar output nucleus during cognitive processing. *Science* 265:949–951.
- Kleim JA, Swain RA, Czerlanis CM, Kelly JL, Pipitone MA, Greenough WT (1997) Learning dependent dendritic hypertrophy of cerebellar stellate cells: plasticity of local circuit neurons. *Neurobiol Learn Mem* 67:29–33.
- Leiner HC, Leiner AL, Dow RS (1986) Does the cerebellum contribute to mental skills? *Behav Neurosci* 100:443–454.
- Leiner HC, Leiner AL, Dow RS (1995) The underestimated cerebellum. *Hum Brain Mapp* 2:244–254.
- Llinas R, Welsh JP (1993) On the cerebellum and motor learning. *Curr Opin Neurobiol* 3:958–965.
- Luft AR, Skalej M, Welte D, Kolb R, Burk K, Schulz JB, Klockgether T, Voigt K (1998) A new semi-automated, three-dimensional technique allowing precise quantification of total and regional cerebellar volume using MRI. *Magn Reson Med* 40:143–151.
- Luft AR, Skalej M, Schulz JB, Welte D, Kolb R, Burk K, Klockgether T, Voigt K (1999) Patterns of age-related shrinkage in cerebellum and brainstem observed *in vivo* using three-dimensional MRI volumetry. *Cereb Cortex* 9:712–721.
- Maguire EA, Gadian DG, Johnsrude IS, Good CD, Ashburner J, Frackowiak RSJ, Frith CD (2000) Navigation-related structural change in the hippocampi of taxi drivers. *Proc Natl Acad Sci* 97:4398–4403.
- Marr D (1969) A theory of cerebellar cortex. *J Physiol* 202:437–470.
- Mauk MD, Garcia KS, Medina JF, Steele PM (1998) Does cerebellar LTD mediate motor learning? Toward a resolution without a smoking gun. *Neuron* 20:359–362.
- Meyer A (1977) The search for a morphological substrate in the brains of eminent persons including musicians: a historical review. In: *Music and the brain* (Critchley M, Henson RA, eds), pp. 255–281. London: Heinemann.
- Middleton FA, Strick PL (1994) Anatomical evidence for cerebellar and basal ganglia involvement in higher cognitive function. *Science* 266:458–461.
- Nicholson KG, Kimura D (1996) Sex difference for speech and manual skill. *Percept Mot Skills* 82:3–13.
- Nixon PD, Passingham RE (2000) The cerebellum and cognition: cerebellar lesions impair sequence learning but not conditional visuomotor learning in monkeys. *Neuropsychologia* 38:1054–1072.
- Nopoulos P, Flaum M, O'Leary D, Andreasen NC (2000) Sexual dimorphism in the human brain: evaluation of tissue volume, tissue composition and surface anatomy using magnetic resonance imaging. *Psychiatry Res* 98:1–13.
- Pantev C, Oostenveld R, Engelien A, Ross B, Roberts LE, Hoke M (1998) Increased auditory cortical representation in musicians. *Nature* 392:811–814.
- Parsons LM (2001) Exploring the functional neuroanatomy of music performance, perception and comprehension. *Ann N Y Acad Sci* 930:211–231.
- Passingham RE (1979) Brain size and intelligence in man. *Brain Behav Evol* 16:253–270.
- Paulson MJ, Lin T (1970) Predicting WAIS IQ from Shipley-Hartford scores. *J Clin Psychol* 26:453–461.
- Peters M (1991) Sex differences in human brain size and the general meaning of differences in brain size. *Can J Psychol* 45:507–522.
- Peters M, Dürding BM (1978) Handedness measured by finger tapping: a continuous variable. *Can J Psychol* 32:257–260.
- Peters M, Jancke L, Staiger JF, Schlaug G, Huang Y, Steinmetz H (1998) Unsolved problems in comparing brain sizes in *Homo sapiens*. *Brain Cogn* 38:254–285.
- Peters M, Jancke L, Zilles K (2000) Comparison of overall brain volume and midsagittal corpus callosum surface area as obtained from NMR scans and direct anatomical measurements: a within-subject study on autopsy brains. *Neuropsychologia* 38:1375–1381.
- Press GA, Murakami J, Courchesne E, Berthoty DP, Grafe M, Wiley CA, Hesselink JR (1989) The cerebellum in sagittal plane – anatomic-MR correlation: 2. The cerebellar hemispheres. *Am J Radiology* 153:837–846.
- Pysh JJ, Weiss GM (1979) Exercise during development induces an increase in Purkinje cell dendritic tree size. *Science* 206:230–232.
- Raichle ME, Fiez JA, Videen TO, MacLeod AM, Pardo JV, Fox PT, Petersen

- SE (1994) Practice-related changes in human brain functional anatomy during nonmotor learning. *Cereb Cortex* 4:8–26.
- Raz N, Gunning-Dixon F, Head D, Williamson A, Acker JD (2001) Age and sex differences in the cerebellum and the ventral pons: a prospective MR study of healthy adults. *AJNR Am J Neuroradiol* 22:1161–1167.
- Sanders G, Wenmoth D (1998) Verbal and music dichotic listening tasks reveal variations in functional cerebral asymmetry across the menstrual cycle that are phase and task dependent. *Neuropsychologia* 36:869–874.
- Schlaug G, Jancke L, Huang Y, Steinmetz H (1995a) *In vivo* evidence of structural asymmetry in musicians. *Science* 267:699–701.
- Schlaug G, Jaencke L, Huang Y, Steinmetz H. (1995b) Increased corpus callosum size in musicians. *Neuropsychologia* 33:1047–1055.
- Schmahmann JD, Sherman JC (1998) The cerebellar cognitive affective syndrome. *Brain* 121: 561–579.
- Schneider P, Scherg M, Dosch HG, Specht HJ, Gutschalk A, Rupp A (2002) Morphology of Heschl's gyrus reflects enhanced activation in the auditory cortex of musicians. *Nat Neurosci* 5:688–694.
- Seitz RJ, Canavan AC, Yaguez L, Herzog H, Tellman L, Knorr U, Huang Y, Homberg V (1994) Successive roles of the cerebellum and premotor cortices in trajectory learning. *Neuroreport* 5:2541–2544.
- Sergent J, Zuck E, Terriah S, MacDonald B (1992) Distributed neural network underlying musical sight-reading and keyboard performance. *Science* 257:106–109.
- Steinmetz H, Staiger JF, Schlaug G, Huang Y and Jancke L (1995) Corpus callosum and brain volume in women and men. *Neuroreport* 6:1002–1004.
- Teskey GC, Hutchinson JE, Kolb B (1999) Sex differences in cortical plasticity and behavior following anterior cortical kindling in rats. *Cereb Cortex* 9:675–682.
- Thach WT (1998) A role for the cerebellum in learning movement coordination. *Neurobiol Learn Mem* 70:177–188.
- Timmann D, Drepper J, Maschke M, Kolb FP, Boring D, Thilman AF, Diener HC (2002) Motor deficits cannot explain impaired cognitive associative learning in cerebellar patients. *Neuropsychologia* 40:788–800.
- Toni I, Krams M, Turner R, Passingham RE (1998) The time course of changes during motor sequence learning: a whole-brain fMRI study. *Neuroimage* 8:50–61.
- Volkow ND, Wang GJ, Fowler JS, Hitzemann R, Pappas N, Pascani K, Wong C (1997) Gender differences in cerebellar metabolism: test-retest reproducibility. *Am J Psychiatry* 154:119–121.
- Witelson SF (1989) Hand and sex differences in the isthmus and genu of the human corpus callosum: a post-mortem morphological study. *Brain* 112:799–835.
- Witelson SF, Kigar DL (1992) Sylvian fissure morphology and asymmetry in men and women: bilateral differences in relation to handedness in men. *J Comp Neurol* 323:326–340.
- Woolley CS, McEwen BS (1992) Estradiol mediates fluctuation in hippocampal synapse density during the estrous cycle in the adult rat. *J Neurosci* 12:2549–2554.
- Zatorre RJ, Perry DW, Beckett CA, Westbury CF, Evans AC (1998) Functional anatomy of musical processing in listeners with absolute pitch and relative pitch. *Proc Natl Acad Sci* 95:3172–3177.