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ORIGINAL ARTICLE

Early musical training shapes cortico-cerebellar structural covariation

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Abstract

Adult abilities in complex cognitive domains such as music appear to depend critically on the age at which training or experience begins, and relevant experience has greater long-term effects during periods of peak maturational change. Previous work has shown that early trained musicians (ET; < age 7) out-perform later-trained musicians (LT; > age 7) on tests of musical skill, and also have larger volumes of the ventral premotor cortex (vPMC) and smaller volumes of the cerebellum. These cortico-cerebellar networks mature and function in relation to one another, suggesting that early training may promote coordinated developmental plasticity. To test this hypothesis, we examined structural covariation between cerebellar volume and cortical thickness (CT) in sensorimotor regions in ET and LT musicians and non-musicians (NMs). Results show that ETs have smaller volumes in cerebellar lobules connected to sensorimotor cortices, while both musician groups had greater cortical thickness in right pre-supplementary motor area (SMA) and right PMC compared to NMs. Importantly, early musical training had a specific effect on structural covariance between the cerebellum and cortex: NMs showed negative correlations between left lobule VI and right pre-SMA and PMC, but this relationship was reduced in ET musicians. ETs instead showed a significant negative correlation between vermal IV and right pre-SMA and dPMC. Together, these results suggest that early musical training has differential impacts on the maturation of cortico-cerebellar networks important for optimizing sensorimotor performance. This conclusion is consistent with the hypothesis that connected brain regions interact during development to reciprocally influence brain and behavioral maturation.

Keywords Music · Cerebellum · Sensorimotor · Plasticity · Experience · Sensitive period

Introduction

Adult abilities in complex cognitive domains such as music appear to depend critically on the age at which training or experience begins, with early age of start associated with long-term effects on behavior and the brain (Berken et al. 2016; Penhune 2019; Werker and Hensch 2015). Across all major neural systems, it has been shown that relevant experience has greater long-term effects during periods of peak maturational change, termed sensitive or critical periods (Knudsen 2004; Penhune 2020; Werker and Hensch 2015). Studies from our laboratory have shown that early trained musicians (ET; < age 7) out-perform later-trained musicians (LT; > age 7) on tests of musical skill, even when controlling for practice and training (Baer et al. 2015; Bailey and Penhune 2010, 2013; Ireland et al. 2019; Penhune 2020; Vaquero et al. 2016). Furthermore, ET musicians exhibit structural differences in brain regions involved in motor control and auditory-motor integration. For example, Bailey

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Significance Statement: Musical abilities appear to depend critically on the age at which training or experience begins: early trained musicians (ET; < 7) out-perform later-trained musicians (LT; > 7) on tests of musical skill, and also exhibit neuroanatomical differences. This study shows that ET musicians have smaller volumes of cerebellar lobules connected to sensorimotor cortices, while both ET and LT groups had greater cortical thickness in right pre-supplementary motor area, dorsal premotor cortex, and ventral premotor cortex. Most importantly, ET had a specific effect on structural covariance between the cerebellum and cortex. The results of this study show that musical training before age 7 affects cortico-cerebellar structural covariation in adulthood, indicating that early experience has differential impacts on the maturation of these connected regions.

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Extended author information available on the last page of the article et al. (2014) identified greater cortical surface area and gray matter volume in the ventral premotor cortex (vPMC) of ET musicians that was correlated with performance on a rhythm synchronization task. The vPMC plays a role in sensorimotor integration (Binkofski and Buccino 2006; Zatorre et al. 2007) and appears to have its peak maturational change at or prior to age 8, the period when early training begins (Ducharme et al. 2016; Gogtay et al. 2004). A second study in our laboratory found that ET musicians had smaller volumes in right lobules IV, V, and VI of the cerebellum compared to LT musicians, and that these reductions were correlated with better performance on a timed finger tapping task (Baer et al. 2015). The cerebellum is indirectly connected to cortical motor regions—including the premotor cortex (PMC)—through the thalamus (Bostan et al. 2013; Daskalakis et al. 2004; Percheron et al. 1996) and has been implicated in musical performance, timing, and error correction (Brown et al. 2015; Keren-Happuch et al. 2014). Critically, these cortico-cerebellar networks mature and function in relation to one another rather than in isolation (Kipping et al., 2017; Wang et al. 2016).

Thus, smaller cerebellar volumes in parallel with larger volumes in vPMC suggest the possibility that early training promotes coordinated developmental plasticity in these connected regions. Based on this concept, we hypothesized that structural differences as a function of musical training in the cerebellum should show coordinated patterning with functionally connected motor cortical regions, and that this pattern would differ depending on the age of start of such training. This prediction is consistent with the *interactive specialization* framework of neurocognitive maturation, which proposes that anatomically connected and functionally related regions change together across development (Fjell et al. 2019; Johnson 2011; Lerch et al. 2006). However, no previous studies have shown a direct relationship between structural differences in the cortex and cerebellum.

To test the hypothesis that early musical training might differentially affect cortico-cerebellar covariation, the present study therefore examined the relationship between cerebellar volume and cortical thickness (CT) and surface area (SA) in sensorimotor regions in ET and LT musicians, matched for years of experience and hours of current practice, as well as non-musician controls (NMs). We selected cortical sensorimotor and connected cerebellar regions, a subset of which were previously found to be associated with early musical training. After first assessing differences in cerebellar volume and CT and SA in sensorimotor regions between ET, LT, and NM groups, we performed correlation and regression analyses to examine structural covariation between the cerebellum and cortical motor regions between groups. We hypothesized that (1) ET musicians would show smaller overall and regional cerebellar volumes compared to both LTs and NMs; (2) ET musicians would show greater CT and/or SA in vPMC and possibly other motor regions; and (3) reductions in cerebellar volume in ET musicians would be associated with enlargements in connected cortical motor regions.

Materials and methods

Participants

Participant data were aggregated across a set of studies using the same T1 data acquisition protocol on the same scanner (see below). Participants gave informed consent at the time of the original studies, and only those who had agreed to the re-use of their data were included. Protocols were approved by the Concordia University Human Research Ethics Committee and the Human Research Ethics Board of the Montreal Neurological Institute.

All participants were right-handed, and were administered variants of the Musical Experience Questionnaire (Bailey and Penhune 2010), from which information on musical training was extracted. The full sample included 76 ET musicians and 54 LT musicians, as well as 45 non-musicians (NM: <3 years of musical training or experience, not currently practicing). To maintain consistency with the previous research, ET musicians were defined as those who began musical training before the age 7 (Amunts et al. 1997; Bailey and Penhune 2013; Schlaug et al. 1995). A subsample of individuals in both the ET (25%) and LT (37%) musician groups were previously included in the samples used in the Bailey et al. (2014) and Baer et al. (2015) studies. As in the previous studies (see, for example, Baer et al. 2015; Bailey and Penhune 2010, 2013; Bailey et al. 2014; Steele et al. 2013), ET and LT musician groups were matched for years of musical experience, years of formal music training, and current hours of practice. To create matched ET and LT groups with an optimal covariate balance, we used the MatchIt and Matching packages in R (Ho et al. 2007; Sekhon 2011). The resulting ET and LT groups each comprised 54 participants, in addition to the NM group which comprised 45 participants. The primary instruments reported by participants were: piano (40), strings (27), wind (10), drums (7), and voice (4). Group characteristics and comparison statistics are summarized in Table 1.

ET, LT, and NM groups did not significantly differ by age. ET and LT groups did not significantly differ on years of musical training, years of musical experience, or current hours of practice. Groups differed significantly in the distribution of sex, with the LT group weighted toward males and the NM group weighted toward females. To control for this, all analyses included sex as a covariate.

Table 1 Group demographics and comparison statistics

	ET($n=54$)	LT($n=54$)	NM($n=45$)	Statistic	p value
Age (years)	23.1 ± 3.6	24.7 ± 5.07	24.9 ± 4.7	$F=2.654$	$p=0.074$
Sex (m/f)	**29/25**	**38/16**	**17/28**	$\mathbf{X^2=10.5}$	$\boldsymbol{p=0.005}$
Age of onset musical training	**5.7 ± 1.1**	**10.9 ± 2.7**	–	$\boldsymbol{t(106)=22.5}$	$\boldsymbol{p<0.000}$
Years of musical training	10.9 ± 3.7	9.2 ± 4.6	–	$t(106)=1.754$	$p=0.18$
Years of musical experience	14.4 ± 4.7	13.3 ± 5.2	–	$t(106)=0.571$	$p=0.45$
Current hours of practice per week	9.8 ± 9.5	8.5 ± 10.2	–	$t(106)=1.330$	$p=0.25$

Values are means (± SD). M = Male, F = Female

Image acquisition and pre-processing

Structural MRI scans were acquired using a Siemens Trio 3T MRI scanner with a 32-channel head coil (TR = 2300 ms, TE = 2.98 ms, voxel size = $1 \times 1 \times 1$ mm^3). T1 images were converted to the MINC file format and pre-processed with the CoBrA Laboratory bpipe library (https://github.com/CobraLab/minc-bpipe-library) to perform N4 bias field correction and cropping to constrain the field of view to primarily skull and brain tissue. Total brain volume (TBV) was estimated from the whole-brain mask produced by BEaST brain extraction (Eskildsen et al. 2012).

Cerebellar segmentation and volume calculation

The cerebellum was segmented into 33 regions (13 in each hemisphere and seven in the vermis) using MAGeTBrain as described in Park et al. (2014; Chakravarty et al. 2013; Fig. 1, Panel A). This tool uses five expert-defined cerebellar atlases to segment a subset of participant scans to generate an expanded set of study-specific atlases, or templates. These study-specific templates are then registered to all study scans to produce a large number of candidate segmentations for each participant. Finally, a process of majority voxel voting produces the final labeled images for computing volume.

The atlases used for cerebellar segmentation in our previous study (Baer et al. 2015, as described in Park et al., 2014) divided the left and right hemispheres of the cerebellum at the mid-line, thus combining vermal and lateral regions. Hemispheric and vermal regions are known to have differential connectivity (Buckner et al. 2011; Grodd et al., 2001) and are thought to subserve different functions (King et al., 2019; Stoodley and Schmahmann 2009). Thus, a new set of atlases was developed which include seven vermal regions: vermal lobules VI through X were defined based on the protocol from Bogovic et al. (2013), which was informed by the Schmahmann atlas (1999). For vermal lobules III–V, a planar lateral boundary was set for each hemisphere based on the coronal view. As described by Schmamann et al. (1999, see page 16), this boundary was defined by the paramedian sulcus (if present); the lateral edge of buried vermal cortex; and/or the lateral edge of the paramedian white matter. These atlases including the vermis have been used in several subsequent studies (see, for example, Mankiw et al. 2017; Steele and Chakravarty 2018).

To assess the reliability of the cerebellar segmentation in the current study and to confirm the validity of the NMs as a comparison group, we performed a Pearson correlation to compare mean regional volumes obtained from the NM group to a large, well-defined sample of 327 individuals from the Human Connectome Project in which cerebellar volumes were also estimated using MAGeTBrain (Steele and Chakravarty 2018).

Fifteen regions of the cerebellum were included in the current study: bilateral lobules IV, V, VI, VIIIA, and VIIIB as well as their mid-line vermal components. These regions are associated with motor and timing functions and are the same lobules that were examined in our previous study, with the addition of the vermis (Baer et al. 2015; Stoodley and Schmahmann 2009). To reduce the possibility of type I error, analyses of the sub-regions of the cerebellum were grouped into three macro regions according to anatomically and functionally relevant hemispherical/vermal boundaries: left and right hemispheres and the mid-line vermis. Differences between groups were assessed for each macro-region using MANCOVA with sex and TBV as covariates to control for both the normal variation in brain size across participants as well as the unequal distribution of sex across groups [false discovery rate (FDR)-corrected at 0.05]. Lobules within any macro-region which achieved significance between groups were subsequently tested in a series of post hoc comparisons (FDR-corrected at 0.05).

Segmentation of cortical sensorimotor regions

To examine cortical thickness (CT) and surface area (SA) in sensorimotor regions, anatomical boundaries were identified based on the volumetric Human Motor Area Template (HMAT; see Fig. 2, Panel B) which includes: bilateral primary motor cortex (M1), ventral and dorsal premotor cortex (vPMC and dPMC), supplementary motor area (SMA), pre-supplementary motor area (pre-SMA), and primary somatosensory cortex (S1) (Mayka et al. 2006). The anatomical boundaries in HMAT were computed by analyzing probability distributions of the normalized stereotaxic coordinates of these regions across 126 previous studies. To extract CT

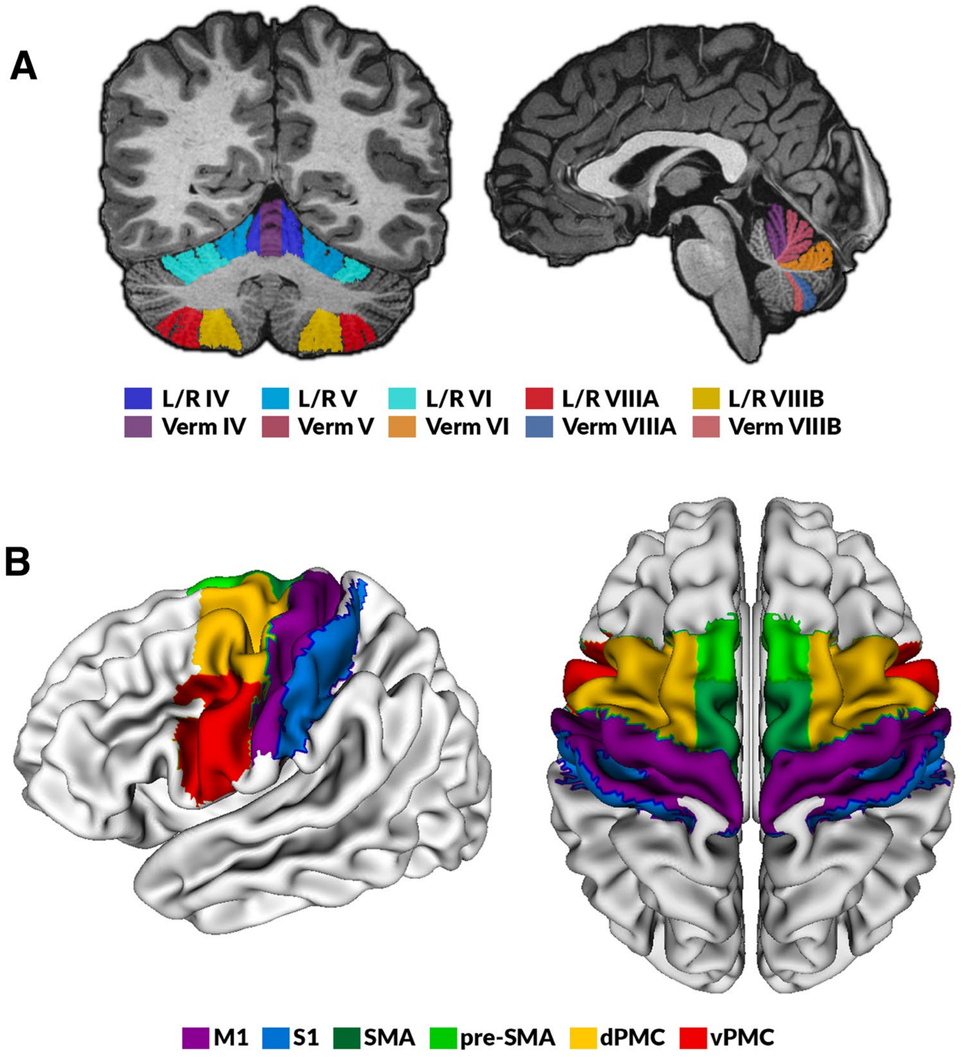

Fig. 1 Segmentations of cerebellar and cortical regions. Panel A: example segmentation and labeling of cerebellar regions on one subject using MAGeTBrain (Chakravarty et al. 2013). Panel B: example segmentation and labeling of cortical sensorimotor regions on one subject using the HMAT parcellation (Mayka et al. 2006) applied to the surface mesh output of CIVET (Ad-Dab'bagh, 2006)

and SA values, T1-weighted MRI images were converted to MINC and pre-processed via the CIVET pipeline, version 2.1.0 (Ad-Dab'bagh, 2006). CIVET is a fully automated image-processing pipeline which performs tissue classification and extraction of gray and white matter surfaces. Following surface extraction by CIVET, cortical surface vertices were labeled according to the HMAT template in MNI space. Average CT and total SA within each cortical sensorimotor region were calculated and extracted. As in the cerebellar volume analysis described above, in the first step, differences between groups were assessed across the six cortical regions collapsed within each hemisphere using MANCOVA (FDR-corrected at 0.05). Only sex was used as a covariate in these analyses, since there is evidence that CT is only marginally related to brain size (Im et al. 2008) and that correcting for TBV is not recommended (Schmansky 2020). If a significant effect of group was observed for either hemisphere (FDR-corrected at 0.05), post hoc comparisons for individual regions were carried out (FDR-corrected at 0.05).

Correlation analyses

To examine the relationship between cerebellar volumes that differed across groups and those of the cortical sensorimotor regions identified by HMAT, a series of correlations were performed. Cerebellar volumes were first normalized by each participant's TBV, and a series of partial correlations were conducted using sex as a covariate (FDR-corrected at 0.05). A correlation matrix was produced for each group (ET, LT, and NM), which related the volumes of cerebellar regions against the average cortical thickness and total surface area of each cortical sensorimotor region. To compare the directionality of these relationships across groups, a series of multiple regressions were performed on each pair of regions which

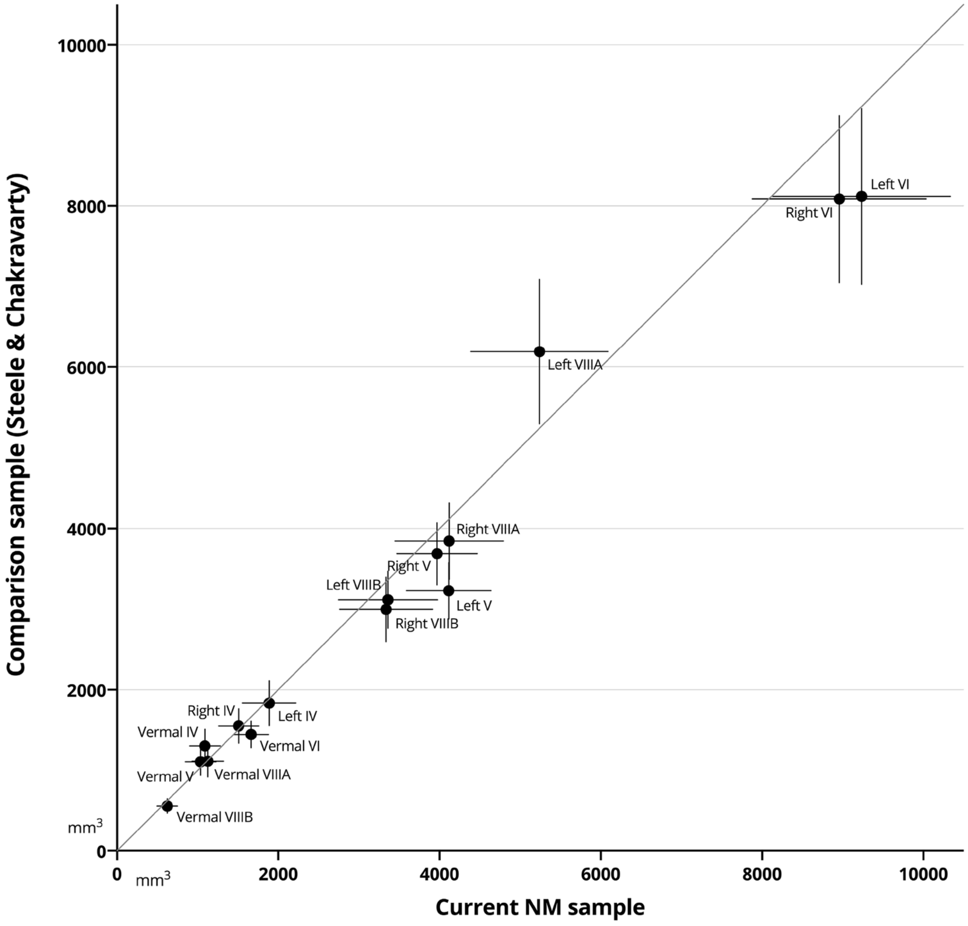

Fig. 2 Regional cerebellar volumes of current NM group and those of the normative sample from Steele and Chakravarty (2018). Error bars are ± 1 standard deviation; no direct statistical comparison was made

were found to be significantly correlated. Each regression compared the relationship between cerebellar volume and CT between all three groups.

Results

Validation of cerebellar volumes in the non-musician control group

Mean cerebellar volumes for all 15 regions of interest were found to be within one standard deviation of the comparison normative sample (see Fig. 2), and a Pearson correlation revealed these samples to be highly correlated ($r = 0.986$, $p < 0.001$). In addition to confirming the robustness of the segmentation method, this result confirms that our NM group represents a normal subsample of the population and is thus an adequate comparison group for the ET and LT musicians, allowing us to accurately assess the directionality of differences.

Comparison of cerebellar volumes across groups

Results revealed a significant main effect of group in all three macro regions of the cerebellum, such that ET musicians had overall smaller volumes compared with LTs and NMs (see Table 2 and Fig. 3A). Subsequent FDR-corrected post hoc comparisons revealed a number of significant group differences in the following regions: vermal IV, right V, left VI, right VIIIA, and vermal VIIIB (see Table 2). In all of these comparisons, ET musicians had smaller regional volumes than LT musicians and/or NMs. In right VIIIA, however, although ET musicians had significantly smaller volumes than LT musicians, this was due to LT musicians having significantly larger volumes than NM.

Cortical thickness and surface area in sensorimotor regions

Results of the MANCOVA analysis comparing the six sensorimotor regions from HMAT collapsed across hemisphere for the three groups revealed a significant main effect of

Table 2 Results of cerebellar volume analyses

Region	F	p	Post hoc
Left hemisphere	**1.851**	**0.05**	
Left IV	2.595	0.078	
Left V	2.158	0.119	
Left VI	**3.049**	**0.05**	
Left VIIIA	2.740	0.062	
Left VIIIB	0.675	0.511	
Right hemisphere	**2.567**	**0.01**	
Right IV	2.423	0.092	
Right V	**4.759**	**0.01**	**ET < LT, $p = 0.016$ ($d = 0.54$)** **ET < NM, $p = 0.018$ ($d = 0.13$)**
Right VI	1.565	0.213	
Right VIIIA	**5.539**	**0.005**	**ET < LT, $p = 0.015$ ($d = 0.58$)** **LT > NM, $p = 0.024$ ($d = 0.94$)**
Right VIIIB	2.747	0.067	
Vermis	**2.499**	**0.01**	
Vermal IV	**4.789**	**0.01**	**ET < NM, $p = 0.009$ ($d = 0.47$)**
Vermal V	2.488	0.087	
Vermal VI	0.53	0.589	
Vermal VIIIA	0.684	0.506	
Vermal VIIIB	**5.574**	**0.005**	**ET < LT, $p = 0.006$ ($d = 0.73$)**

Omnibus & post hoc tests are FDR-corrected at 0.05; all p values are Benjamini–Hochberg adjusted

group in the right hemisphere for CT (See Table 3). Subsequent FDR-corrected post hoc comparisons revealed group differences in right pre-SMA, dPMC, and vPMC, such that both musician groups had greater cortical thickness than NMs in pre-SMA, while ETs had greater cortical thickness in vPMC and LTs had greater cortical thickness in dPMC (see Fig. 3B). There were no significant group differences for SA.

Cerebellum and cortical sensorimotor correlations

To assess the relationship between changes in cerebellar volumes and CT, we performed a series of correlations across the regions found to differ in the group comparisons (Table 4). The results of this analysis identified significant negative relationships between cerebellar left VI and right pre-SMA and PMC for NMs, as well as significant negative relationships between cerebellar vermal IV and right pre-SMA and dPMC for ET musicians. There were no significant correlations for LT musicians. Furthermore, the directionality of these correlations indicated an inverse relationship between cerebellar volume and cortical thickness of the sensorimotor regions. To be able to compare the directionality of these relationships between groups, we performed a multiple regression on each pair of regions which were found to be significantly correlated (Fig. 4). The results of these regressions paralleled those of the correlation analyses: regressions between left VI and pre-SMA, dPMC, and vPMC were significant for NMs only, while regressions between vermal IV and pre-SMA and dPMC were significant only for ETs. There were no significant regressions for LT musicians.

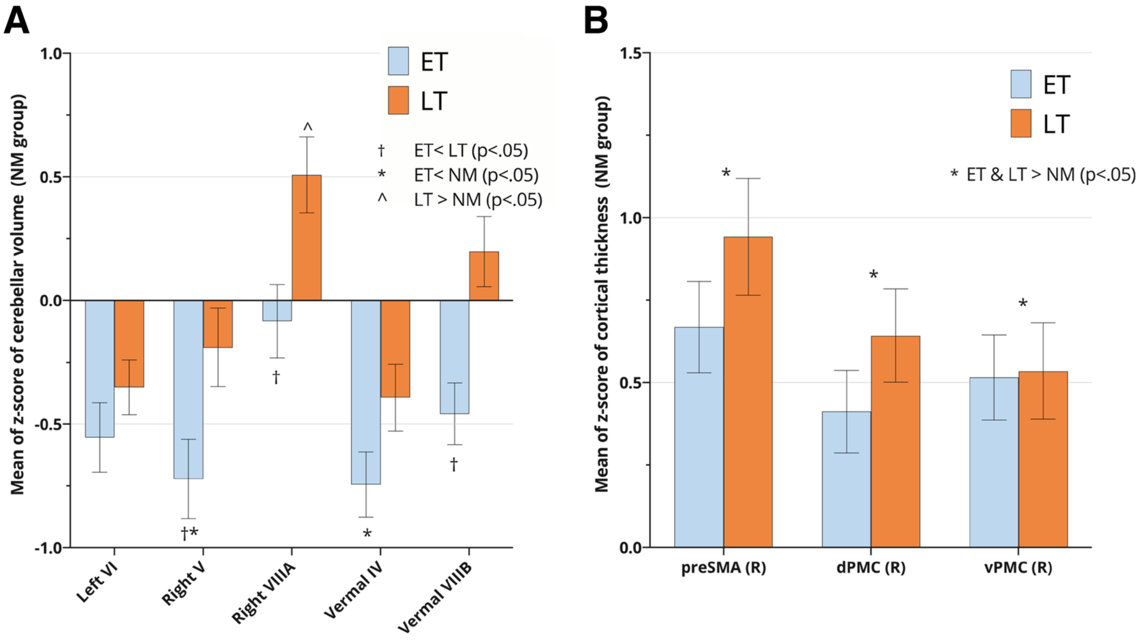

Fig. 3 Panel **A**: regional cerebellar volumes of ET and LT groups relative to NMs. Panel **B**: regional cortical thickness of ET and LT groups relative to NMs

Table 3 Results of cortical thickness and surface area analyses

Region	*F*	*P*	Post hoc
Cortical thickness			
Right hemisphere	**1.987**	**0.05**	
M1	1.665	0.193	
S1	0.642	0.528	
SMA	2.808	0.064	
pre-SMA	**7.472**	**0.001**	**ET > NM, $p = 0.018$ ($d = 0.66$)** **LT > NM, $p < 0.000$ ($d = 0.8$)**
dPMC	**5.125**	**0.007**	**LT > NM, $p = 0.009$ ($d = 0.63$)**
vPMC	**3.223**	**0.043**	**ET > NM, $p = 0.04$ ($d = 0.53$)**
Left hemisphere	1.387	0.171	
Surface area			
Right hemisphere	0.981	0.467	
Left hemisphere	1.315	0.209	

Omnibus & post hoc tests are FDR-corrected at 0.05; all *p* values are Benjamini–Hochberg adjusted

Table 4 Correlations between cerebellar volume and sensorimotor cortical thickness

	Right		
	Pre-SMA	dPMC	vPMC
Early trained musicians (ET)			
Left VI	0.1	0.21	0.2
Right V	0.04	0	−0.04
Right VIIIA	0.09	0.07	0.04
Vermal IV	**−0.34**	**−0.27**	−0.15
Vermal VIIIB	−0.22	−0.17	−0.09
Late-trained musicians (LT)			
Left VI	−0.05	−0.06	−0.07
Right V	−0.07	−0.16	−0.14
Right VIIIA	−0.08	−0.11	−0.14
Vermal IV	0.03	0.01	−0.03
Vermal VIIIB	−0.16	−0.18	−0.21
Non-musicians (NM)			
Left VI	**−0.39**	−0.28	**−0.31**
Right V	−0.01	0.04	−0.05
Right VIIIA	0.02	−0.09	−0.23
Vermal IV	0	−0.02	−0.01
Vermal VIIIB	0.16	0.12	−0.03

Highlighted in bold cells are statistically significant at $p < 0.05$ after FDR correction at 0.05. *M1* Primary motor cortex, *S1* Primary somatosensory cortex, *SMA* Supplementary motor area, *pre-SMA* Pre-supplementary motor area; *dPMC* Dorsal premotor cortex, *vPMC* Ventral premotor cortex

Discussion

The goal of this study was to investigate whether experience-dependent plasticity effects on cortical and cerebellar regions are related, as well as to test whether early musical training has a differential effect on structural covariation between connected regions of the cerebellum and motor cortex. Our results show that ET musicians have decreased volumes of cerebellar lobules connected to sensorimotor cortices, extending our previous findings in a larger sample (Baer et al. 2015). In parallel, we found that both musician groups had greater cortical thickness in right pre-SMA, dPMC, and vPMC compared to NMs. Most importantly, early musical training had a specific effect on structural covariance between the cerebellum and cortex. While NM controls showed a pattern of negative correlations between left lobule VI and right pre-SMA and PMC, this relationship was reduced in ET musicians. In addition, NMs showed no significant relationship between volumes of vermal lobule IV and motor cortical regions, while ET musicians showed a significant negative correlation between vermal IV and right pre-SMA and dPMC. These differences in the pattern of structural covariance suggest that early musical training has specific developmental effects on cortico-cerebellar networks important for optimizing sensorimotor performance.

Our findings of greater CT in cortical sensorimotor regions and smaller cerebellar volumes in ET musicians extend those of previous research. Previous work from our lab using deformation-based morphometry showed greater expansion of the deformation field and greater surface area in the right vPMC in ET compared to LT musicians (Bailey et al. 2014). In the current study, both ET and LT musicians show greater CT in premotor regions and SMA compared to non-musicians, but there are no differences between the musician groups. This may be the result of differing measures (CT vs DBM). These findings are consistent with work, showing that professional musicians exhibited greater gray matter volume in primary, premotor, and somatosensory areas compared to amateur musicians and non-musicians (Bermudez et al. 2009; Gaser and Schlaug 2003), as well as work showing that in identical twin pairs, the twins who practiced showed enhancements in gray matter volume in premotor regions (de Manzano and Ullen 2018).

Interestingly, both our result and prior results of differential cortical effects are lateralized to the right hemisphere. While one might expect this effect to be associated with handedness, we believe that the laterality of our cortical findings is related to hemispheric specialization in music perception and performance which has been investigated in the previous research (see, for example: Bermudez et al. 2005; Halwani et al. 2011). In addition, the majority of musical instruments played by our participants require bimanual control, which, for right-handed individuals, entails extensive training of the non-dominant left hand. Additionally, studies of motor control and learning demonstrate greater bilateral engagement of motor regions when tasks are bimanual and/or more complex (Puttemans et al. 2005). Finally, studies

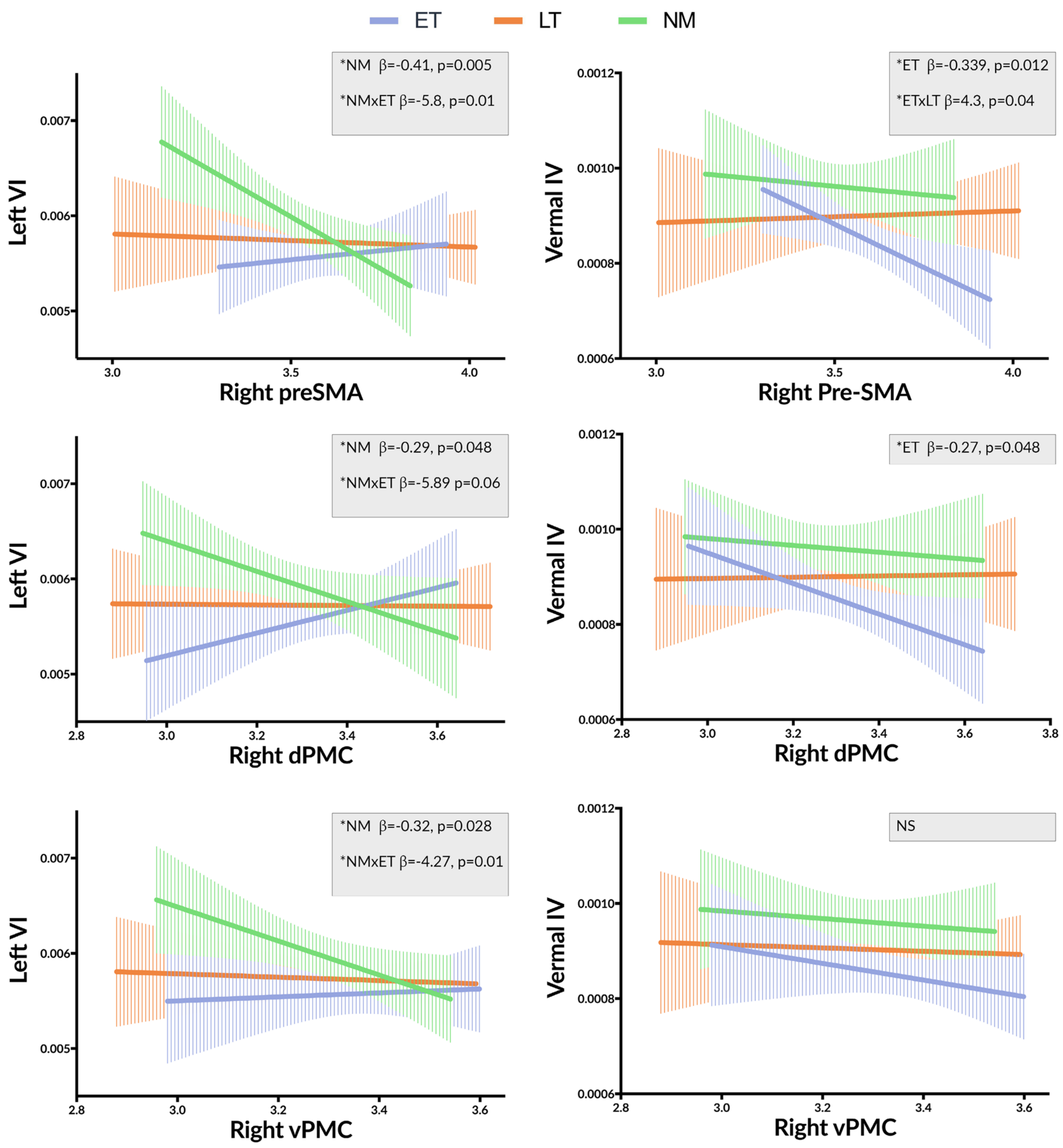

Fig. 4 Regressions on pairs of regions with statistically significant correlations

of brain structural differences between musicians and non-musicians typically show changes in right hemisphere auditory and motor regions (Brown et al. 2015; Herholz, S. C. & Zatorre, 2012). This has been interpreted as relating to both the bimanual training effects described above and to the right hemisphere dominance for the processing of musical stimuli.

Our finding of smaller cerebellar volumes in ET musicians is also supported by recent work showing reductions in volume that are related to training and relevant skill (but see Hutchinson et al. (2003), who found larger total cerebellar volume in male musicians). As described in the Introduction, work from our laboratory has found that, compared to LT musicians, ET musicians had smaller volumes in bilateral cerebellar white matter and right lobules IV, V, and VI, and that smaller volumes were correlated with better performance on a test of timed finger tapping (Baer et al. 2015). Our analyses identified similar volumetric reductions in regions IV, V, and VI; however, the reductions in lobules IV and VI were in the vermal area and left hemisphere, respectively. Given that our previous work had shown that ET musicians had GM enhancements in the right ventral premotor cortex, we anticipated that there might be specific effects in structural covariance between the right hemisphere motor regions and the connected left hemisphere cerebellar regions.

Support for our finding that training can produce concurrent reductions in cerebellar volume and increases in cortical volume comes from longitudinal neuroimaging studies of sensorimotor learning in mice. Adolescent mice that spent 3 weeks training in a re-configurable maze showed decreased volume of lobule VI (Scholz et al. 2015a, b), and adult mice that had been trained to balance on a rotating rod showed reduced cerebellar volume in lobules III and IX (Scholz et al. 2015a, b). Importantly, in both of these studies, decreases in cerebellar volume were accompanied by increases in the volume of connected regions, including M1 and frontal cortex, providing evidence of widespread structural reorganization in cortico-cerebellar networks with intensive training that mirrors the effects we describe.

Our finding of changes in cortico-cerebellar structural covariation with early musical training is also consistent with previous research, showing that these regions are anatomically and functionally related. Trans-neuronal tracing studies in macaque monkeys have demonstrated that lobules IV–VI are connected to frontal motor and association regions, including M1 and PMC (Kelly and Strick 2003), and functional connectivity studies based on resting-state fMRI data in humans have shown that these regions are functionally connected to sensorimotor and prefrontal areas of the cortex (Wang, C. et al., 2016). Furthermore, research has demonstrated that cortico-cerebellar functional connectivity changes with maturation across the lifespan. These fluctuations in connectivity may underlie maturational changes in the development of motor and cognitive function, and thus contribute to sensitive periods for the effects of training.

In an initial study in adults, Wang & Kipping (2016) investigated cortico-cerebellar functional connectivity networks using resting-state fMRI. They found that lobule VI was connected to premotor areas, but also to more widespread cortical regions in the parietal and frontal—a finding consistent with earlier work (Buckner et al. 2011). In contrast, lobule IV was part of the “motor cerebellum,” connected primarily to premotor and sensorimotor cortical areas. A subsequent study using the same approach compared functional connectivity in children aged 4–5, 6–7, and 9–10, identifying age-related differences in both the extent and strength of these cortico-cerebellar networks (Kipping et al., 2017). Their results showed that functional connectivity in the majority of these networks peaked at age 6–7, including those involving lobules IV and VI, at which point connectivity within the executive control and default mode networks began to emerge. These findings support the hypothesis that musical training before age 7 may have a differential effect on structural and functional covariation in sensorimotor networks, changing the relationships between these regions, whereas later musical training—beginning after peak connectivity of this network gives way to more widespread connectivity—does not show similar effects.

While the association between larger cortical volumes and training is well established, it is less clear why smaller cerebellar volumes might be associated with early training and enhanced performance. The cerebellum is critical for error correction and optimization within the motor system (Koziol et al. 2014; Sokolov et al. 2017), and cerebellar activity decreases as new skills and rules are learned, become automatic, and fewer errors are produced (Balsters and Ramnani 2011; Penhune and Steele 2012). It is therefore plausible that musical training during early childhood, the period of strongest connectivity between the motor cerebellum and cortical sensorimotor regions (Kipping et al. 2013, 2017), might influence error correction circuitry. Rats trained to navigate a series of obstacles had significantly reduced Purkinje cell densities compared to controls (Kleim et al. 1997), and mice exposed to 5 days of optokinetic response training—a series of slow- and fast-phase eye movements for tracking motion—showed a significant reduction in synapses in the cerebellum (Wang et al. 2014). Cerebellar Purkinje cells drive motor learning and coordination through inhibitory projections (Lee et al. 2015), and are themselves influenced through GABAergic inhibition from their inputs (Steuber et al., 2007). It has therefore been proposed that volume reductions in the cerebellum could be the result of synaptic pruning following training-induced inhibition of Purkinje cells (Scholz et al. 2015a, b).

Although both structural and functional connections between the cerebellum and cortical motor regions have been established, it remains unclear by what mechanism these regions co-develop. The *interactive specialization* framework proposes that connected brain regions or networks interact during development to reciprocally influence maturation (Johnson 2011). In the current context, we propose that musical training engages the cortical sensorimotor and cerebellar networks, driving plasticity in both (Penhune 2020). Critically, maturation of particular regions of the brain happens at different ages, and interactive specialization proposes that earlier-maturing sensorimotor networks interact with later-maturing networks controlling higher order functions. Earlier developing functions therefore benefit from top–down cognitive input, but at the same time can promote maturation in later-developing regions. In the case of musical training, earlier-developing motor regions may interact with later-developing cerebellar circuits, driving coordinated change. Earlier onset of musical training when sensorimotor regions are rapidly developing (Ducharme et al. 2016; Gogtay et al. 2004) may be particularly effective in stimulating plasticity, both locally and in connected regions. Evidence that functional connectivity between the cerebellum and cortex is greatest at age 6–7 (Kipping et al. 2017) further supports the possibility of correlated change.

Although the cerebellum itself is thought to exhibit peak developmental change in adolescence (Tiemeier et al. 2010), early start of music training may still enhance plasticity, both directly and through its network connections. Furthermore, early experience may have a metaplastic effect, such that early plasticity may serve as a scaffold on which later experience can build (Steele and Penhune 2010).

Evidence for metaplastic effects of music training comes from studies showing that musicians have enhanced learning of sensory and motor skills (Herholz, Sibylle C. et al., 2011; Ragert et al. 2004; Rosenkranz et al. 2007), and greater increases in M1 activity during learning (Hund-Georgiadis and von Cramon 1999). Finally, given the diverse sensory, motor, and cognitive functions engaged by music training and their widespread loci within the brain (Brown et al. 2015; Zatorre et al. 2007), it is likely that other connected regions—such as prefrontal cortex—may influence experience-dependent network changes in early and late-trained musicians.

Conclusion

The results of this study show that musical training before age 7 affects cortico-cerebellar structural covariation in adulthood, indicating that early experience has differential impacts on the maturation of these connected regions. Our findings emphasize that early experience promotes plasticity at a network level and are consistent with the hypothesis that reciprocal communication within and between networks is an important ongoing contributor to brain and behavioral maturation. Together with our previous work, this study contributes to building a more complex picture of sensitive period effects, in which long-term plasticity is the product of experience during periods of peak maturational change at both the local circuit and network levels.

Author contributions JJS, CJS, RJZ, and VBP contributed to the study conception and design. Data collection, preparation, and analysis were performed by JJS. CJS and MMC provided analytic tools. JJS and VBP wrote the first draft of the manuscript, and all authors contributed to the final version. All authors read and approved the final manuscript.

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Data availability Not applicable.

Code availability All software used in this research has been cited in the main text, including—where applicable—URLs where it can be obtained.

Declarations

Conflicts of interest The authors have no conflicts of interest to declare that are relevant to the content of this article.

Ethics approval Protocols were approved by the Concordia University Human Research Ethics Committee and the Human Research Ethics Board of the Montreal Neurological Institute.

Consent to participate Participants gave informed consent at the time of the original studies, and only those who had agreed to the re-use of their data were included.

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