



RESEARCH ARTICLE

WILEY

Using cortico-cerebellar structural patterns to classify early- and late-trained musicians

Joseph J. Shenker^{1,2}  | Christopher J. Steele^{1,3}  | Robert J. Zatorre^{2,4}  |
Virginia B. Penhune^{1,2} 

¹Department of Psychology, Concordia University, Montreal, Quebec, Canada

²BRAMS: International Laboratory for Brain, Music, and Sound Research, Montreal, Quebec, Canada

³Department of Neurology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

⁴Cognitive Neuroscience Unit, Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada

Correspondence

Joseph J. Shenker PhD, Department of Psychology, Concordia University, Montreal, Quebec, Canada.
Email: jake.shenker@gmail.com

Funding information

Canadian Institute for Advanced Research; Canadian Institutes of Health Research, Grant/Award Numbers: 143217, HNC 170723; Heart and Stroke Foundation of Canada; Natural Sciences and Engineering Research Council of Canada, Grant/Award Numbers: DGEER-2020-00146, RGPIN-2020-06812

Abstract

A body of current evidence suggests that there is a sensitive period for musical training: people who begin training before the age of seven show better performance on tests of musical skill, and also show differences in brain structure—especially in motor cortical and cerebellar regions—compared with those who start later. We used support vector machine models—a subtype of supervised machine learning—to investigate distributed patterns of structural differences between early-trained (ET) and late-trained (LT) musicians and to better understand the age boundaries of the sensitive period for early musicianship. After selecting regions of interest from the cerebellum and cortical sensorimotor regions, we applied recursive feature elimination with cross-validation to produce a model which optimally and accurately classified ET and LT musicians. This model identified a combination of 17 regions, including 9 cerebellar and 8 sensorimotor regions, and maintained a high accuracy and sensitivity (true positives, i.e., ET musicians) without sacrificing specificity (true negatives, i.e., LT musicians). Critically, this model—which defined ET musicians as those who began their training before the age of 7—outperformed all other models in which age of start was earlier or later (between ages 5–10). Our model's ability to accurately classify ET and LT musicians provides additional evidence that musical training before age 7 affects cortico-cerebellar structure in adulthood, and is consistent with the hypothesis that connected brain regions interact during development to reciprocally influence brain and behavioral maturation.

KEYWORDS

experience, music, plasticity, sensitive period, support vector machine

1 | INTRODUCTION

A body of current evidence suggests that there is a sensitive period for musical training: people who begin training before the age of seven show better performance on certain tests of musical skill, and

also show differences in brain structure—especially in motor cortical and cerebellar regions—compared with those who start later. In both children and adults, those who begin early (≤ 7 ; early-trained [ET]) outperform those who begin later (> 7 ; late-trained [LT]) on tests of melody discrimination and rhythm reproduction (Baer et al., 2015;

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2023 The Authors. *Human Brain Mapping* published by Wiley Periodicals LLC.

Bailey & Penhune, 2010; Ireland et al., 2019; Kraus et al., 2009; Penhune, 2020; Vaquero et al., 2016; Watanabe et al., 2007). In addition, ET musicians exhibit greater cortical surface area and gray matter volume in the ventral premotor cortex (vPMC) (Bailey et al., 2014), and smaller volumes in the basal ganglia (Vaquero et al., 2016) and the cerebellum (Baer et al., 2015; Shenker et al., 2022) as compared to LT musicians.

Previous studies, however, have all relied on univariate methods to assess differences in brain structure across multiple regions independently. However, it seems likely that experience-dependent plasticity for complex skills such as music would engage a more spatially distributed network, and that a multivariate technique would be more sensitive to the distributed pattern of changes associated with early training. The current research therefore uses support vector machine (SVM) models—a subtype of supervised machine learning (ML)—to investigate distributed patterns of structural differences between ET and LT musicians in cortical motor and cerebellar regions known to be structurally and functionally connected.

Brain structural differences between ET and LT musicians were initially observed in a study examining the corpus callosum (Schlaug et al., 1995). Musicians were found to have larger surface area of the anterior corpus callosum, an effect that was greater in those who began their training at or before the age of 7. A subsequent study of musicians found that the size of the primary motor cortex (M1) was inversely correlated with the age of start (AoS) of musical training: those who began training at an earlier age showed larger M1 than those who began later in life (Amunts et al., 1997). Following these early studies, research from our group and others identified additional neuroanatomical differences associated with early musical training: greater cortical surface area and gray matter in the right vPMC (Bailey et al., 2014); greater functional anisotropy—a proxy measure of white matter fiber density—in the posterior midbody/isthmus of the corpus callosum (Steele et al., 2013); smaller gray matter volume in the right putamen (Vaquero et al., 2016); and smaller volumes in hemispheric and vermal cerebellar regions (Baer et al., 2015; Shenker et al., 2022; van Vugt et al., 2021).

In a recent study using a large sample ($N = 108$) we identified a differential pattern of structural differences between ET and LT musicians in the motor cortex and cerebellum (Shenker et al., 2022). Our results identified negative correlations between cerebellar volume and motor cortical thickness and surface area in ET musicians, suggesting that early musical training has differential impacts on the maturation of cortico-cerebellar networks important for optimizing sensorimotor performance (Shenker et al., 2022). This result is consistent with the *interactive specialization* framework, which proposes that connected brain regions or networks interact during development to reciprocally influence maturation (Johnson, 2011). Indeed, widespread structural changes occur as the brain matures, and cognitive and behavioral maturation is likely the result of distributed patterns of subtle changes that are influenced by experience and its timing (Bray et al., 2009). As a multivariate method, SVM is well suited to identify patterns of linked differences in structure characteristic of early musicianship.

In much previous work, ET musicians have typically been defined as those who began musical training at or before age 7. As described above, Schlaug et al. (1995) observed that differences between musicians and non-musicians were driven by those who began before age 7. Subsequent studies showing behavioral and anatomical differences between ET and LT musicians have used this age cut-off. However, we know that the maturational trajectories of brain and behavior are variable, and that maturation or experience in one domain influences maturation in other domains (Werker & Hensch, 2015). It is therefore unlikely that there is an abrupt change in sensitivity to musical experience at age 7, but rather gradual changes in sensitivity to different aspects of training.

Evidence for a broader range of sensitivity comes from a study which aggregated behavioral data in a large sample of musicians and examined how different age cut-offs affected the relationship between AoS and performance on a rhythm synchronization task (Bailey & Penhune, 2013). The authors applied different AoS cutoffs to produce varying ET versus LT group splits, and examined whether AoS was correlated with performance on the task. The results showed that AoS was correlated with rhythm synchronization performance if musicians began their training at or prior to age 9, but not afterwards. This correlation was strongest when age 7 was used to divide the groups.

Further, a recent study of child musicians found that children who began musical training before age 7 performed better on a melody discrimination task, but not the rhythm synchronization task, compared to children who began later (Ireland et al., 2019). This observation suggests that children's rhythmic abilities may take time to mature, and that on-going training after age 7 may be required for adult behavioral differences to appear; indeed, 7–13 year-old children showed continuing improvement on rhythm synchronization tasks with increasing age (Ireland et al., 2018). Although the ET/LT cut-off at age 7 has persisted in the literature—and has often led to interesting results—there has been little systematic study of whether it is, in fact, the optimal point by which to split these groups. Therefore, an additional goal of the current study was to investigate the age cut-off for defining early musicianship by comparing the predictive power of ML models using different AoS cut-offs.

Using ML to identify patterns of structural differences between ET and LT groups requires a classification method that attempts to predict group membership based on a combination of features (Bray et al., 2009). Of the multitude of classification methods, SVM is probably the most common. SVM aims to calculate a linear vector—known as a hyperplane—which separates a cluster of data points into two distinct categories (Amari & Wu, 1999). SVM has been widely used for classifying data across multiple domains, from identifying cancerous tissues (Furey et al., 2000) and brain tumors (Othman et al., 2011) to distinguishing individuals with Alzheimer's disease from healthy individuals (Kloppel et al., 2008; Magnin et al., 2009).

Albouy et al. (2019) combined SVM with both structural and functional magnetic resonance imaging (fMRI) to identify patterns of activations which could distinguish healthy controls from participants with congenital amusia (although the authors noted that the relatively

low sensitivity of the model might limit its predictive capacity). Another study used SVM to try to classify musicians and non-musicians based on cortical thickness (Puoliväli et al., 2020). They produced a predictive model that was capable of classifying musicians and nonmusicians with a pattern of cortical thickness differences mostly in the frontal, parietal, and occipital lobes of the left hemisphere. However, this model was only accurate in classifying nonmusicians, while its ability to correctly identify musicians was near chance, possibly due to the heterogeneity of musicians comprising the sample. Given that the pattern of differences between expert and nonexpert groups is likely to be nuanced, larger, more well-defined samples are crucial for more accurate predictive power.

Overall, the existing research provides significant evidence of the differences between musicians with an AoS before or after age 7, although the application of ML tools within this area of study is minimal. The present study employed SVM to identify patterns of cortico-cerebellar structural variation in regions known to be structurally and functionally connected which can differentiate between ET and LT musicians. Cortical thickness and surface area of cortical sensorimotor regions as well as the volume of cerebellar regions—a subset of which were previously found to be associated with early musical training—were provided to the SVM classifier for training. Using recursive feature elimination (RFE) with cross-validation (Sanz et al., 2018), the most salient features were identified to produce a classifier which could accurately predict ET and LT musicianship. The performance of the classifier was evaluated by comparing accuracy, specificity, and sensitivity of the model. To investigate the optimal AoS to distinguish the effects of early musicianship, we produced and compared several models using different cut-offs from ages 5 through 10. We hypothesized that SVM could be used to successfully predict ET and LT musicians using a sub-selection of regional cerebellar volumes and cortical sensorimotor surface area and cortical thickness. Additionally, we used SVM to explore the fit of the classifier at different AoS cut-offs to better understand the age boundaries of the sensitive period for early musicianship.

2 | MATERIALS AND METHODS

2.1 | Participants

A total of 133 participants were included, comprising 79 ET musicians and 54 LT musicians. As per previous research, ET musicians were defined as those who began musical training at or before the age 7 (Amunts et al., 1997; Bailey & Penhune, 2013; Schlaug et al., 1995; Shenker et al., 2022). Participant data were aggregated from 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 also administered the Musical Experience Questionnaire (Bailey & Penhune, 2010), from which information on musical training was extracted. Participants

TABLE 1 Group demographics.

	ET (n = 79)	LT (n = 54)
Age (years)	22.8 ± 3.5	24.7 ± 5.2
Sex (m/f)	40/39	38/16
Age of onset musical training	5.4 ± 1.1	10.4 ± 2.7
Years of musical training	12.2 ± 4	9.2 ± 4.6
Years of musical experience	15.2 ± 4.4	13.3 ± 5.1
Current hours of practice per week	11.8 ± 11.3	8.5 ± 10.2

Note: Values are means (±SD).

Abbreviations: F, female; M, male.

were the same as those in Shenker et al. (2022). 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. The primary instruments reported by participants were: piano/keyboard (55), strings (12), wind (10), drums/percussion (7), voice (14), guitar (21), bass (8), and brass (5). One musician did not report his/her primary instrument. There were no statistically significant differences between the groups for years of musical experience and current hours of practice. Group characteristics are summarized in Table 1.

2.2 | Image acquisition and preprocessing

Structural MRI scans were acquired using a Siemens Trio 3 T MRI scanner with a 32-channel head coil (TR = 2300 ms, TE = 2.98 ms, voxel size = $1 \times 1 \times 1$ mm³). T1 images were converted to the MINC file format and preprocessed with the CoBra Laboratory bpipe library (<https://github.com/CobraLab/minc-bpipe-library>) to perform N4 bias field correction and cropping in order 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 BFAST brain extraction (Eskildsen et al., 2012).

2.3 | Cerebellar segmentation and volume calculation

The cerebellum was segmented using MAGeTBrain (<https://github.com/CoBrALab/MAGeTbrain>), an automated method using multiple automatically generated templates of different brains (Chakravarty et al., 2013; Park et al., 2014). 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—where the most frequently occurring label among all the candidate segmentations at each voxel is retained—produces the final labeled images for computing volume. Segmentation parameters and cerebellar atlas were consistent with our previous work (Shenker et al., 2022): the cerebellum was

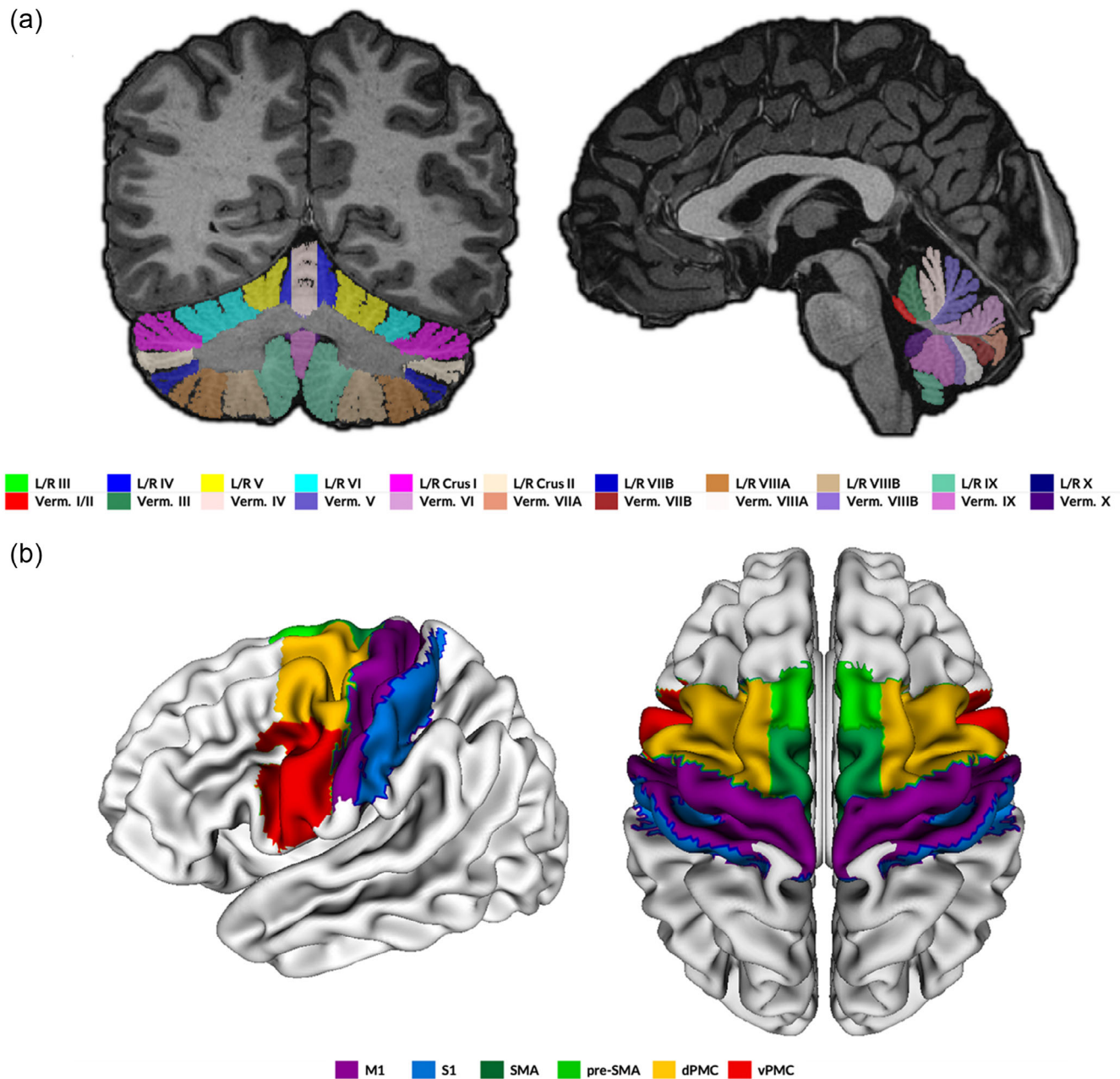


FIGURE 1 Segmentations of cerebellar and cortical regions. (a) Example segmentation and labeling of cerebellar regions on one subject using MAGEtBrain (Chakravarty et al., 2013). (b) Example segmentation and labeling of cortical sensorimotor regions on one subject using the HMAT parcellation (Mayka et al., 2006) applied to the surface mesh output of CIVET (Ad-Dab'bagh, 2006).

segmented into 33 separate regions across left and right hemispheres and vermal region as described in Park et al. (2014) (Figure 1a), and volumes were weighted by each participant's total brain volume (TBV). All cerebellar regions were included in the analysis.

2.4 | Segmentation of cortical sensorimotor regions

To examine cortical thickness and surface area in sensorimotor regions, anatomical boundaries were identified based on the

volumetric Human Motor Area Template (HMAT; see Figure 1b) which includes: bilateral primary motor cortex (M1), ventral and dorsal premotor cortex (vPMC and dPMC), supplementary motor area (SMA), presupplementary motor area (pre-SMA), and primary somatosensory cortex (S1) for a total of 24 variables (Mayka et al., 2006). To extract these values, T1-weighted MRI images were converted to MINC and pre-processed via the CIVET pipeline, version 2.1.0 (Ad-Dab'bagh, 2006), and average cortical thickness and total surface area within each cortical sensorimotor region were calculated and extracted (for additional details, see Shenker et al., 2022).

2.5 | Machine learning

ML was used in order to more directly investigate structural patterns and salient features which can more accurately delineate ET and LT musicians. SVM models were implemented in scikit-learn (version 1.0.2), a Python-based ML framework (Pedrosa et al., 2018). Fifty-seven features were included in all SVMs: cerebellar volume from MAGeTBrain (33 variables) and cortical thickness (12 variables) and surface area from HMAT (12 variables). The hyperparameters C and gamma were optimized using scikit-optimize, and these optimal values were calculated and used uniquely for each model. Two-fold recursive feature elimination (RFE) was used to identify the optimal number of features for SVM models. The RFE algorithm uses weights generated by the SVM classifier as a ranking criterion, eliminating features one-by-one in order to find an optimal subset of features for classification (Huang et al., 2014; Kuhn & Johnson, 2018). These features were then fed back into the classifier using 10-fold cross validation. A linear kernel was used for each SVM model, as it has been suggested that this is required for RFE to perform most accurately (Guyon et al., 2002; Kuhn & Johnson, 2018). For each model, the following steps were performed: (1) optimize hyperparameters C and gamma;

(2) train the model using all predictors; (3) perform feature ranking using RFE; (4) keep the most relevant features as identified by RFE; (5) reoptimize hyperparameters; (6) train the model using only the most relevant features; (7) evaluate model performance. To evaluate the outcome of the models, we used permutation tests to estimate chance performance: using 1000 permutations, chance was estimated at 54% ($p = .316$).

Our primary model defined ET musicians as those who began their musical training at or before the age of 7. Additional models using different AoS cut-offs (age of onset \leq age 5, 6, 8, 9, 10, respectively) were tested in order to better understand the age boundaries of the sensitive period for early musicianship.

3 | RESULTS

Of the 57 features included in the model, RFE identified 17 that were optimal for classifying ET and LT musicians. These included volumes of cerebellar motor lobules III–VI and inferior lobule VIIB, as well as cortical thickness in right primary motor, sensorimotor and vPMC (see Figure 2 for the list of regions). These features are consistent with

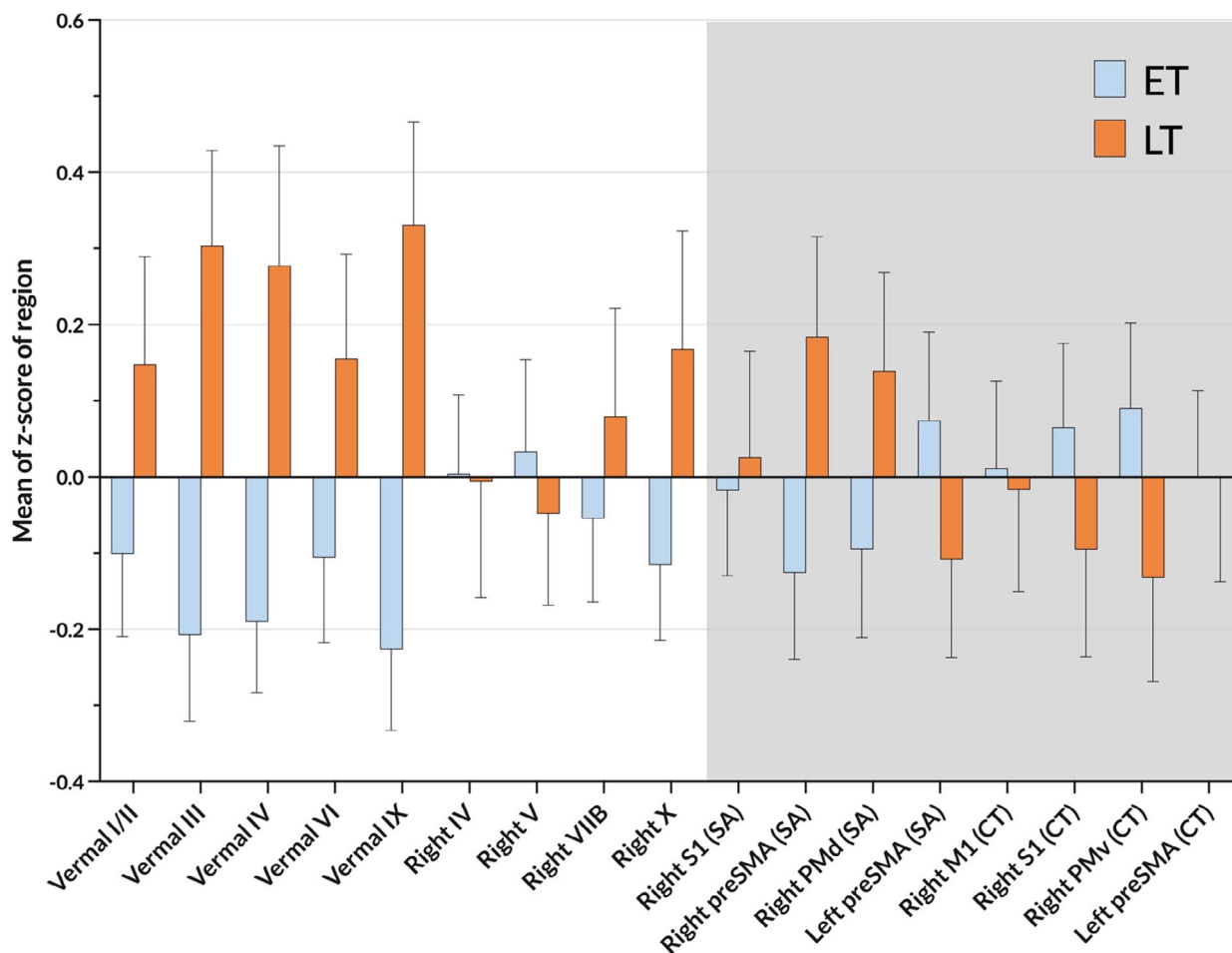


FIGURE 2 Comparison of standardized mean regional volume (cerebellum), surface area, or cortical thickness for optimal 19 regions included in SVM models.

regions showing differences in our previous study examining cortico-cerebellar covariation in the same groups (Shenker et al., 2022). The average cerebellar volume, surface area, or cortical thickness of each region within each group (ET/LT) is visualized in Figure 2. Although no direct statistical comparisons are made, the overall pattern is consistent with the inverted correlational relationship between cerebellar and motor cortical regions in ET musicians seen in our previous study with overall smaller cerebellar volumes being related to greater cortical thickness (Shenker et al., 2022).

Our primary model, in which ET musicians began their training at or before age 7, achieved an overall accuracy of 74% (sensitivity = 78%, specificity = 69%) with a Cohen's kappa of 0.47, denoting “moderate” agreement (Artstein & Poesio, 2008; Landis & Koch, 1977) and an area under the curve (AUC) value of 0.735. Models in which AoS was defined at 1 year earlier or 1 year later than the primary model (i.e., $AoS \leq 6, \leq 8$) performed moderately well, but with greater false positives and/or fewer true positives than the $AoS \leq 7$ model. Additional models with ages of start $\leq 5, 9$, and 10 all performed more poorly, with a range of Cohen's kappa coefficients from 0.13 to 0.27 and two which were noncalculable (denoting “poor” agreement) and AUC values ranging from 0.5 to 0.541. Metrics of all models are summarized in Table 2 and compared as a series of receiver operating characteristic (ROC) curves—which were produced by calculating and plotting the true positive rate against the false positive rate for each AoS model—in Figure 3.

4 | DISCUSSION

The goal of this study was to identify the most salient motor cortical and cerebellar structural features which could be used by a ML algorithm to accurately classify ET and LT musicians. The performance of the classifier was evaluated by comparing accuracy, specificity, and sensitivity of the model. Our primary model ($AoS \leq$ age 7) identified a combination of 17 regions which most optimally and accurately classified ET and LT regions, including bilateral motor-related regions of the cerebellum and motor and premotor regions of the cortex, predominantly in the right hemisphere. Critically, this model—which defined ET musicians as those who began their training before the age of 7—outperformed all other models in which AoS was earlier or later (between ages 5–10).

These results parallel and expand upon those of our previous study: we examined differences in cortico-cerebellar covariation in ET and LT groups and found that ET musicians had decreased overall and regional cerebellar volume, and that this effect was associated with increased cortical thickness in right premotor regions (Baer et al., 2015; Bailey et al., 2014; Shenker et al., 2022). As depicted in Figure 2, mean volume, surface area, and cortical thickness of features used by our SVM model follow these same patterns. The cerebellar regions identified by our model are largely those which are known to exhibit denser connectivity to sensorimotor areas: both human and non-human primate studies have identified connections between sensorimotor areas M1, PMC, and SMA and cerebellar lobules III–VI and

TABLE 2 Confusion matrices and performance metrics of SVM models.

ET \leq 5

	ET	LT	
ET	4	35	Accuracy: 72% Sensitivity: 66% Specificity: 72% Cohen's kappa: 0.13
LT	2	92	

ET \leq 6

	ET	LT	
ET	36	25	Accuracy: 67% Sensitivity: 65% Specificity: 68% Cohen's kappa: 0.33
LT	19	53	

ET \leq 7

	ET	LT	
ET	62	17	Accuracy: 74% Sensitivity: 78% Specificity: 69% Cohen's kappa: 0.47
LT	17	37	

ET \leq 8

	ET	LT	
ET	72	22	Accuracy: 69% Sensitivity: 79% Specificity: 47% Cohen's kappa: 0.27
LT	19	20	

ET \leq 9

	ET	LT	
ET	105	0	Accuracy: 79% Sensitivity: 78% Specificity: noncalculable Cohen's kappa: noncalculable
LT	28	0	

ET \leq 10

	ET	LT	
ET	114	0	Accuracy: 85% Sensitivity: 14% Specificity: noncalculable Cohen's kappa: noncalculable
LT	19	0	

Note: True positives and true negatives (ET and LT musicians, respectively) are found in the top left and bottom right cell of each matrix. Our primary model ($AoS \leq 7$) is highlighted.

VIIA–VIIIB (Kelly & Strick, 2003; Palesi et al., 2017; Salmi et al., 2010). In addition, the salient cerebellar features identified by this model are not lateralized—three regions in both the left and right hemisphere

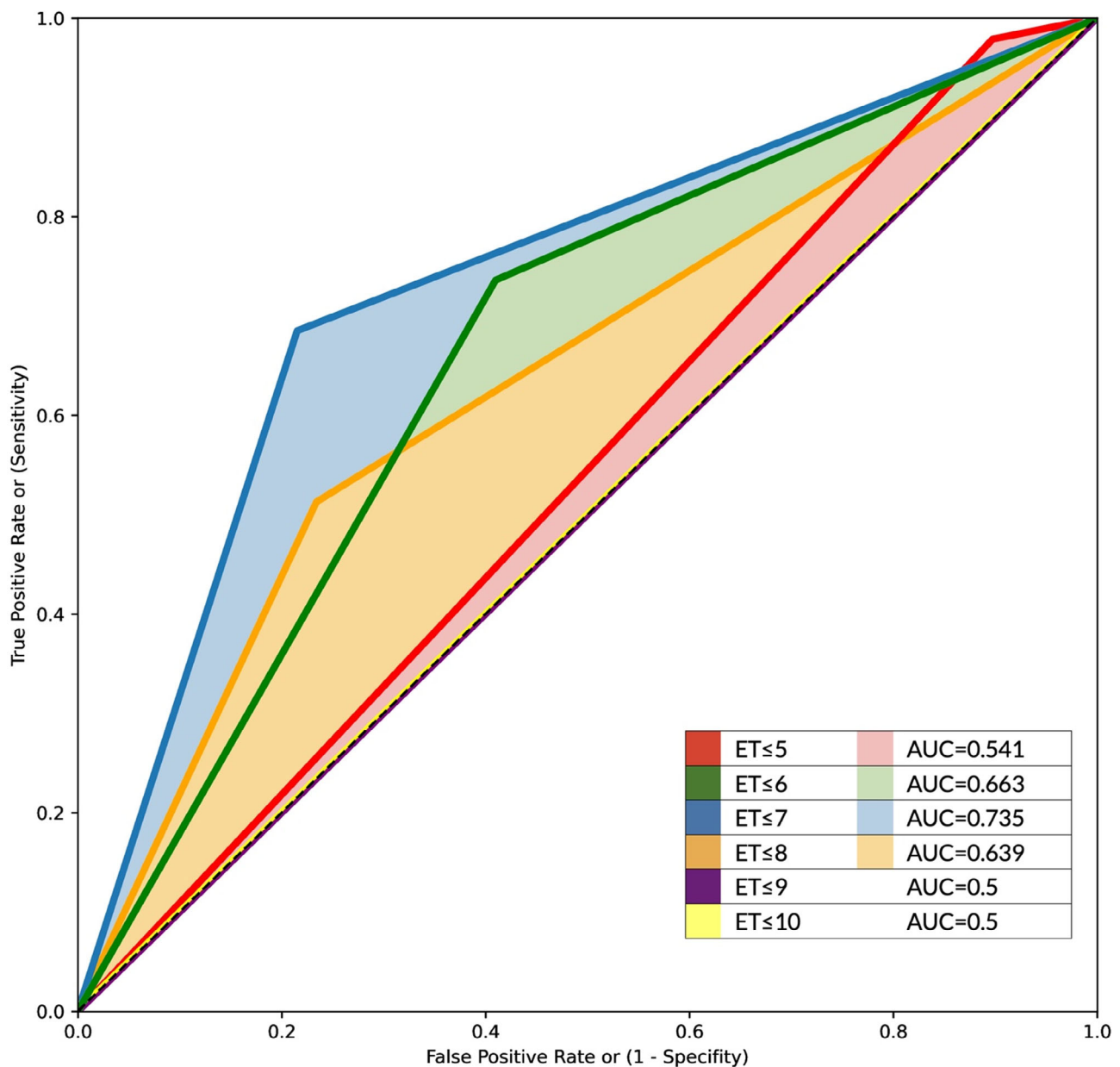


FIGURE 3 ROC curves and AUC values of models varying the age of onset of musical training criterion. The blue line represents the model based on AoS ≤ 7 , the classifier that most accurately predicted group membership.

and six vermal regions—which is consistent with previous findings identifying ET/LT differences across both hemispheres of the cerebellum (Baer et al., 2015; Shenker et al., 2022). In contrast, the majority of the salient cortical features are lateralized to the right hemisphere—including the right vPMC, larger in ET musicians, as previously identified by Bailey et al. (2014). This finding is consistent with previous research suggesting hemispheric specialization in music perception and performance research (see, e.g., Bermudez & Zatorre, 2005; Halwani et al., 2011; Palomar-García et al., 2016).

By leveraging a multivariate ML approach, we have been able to identify a distributed pattern of cerebellar and cortical features predictive of early and late musical training. Previous research studies have each identified separate features in cortical and subcortical

regions related to early training (Baer et al., 2015; Bailey et al., 2014; Steele et al., 2013; van Vugt et al., 2021). However, using a multivariate approach has allowed us to examine not just individual structural differences but more nuanced patterns of coordinated change. Our current findings suggest that early training in musicianship is, indeed, associated with a broad pattern of differences across a larger network. This outcome is consistent with the *interactive specialization* model of brain development, which posits that functionally connected regions develop in tandem, and that experience that promotes plasticity in one part of the network will promote plasticity in the others (Johnson, 2011). Indeed, complex abilities such as music perception and performance—which comprise multiple, overlapping skills—require the contribution of interacting brain networks (Zatorre et al., 2007).

In addition, our primary model—based on $\text{AoS} \leq 7$ —outperformed models with other AoS cutoffs (≤ 6 , ≤ 8 , ≤ 9 , and ≤ 10). The $\text{AoS} \leq 7$ model demonstrated high accuracy and sensitivity (true positives, i.e., correct classification of ET musicians when they really were ET musicians) without sacrificing specificity (true negatives, i.e., correct classification of LT musicians when they really were LT musicians). Models testing classification at other age cut-offs were less accurate: models in which AoS was defined at 1 year earlier or 1 year later than the primary model (i.e., $\text{AoS} \leq 6$, ≤ 8) performed moderately well, but $\text{AoS} \leq 6$ produced more false positives and $\text{AoS} \leq 8$ produced fewer true positives than the $\text{AoS} \leq 7$ model. Models using $\text{AoS} \leq 5$, $\text{AoS} \leq 9$, and $\text{AoS} \leq 10$ showed little to no predictive power. In other words, the unique pattern of cortico-cerebellar structural variation identified by the classifier could most accurately predict groups based on the $\text{AoS} \leq 7$ cut-off, and other models were capable of classifying one group but not the other or were prone to classification errors. Together, these results indicate that musical training at or before age 7 has a joint effect on cortical and cerebellar structure in adulthood and supports the hypothesis that the sensitive period for coordinated developmental plasticity in cortico-cerebellar regions—promoted by early musical training—may end at or around age 7. However, sensitive periods for complex skills such as music or language are unlikely to exhibit abrupt cut-offs. Instead, such skills are likely to depend on a cascade of developmental and experience-dependent plasticity effects with basic sensory processes being affected earlier and more complex processes affected later (Penhune, 2022; Werker & Hensch, 2015).

Previous research has demonstrated that the cortico-cerebellar connectivity underlying the motor and cognitive functions associated with musicianship changes across the lifespan and may therefore contribute to sensitive periods for the effects of training (Fjell et al., 2019; Kipping et al., 2017; Tiemeier et al., 2010). 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. Grey matter volume of anterior motor regions—including M1 and PMC—have a peak rate of change between the ages of 6 and 8 (Giedd et al., 1999). Evidence that functional connectivity between the cerebellum and cortex is greatest at age 6–7 further supports the possibility of correlated change. Kipping et al. (2017) investigated cortico-cerebellar functional connectivity networks using resting-state fMRI in children aged 4–5, 6–7, and 9–10. They identified age-related differences in both the extent and strength of these cortico-cerebellar networks and found that functional connectivity in the majority of these networks peaked at age 6–7. These observations suggest that plasticity is heightened during these developmental windows, and that long-term plasticity may be the product of experience during periods of peak maturational change at both the local circuit and network levels.

It is unlikely, however, that all musician-associated skills fall into one distinct sensitive period. There is evidence of multiple sensitive periods across the cortex associated with diverse behaviors, and these cascading sensitive periods occur at different temporal windows and

are sensitive to different types of behavior (Penhune, 2021). Studies in language acquisition, for example, have noted multiple sensitive periods—with windows opening and closing at different ages—for distinct aspects of language: a window for the acquisition of syntax which appears to close around age 7, while that of consonant discrimination of non-native speech sounds begins closing after 10–12 months of age (Werker & Hensch, 2015). While the sensitive period described in the current research appears to close around age 7, this window—possibly one of many—may be unique to the complex pattern of cortico-cerebellar plasticity and may not represent the totality of differences between ET and LT musicians. Research in children supports this hypothesis: while children who began musical training before age 7 outperformed same-aged LT peers on simple melody discrimination, there was no difference in children's performance on rhythm synchronization or transposed melody discrimination tasks (Ireland et al., 2019). Adult ET musicians, however, do outperform adult LT musicians on rhythm synchronization tasks (Baer et al., 2015). Early start of music training may enhance plasticity, both directly and through network connections, and early experience may have a metaplastic effect such that early plasticity may serve as a scaffold on which later experience can build (Steele & Penhune, 2010).

Finally, it is important to note that the current research focused only on cortical sensorimotor regions and the cerebellum due to previous evidence of their implication in early musical training. Future studies with a larger number of participants—and enough statistical power—would benefit from replicating these analyses across the whole brain in order to uncover potential contributions from—and interactions between—other brain regions. More specifically, future research in this domain might consider investigating the basal ganglia. Previous work examining structural and functional differences between ET and LT musicians has shown a reduced volume of the putamen (Vaquero et al., 2016) and a pattern of cortico-striatal functional connectivity that was unique to ET musicians (van Vugt et al., 2021). These findings suggest that the cortico-cerebellar network-level differences observed in this study may be part of a larger series of network-level changes associated with early training. Similarly, it would be interesting to examine interactions between the auditory and motor systems given the importance of sensorimotor integration to musical performance (Zatorre et al., 2007). Finally, a larger sample size would additionally allow us to better control for the potential impacts of biological sex, which could be the source of some variance in the current analyses.

5 | CONCLUSION

This study used a multivariate classification approach to identify patterns of cortico-cerebellar structural variation which can differentiate ET and LT musicians, emphasizing that early experience promotes plasticity at a network level. In addition, these patterns were most robust when classifying musicians who began their training at or before age 7, providing new evidence for a sensitive period for music experience in middle childhood. Together with previous work, this

study helps build a more nuanced understanding of how early musical experience interacts with sensitive periods to effect network-level changes in the brain.

AUTHOR CONTRIBUTIONS

Joseph J. Shenker: Conceptualization, Methodology, Software, Formal analysis, Investigation, Writing—Original draft, Visualization. **Christopher J. Steele:** Conceptualization, Validation, Writing—Review & editing. **Robert J. Zatorre:** Conceptualization, Validation, Writing—Review & editing. **Virginia B. Penhune:** Conceptualization, Validation, Writing—Original draft, Review & editing, Supervision.

ACKNOWLEDGMENTS

JJS is funded by the by a Graduate Scholarship from the Natural Sciences and Engineering Research Council of Canada (NSERC). CJS is supported by the Heart & Stroke Foundation New Investigator Award, Canadian Institutes of Health Research (CIHR) (HNC 170723), and NSERC (RGPIN-2020-06812, DGECR-2020-00146). RJZ is a fellow of the Canadian Institute for Advanced Research. Funding to RJZ and VBP is from the Canadian Institutes of Health Research (#143217).

CONFLICT OF INTEREST STATEMENT

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

DATA AVAILABILITY STATEMENT

Original code used in this study will be made available upon reasonable request to the corresponding author. The data are not publicly available as subjects did not provide specific consent.

ORCID

Joseph J. Shenker  <https://orcid.org/0000-0002-7874-5040>

Christopher J. Steele  <https://orcid.org/0000-0003-1656-7928>

Robert J. Zatorre  <https://orcid.org/0000-0003-1730-7423>

Virginia B. Penhune  <https://orcid.org/0000-0002-9475-5724>

REFERENCES

- Ad-Dab'bagh, Y., Einarson, D., Lyttelton, O., Muehlboeck, J.-S., Mok, K., Ivanov, O., Vincent, R. D., Lepage, C., Lerch, J., Fombonne, E., & Evans, A. C. (2006). The CIVET image-processing environment: A fully automated comprehensive pipeline for anatomical Neuroimaging research. In *Paper presented at the 12th annual meeting of the Organization for Human Brain Mapping*.
- Albouy, P., Caclin, A., Norman-Haignere, S. V., Lévêque, Y., Peretz, I., Tillmann, B., & Zatorre, R. J. (2019). Decoding task-related functional brain imaging data to identify developmental disorders: The case of congenital amusia. *Frontiers in Neuroscience*, 13. <https://doi.org/10.3389/fnins.2019.01165>
- Amari, S., & Wu, S. (1999). Improving support vector machine classifiers by modifying kernel functions. *Neural Networks*, 12(6), 783–789. [https://doi.org/10.1016/S0893-6080\(99\)00032-5](https://doi.org/10.1016/S0893-6080(99)00032-5)
- 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. *Human Brain Mapping*, 5(3), 206–215. [https://doi.org/10.1002/\(SICI\)1097-0193\(1997\)5:3<206::AID-HBM5>3.0.CO;2-7](https://doi.org/10.1002/(SICI)1097-0193(1997)5:3<206::AID-HBM5>3.0.CO;2-7)
- Artstein, R., & Poesio, M. (2008). Inter-coder agreement for computational linguistics. *Computational Linguistics*, 34(4), 555–596. <https://doi.org/10.1162/coli.07-034-R2>
- Baer, L. H., Park, M. T., Bailey, J. A., Chakravarty, M. M., Li, K. Z., & Penhune, V. B. (2015). Regional cerebellar volumes are related to early musical training and finger tapping performance. *NeuroImage*, 109, 130–139. <https://doi.org/10.1016/j.neuroimage.2014.12.076>
- Bailey, J. A., & Penhune, V. B. (2010). Rhythm synchronization performance and auditory working memory in early- and late-trained musicians. *Experimental Brain Research*, 204(1), 91–101. <https://doi.org/10.1007/s00221-010-2299-y>
- Bailey, J. A., & Penhune, V. B. (2013). The relationship between the age of onset of musical training and rhythm synchronization performance: Validation of sensitive period effects. *Frontiers in Neuroscience*, 7, 227. <https://doi.org/10.3389/fnins.2013.00227>
- Bailey, J. A., Zatorre, R. J., & Penhune, V. B. (2014). Early musical training is linked to gray matter structure in the ventral premotor cortex and auditory-motor rhythm synchronization performance. *Journal of Cognitive Neuroscience*, 26(4), 755–767. https://doi.org/10.1162/jocn_a_00527
- Bermudez, P., & Zatorre, R. J. (2005). Differences in gray matter between musicians and nonmusicians. *Annals of the New York Academy of Sciences*, 1060, 395–399. <https://doi.org/10.1196/annals.1360.057>
- Bray, S., Chang, C., & Hoeff, F. (2009). Applications of multivariate pattern classification analyses in developmental neuroimaging of healthy and clinical populations. *Frontiers in Human Neuroscience*, 3, 32. <https://doi.org/10.3389/neuro.09.032.2009>
- Chakravarty, M. M., Steadman, P., van Eede, M. C., Calcott, R. D., Gu, V., Shaw, P., ... Lerch, J. P. (2013). Performing label-fusion-based segmentation using multiple automatically generated templates. *Human Brain Mapping*, 34(10), 2635–2654. <https://doi.org/10.1002/hbm.22092>
- Ducharme, S., Albaugh, M. D., Nguyen, T.-V., Hudziak, J. J., Mateos-Pérez, J. M., Labbe, A., ... Karama, S. (2016). Trajectories of cortical thickness maturation in normal brain development—The importance of quality control procedures. *NeuroImage*, 125, 267–279. <https://doi.org/10.1016/j.neuroimage.2015.10.010>
- Eskildsen, S. F., Coupe, P., Fonov, V., Manjon, J. V., Leung, K. K., Guizard, N., ... Neuroimaging I, A.'s. D. (2012). BEaST: Brain extraction based on nonlocal segmentation technique. *NeuroImage*, 59(3), 2362–2373. <https://doi.org/10.1016/j.neuroimage.2011.09.012>
- Fjell, A. M., Chen, C. H., Sederevicus, D., Sneve, M. H., Grydeland, H., Krogstad, S. K., ... Walhovd, K. B. (2019). Continuity and discontinuity in human cortical development and change from embryonic stages to old age. *Cerebral Cortex*, 29(9), 3879–3890. <https://doi.org/10.1093/cercor/bhy266>
- Furey, T. S., Cristianini, N., Duffy, N., Bednarski, D. W., Schummer, M., & Haussler, D. (2000). Support vector machine classification and validation of cancer tissue samples using microarray expression data. *Bioinformatics*, 16(10), 906–914.
- Giedd, J. N., Blumenthal, J., Jeffries, N. O., Castellanos, F. X., Liu, H., Zijdenbos, A., ... Rapoport, J. L. (1999). Brain development during childhood and adolescence: A longitudinal MRI study. *Nature Neuroscience*, 2(10), 861–863. <https://doi.org/10.1038/13158>
- Gogtay, N., Giedd, J. N., Lusk, L., Hayashi, K. M., Greenstein, D., Vaituzis, A. C., ... Thompson, P. M. (2004). Dynamic mapping of human cortical development during childhood through early adulthood. *Proceedings of the National Academy of Sciences of the United States of America*, 101(21), 8174–8179. <https://doi.org/10.1073/pnas.0402680101>

- Guyon, I., Weston, J., Barnhill, S., & Vapnik, V. (2002). Gene selection for cancer classification using support vector machines. *Machine Learning*, 46(1), 389–422. <https://doi.org/10.1023/A:1012487302797>
- Halwani, G. F., Loui, P., Rüber, T., & Schlaug, G. (2011). Effects of practice and experience on the arcuate fasciculus: Comparing singers, instrumentalists, and non-musicians. *Frontiers in Psychology*, 2, 156. <https://doi.org/10.3389/fpsyg.2011.00156>
- Huang, M. L., Hung, Y. H., Lee, W. M., Li, R. K., & Jiang, B. R. (2014). SVM-RFE based feature selection and Taguchi parameters optimization for multiclass SVM classifier. *ScientificWorldJournal*, 2014, 795624. <https://doi.org/10.1155/2014/795624>
- Ireland, K., Iyer, T. A., & Penhune, V. B. (2019). Contributions of age of start, cognitive abilities and practice to musical task performance in childhood. *PLoS One*, 14(4), e0216119. <https://doi.org/10.1371/journal.pone.0216119>
- Ireland, K., Parker, A., Foster, N., & Penhune, V. (2018). Rhythm and melody tasks for school-aged children with and without musical training: Age-equivalent scores and reliability. *Frontiers in Psychology*, 9, 426. <https://doi.org/10.3389/fpsyg.2018.00426>
- Johnson, M. H. (2011). Interactive specialization: A domain-general framework for human functional brain development? *Developmental Cognitive Neuroscience*, 1(1), 7–21. <https://doi.org/10.1016/j.dcn.2010.07.003>
- Kelly, R. M., & Strick, P. L. (2003). Cerebellar loops with motor cortex and prefrontal cortex of a nonhuman primate. *The Journal of Neuroscience*, 23(23), 8432–8444. <https://doi.org/10.1523/jneurosci.23-23-08432.2003>
- Kipping, J. A., Tuan, T. A., Fortier, M. V., & Qiu, A. (2017). Asynchronous development of cerebellar, cerebello-cortical, and cortico-cortical functional networks in infancy, childhood, and adulthood. *Cerebral Cortex*, 27(11), 5170–5184. <https://doi.org/10.1093/cercor/bhw298>
- Kloppel, S., Stonnington, C. M., Chu, C., Draganski, B., Scahill, R. I., Rohrer, J. D., ... Frackowiak, R. S. (2008). Automatic classification of MR scans in Alzheimer's disease. *Brain*, 131(Pt 3), 681–689. <https://doi.org/10.1093/brain/awm319>
- Kraus, N., Skoe, E., Parbery-Clark, A., & Ashley, R. (2009). Experience-induced malleability in neural encoding of pitch, timbre, and timing. *Annals of the New York Academy of Sciences*, 1169, 543–557. <https://doi.org/10.1111/j.1749-6632.2009.04549.x>
- Kuhn, M., & Johnson, K. (2018). *Applied predictive modeling*. Springer.
- Landis, J. R., & Koch, G. G. (1977). The measurement of observer agreement for categorical data. *Biometrics*, 33(1), 159–174.
- Magnin, B., Mesrob, L., Kinkingnehun, S., Pelegrini-Issac, M., Colliot, O., Sarazin, M., ... Benali, H. (2009). Support vector machine-based classification of Alzheimer's disease from whole-brain anatomical MRI. *Neuroradiology*, 51(2), 73–83. <https://doi.org/10.1007/s00234-008-0463-x>
- Mayka, M. A., Corcos, D. M., Leurgans, S. E., & Vaillancourt, D. E. (2006). Three-dimensional locations and boundaries of motor and premotor cortices as defined by functional brain imaging: A meta-analysis. *NeuroImage*, 31(4), 1453–1474. <https://doi.org/10.1016/j.neuroimage.2006.02.004>
- Othman, M. F. B., Abdullah, N. B., & Kamal, N. F. B. (2011). *MRI brain classification using support vector machine*. Paper presented at the 2011 fourth international conference on modeling, simulation and applied optimization, 19–21 April.
- Palesi, F., De Rinaldis, A., Castellazzi, G., Calamante, F., Muhlert, N., Chard, D., ... Gandini Wheeler-Kingshott, C. A. M. (2017). Contralateral cortico-ponto-cerebellar pathways reconstruction in humans in vivo: Implications for reciprocal cerebro-cerebellar structural connectivity in motor and non-motor areas. *Scientific Reports*, 7(1), 12841. <https://doi.org/10.1038/s41598-017-13079-8>
- Palomar-García, M.-Á., Zatorre, R. J., Ventura-Campos, N., Bueichekú, E., & Ávila, C. (2016). Modulation of functional connectivity in auditory-motor networks in musicians compared with nonmusicians. *Cerebral Cortex*, 27(5), 2768–2778. <https://doi.org/10.1093/cercor/bhw120>
- Park, M. T. M., Pipitone, J., Baer, L. H., Winterburn, J. L., Shah, Y., Chavez, S., ... Chakravarty, M. M. (2014). Derivation of high-resolution MRI atlases of the human cerebellum at 3T and segmentation using multiple automatically generated templates. *NeuroImage*, 95, 217–231. <https://doi.org/10.1016/j.neuroimage.2014.03.037>
- Pedrosa, D. J., Brown, P., Cagnan, H., Visser-Vandewalle, V., Wirths, J., Timmermann, L., & Brittain, J. S. (2018). A functional micro-electrode mapping of ventral thalamus in essential tremor. *Brain*, 141(9), 2644–2654. <https://doi.org/10.1093/brain/awy192>
- Penhune, V. B. (2020). A gene-maturation-environment model for understanding sensitive period effects in musical training. *Current Opinion in Behavioral Sciences*, 36, 13–22. <https://doi.org/10.1016/j.cobeha.2020.05.011>
- Penhune, V. B. (2021). *Understanding Sensitive Period Effects in Musical Training* (pp. 1–22). Springer Berlin Heidelberg.
- Penhune, V. B. (2022). Understanding sensitive period effects in musical training. *Current Topics in Behavioral Neurosciences*, 53, 167–188. https://doi.org/10.1007/7854_2021_250
- Puolivälä, T., Sipola, T., Thiede, A., Kliuchko, M., Bogert, B., Toivaiainen, P., ... Parviainen, T. (2020). Musical skills can be decoded from magnetic resonance images. *bioRxiv*. <https://doi.org/10.1101/2020.07.19.210906>
- Salmi, J., Pallesen, K. J., Neuvonen, T., Brattico, E., Korvenoja, A., Salonen, O., & Carlson, S. (2010). Cognitive and motor loops of the human cerebro-cerebellar system. *Journal of Cognitive Neuroscience*, 22(11), 2663–2676. <https://doi.org/10.1162/jocn.2009.21382>
- Sanz, H., Valim, C., Vegas, E., Oller, J. M., & Reverter, F. (2018). SVM-RFE: Selection and visualization of the most relevant features through non-linear kernels. *BMC Bioinformatics*, 19(1), 432. <https://doi.org/10.1186/s12859-018-2451-4>
- Schlaug, G., Jancke, L., Huang, Y., & Steinmetz, H. (1995). In vivo evidence of structural brain asymmetry in musicians. *Science*, 267(5198), 699–701.
- Shenker, J. J., Steele, C. J., Chakravarty, M. M., Zatorre, R. J., & Penhune, V. B. (2022). Early musical training shapes cortico-cerebellar structural covariation. *Brain Structure & Function*, 227(1), 407–419. <https://doi.org/10.1007/s00429-021-02409-2>
- Steele, C. J., Bailey, J. A., Zatorre, R. J., & Penhune, V. B. (2013). Early musical training and white-matter plasticity in the corpus callosum: Evidence for a sensitive period. *The Journal of Neuroscience*, 33(3), 1282–1290. <https://doi.org/10.1523/JNEUROSCI.3578-12.2013>
- Steele, C. J., & Penhune, V. B. (2010). Specific increases within global decreases: A functional magnetic resonance imaging investigation of five days of motor sequence learning. *The Journal of Neuroscience*, 30(24), 8332–8341. <https://doi.org/10.1523/JNEUROSCI.5569-09.2010>
- Tiemeier, H., Lenroot, R. K., Greenstein, D. K., Tran, L., Pierson, R., & Giedd, J. N. (2010). Cerebellum development during childhood and adolescence: A longitudinal morphometric MRI study. *NeuroImage*, 49(1), 63–70. <https://doi.org/10.1016/j.neuroimage.2009.08.016>
- van Vugt, F. T., Hartmann, K., Altenmüller, E., Mohammadi, B., & Margulies, D. S. (2021). The impact of early musical training on striatal functional connectivity. *NeuroImage*, 238, 118251. <https://doi.org/10.1016/j.neuroimage.2021.118251>
- Vaquero, L., Hartmann, K., Ripolles, P., Rojo, N., Sierpowska, J., Francois, C., ... Altenmüller, E. (2016). Structural neuroplasticity in expert pianists depends on the age of musical training onset. *NeuroImage*, 126, 106–119. <https://doi.org/10.1016/j.neuroimage.2015.11.008>
- Watanabe, D., Savion-Lemieux, T., & Penhune, V. B. (2007). The effect of early musical training on adult motor performance: Evidence for a

- sensitive period in motor learning. *Experimental Brain Research*, 176(2), 332–340. <https://doi.org/10.1007/s00221-006-0619-z>
- Werker, J. F., & Hensch, T. K. (2015). Critical periods in speech perception: New directions. *Annual Review of Psychology*, 66, 173–196. <https://doi.org/10.1146/annurev-psych-010814-015104>
- Zatorre, R. J., Chen, J. L., & Penhune, V. B. (2007). When the brain plays music: Sensory-motor interactions in music perception and production. *Nature Reviews. Neuroscience*, 8, 547–558.

How to cite this article: Shenker, J. J., Steele, C. J., Zatorre, R. J., & Penhune, V. B. (2023). Using cortico-cerebellar structural patterns to classify early- and late-trained musicians. *Human Brain Mapping*, 1–11. <https://doi.org/10.1002/hbm.26395>