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Musical Training Shapes Structural Brain Development

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Krista L. Hyde<sup>1</sup>, Jason Lerch<sup>2</sup>, Andrea Norton<sup>4</sup>, Marie Forgeard<sup>4</sup>, Ellen Winner<sup>3</sup>,  
Alan C. Evans<sup>1</sup> & Gottfried Schlaug<sup>4</sup>

<sup>1</sup> Montreal Neurological Institute, McGill University, 3801 University Street,  
Montreal, Quebec, H3A 2B4, Canada

<sup>2</sup> Mouse Imaging Centre, Hospital for Sick Children, 25 Orde St. Toronto,  
Ontario, M5t 3H7 Canada

<sup>3</sup> Dept. of Psychology, Boston College, 140 Commonwealth Ave., Chestnut Hill,  
MA 02467

<sup>4</sup> Dept. of Neurology, Music and Neuroimaging Lab, Beth Israel Deaconess  
Medical Center and Harvard Medical School, 330 Brookline Avenue, Boston,  
MA 02215, USA

Corresponding authors: Krista L. Hyde (krista.hyde@mail.mcgill.ca) and  
Gottfried Schlaug (gschlaug@bidmc.harvard.edu)

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The human brain has the remarkable capacity to alter in response to environmental demands. Training-induced structural brain changes have been demonstrated in the healthy adult human brain. However, no study has yet directly related structural brain changes to behavioral changes in the developing brain, addressing the question of whether structural brain differences seen in adults (comparing experts with matched controls) are a product of 'nature' (via biological brain predispositions) or 'nurture' (via early training). Long-term instrumental music training is an intense, multisensory and motor experience and offers an ideal opportunity to study structural brain plasticity in the developing brain in correlation with behavioral changes induced by training. Here we demonstrate structural brain changes after only 15 months of musical training in early childhood, that were correlated with improvements in musically-relevant motor and auditory skills. These findings shed light on brain plasticity, and suggest that structural brain differences in adult experts (whether musicians or experts in other areas) are likely due to training-induced brain plasticity.

## INTRODUCTION

Studies comparing adult musicians with matched non-musicians have revealed structural and functional differences in musically-relevant brain regions such as sensorimotor brain areas (Elbert et al., 1995; Hund-Georgiadis and von Cramon, 1999; Schlaug, 2001; Gaser and Schlaug, 2003b), auditory areas (Pantev et al., 1998; Zatorre, 1998; Schneider et al., 2002; Gaab and Schlaug, 2003; Bermudez and Zatorre, 2005; Lappe et al., 2008) and multimodal integration areas (Munte et al., 2001; Sluming et al., 2002; Gaser and Schlaug, 2003a; Lotze et al., 2003; Bangert and Schlaug, 2006; Sluming et al., 2007; Zatorre et al., 2007). While some research has investigated functional brain correlates of musical training in childhood (Overy et al., 2004; Koelsch et al., 2005; Fujioka et al., 2006; Shahin et al., 2008), no studies have yet examined structural brain and behavioral changes in the developing brain in response to long-term music training to specifically address the question of whether structural brain differences seen in adults (comparing experts with matched controls) are a product of 'nature' or 'nurture'.

Such a study could also examine cognitive and behavioral changes in parallel with brain changes in response to music training. There is a widespread view that learning to play a musical instrument in childhood stimulates cognitive development and leads to the enhancement of skills in a variety of extra-musical areas which is commonly referred to as transfer (Bangerter and Heath, 2004). The most commonly observed form of transfer occurs when there is a close resemblance between the training domain and the transfer domain (typically referred to as "near transfer", e.g., fine motor skills

that develop while learning to play a musical instrument lead to increased speed and accuracy in typing). While near transfer effects are relatively common, it is notoriously difficult to demonstrate “far transfer”, where the resemblance between training and transfer domains is much less obvious (e.g., learning to read and perform with precision from musical rhythm notation and understanding fractions in math). There are some claims for far transfer from instrumental music training in the areas of verbal, spatial, mathematical, and IQ performance (Rauscher et al., 1993; Rauscher et al., 1997; Chan et al., 1998; Rauscher et al., 1998; Ho et al., 2003; Schellenberg, 2004; Forgeard et al., 2008), but such findings have also been controversial (Steele et al., 1999).

As part of an ongoing longitudinal study on the effects of music training on brain, behavioral and cognitive development in young children (Norton et al., 2005; Schlaug et al., 2005), here we investigated structural brain changes in relation to behavioral changes in young children who received 15 months of instrumental musical training relative to a group of children who did not. We used deformation based morphometry (DBM), an unbiased and automated approach to brain morphology, to search throughout the whole brain on a voxel-wise basis for local brain size or shape differences between groups (Collins et al., 1994; Robbins et al., 2004). The DBM technique is useful for measuring morphometric brain changes longitudinally, as in the present study, where the DBM metric of interest, the Jacobian determinant, yields a measure of relative voxel size change over time in terms of voxel expansion (growth) or contraction (shrinkage). To investigate a brain-behavioral relationship, we correlated the

brain deformation changes after 15 months with performance changes on behavioral tests.

## **MATERIALS AND METHODS**

### ***Participants***

We tested two groups of children that were recruited from Boston area public schools and who had no prior formal musical training (see Table 1). The 'Instrumental' group consisted of fifteen children (mean age at start of study 6.32 years old, SD 0.82 years) beginning weekly half-hour private (outside of the school system) keyboard lessons and who continued lessons for a mean interval of 15 months. The 'Control' group consisted of sixteen children (mean age at start of study 5.90 years old, SD 0.54 years) who did not receive any instrumental music training during this 15 month period, but did participate in a weekly 40 minute group music class in school consisting of singing and playing with drums and bells. The Instrumental and Control children were all right-handed and matched as close as possible in gender, age at the start of the study, and socioeconomic status (SES). SES was defined by parental education on a 6-point scale, with a score of 1, for children whose parents had some high school education, to a score of 6 for those whose parents had a doctoral degree (see Norton et al., 2005).

At Time 1, all children were tested on a series of behavioral tests (described below), and underwent an MRI scan (scan 1). At Time 2 (15 months later), all children were re-tested on the behavioral tests and underwent a

second MRI scan (scan 2). The children whose results are reported here are drawn from a slightly larger group of Instrumental and Control children (see Norton et al., 2005). Here we only report the results from the children who completed both the behavioral tests and MRI scanning at Times 1 and 2. We tested the hypothesis that brain and behavioral changes after 15 months should be greater in Instrumental than Control children; this time period allows us to compare our results with those of other studies using a similar observation period.

### ***Behavioral Tests and MRI scanning***

Children were tested individually at Times 1 and 2 on measures of handedness and SES, and on two near transfer measures: a 4-finger motor sequencing test for the left and right hands assessing fine finger motor skills, and a custom-made 'Melodic and Rhythmic Discrimination Test Battery' assessing music listening and discrimination skills. Five far transfer measures were also administered: the Object Assembly, Block Design, and Vocabulary subtests of the WISC-III (Wechsler, 1991), the Raven's Progressive Matrices (Colored Progressive Matrices and Standard Progressive Matrices) (Raven, 1976), and the Auditory Analysis Test (Rosner and Simon, 1971) assessing phonemic awareness. The vocabulary subtest of the WISC was used as a proxy for verbal IQ. For a detailed description of these tests and their administration to this group of children, see Norton et al. (2005) and Forgeard et al. (2008).

The two musically-relevant (near transfer) behavioral tests are described in more detail below, since these were the only tests that showed significant

between group differences after 15 months (see results section below). Both of these tests are related to musical activity, but can also be performed by children who do not have any instrumental music training. In the 4-finger motor sequencing test, children pressed a particular number sequence (e.g., 5-2-4-3-5) corresponding to fingers 2-5 of their left or right hand on the number keys of a computer keyboard as often, accurately and as fast as possible over a 30 second period. In the 'Melodic and Rhythmic Discrimination Test Battery', children heard pairs of five-tone musical phrases differing only in melody and pairs of phrases differing only in rhythm. The task was to indicate whether the two musical phrases were the same or different. These musical phrases were designed for this study and are described in more detail elsewhere (Norton et al., 2005; Overy et al., 2004; Forgeard et al., 2008). The melodic and rhythmic subtest scores were combined to form one single behavioral measure of auditory-musical discrimination. Behavioral 'difference scores' measuring the difference in performance on the behavioral tests from Time 1 to 2, were calculated and then correlated with brain deformation measures.

Anatomical MRI scans were obtained for all children on a 3T General Electric MRI scanner using a T1-weighted, magnetization prepared gradient-echo (MPRAGE) volume acquisition with a voxel resolution of 0.93 x 0.93 x 1.5 mm. This research was approved by the ethics committees of the Beth Israel Deaconess Medical Center. Written informed consent was obtained from the parents of all the children, and the children themselves gave assent to participate in this study.

***Brain deformation-based morphometry analyses***

Automated deformation brain analyses were performed on the T1 MRI data for each child (see Supplementary Figure 1). All MRI scans were first non-uniformity corrected, and registered to MNI-Talairach space with a 9-parameter linear transform using `mni_autoreg` tools (Collins et al., 1994; Robbins et al., 2004). Next, brain deformation measures in terms of the Jacobian determinants (yielding a measure of relative voxel expansion or contraction) were calculated so that we could perform three different statistical analyses. First, to test for any brain deformation differences at baseline (before musical training), for each group, all Time 1 MRI scans (0 months) iteratively underwent non-linear registration towards the previous group average (starting with the linear group average). The Jacobian determinants of the final non-linear registration were computed and blurred with a 10 mm Gaussian kernel. Statistical analyses were then performed comparing the Jacobian determinant data between groups at baseline, at each voxel. Second, to test for brain deformation differences between groups over time, each child's Time 1 scan (at 0 months) was non-linearly aligned to his or her Time 2 scan (15 months later). The resulting displacement field was blurred with a 10 mm Gaussian kernel and the Jacobian determinant of the blurred displacement field was computed. Statistical analyses were then performed comparing the longitudinal Jacobian determinant data between groups, at each voxel. Third, to test for a brain-behavioral relationship, brain deformation differences (Jacobian determinants of scan 2-1 as above) were regressed on the behavioral difference scores (difference in test performance Time 1 to Time 2), for each subject, at each voxel.

The general linear model was used in the group statistical analyses with age at Time 1, gender, and SES entered as covariates. The results from the group comparison were thresholded at a whole-brain level using the false discovery rate theory (Genovese et al., 2002) with  $q = 0.05$ . This means that only 5% of the significant results may be false positives, and that we are 95% confident that the significant results are true positives. The results were deemed significant at a  $t$ -threshold of 3.0 ( $q = 0.05$ ). The significant brain deformation differences from the group comparison were then used to define a volume of interest in which to test for brain-behavior correlations with the scores on the motor and auditory-musical tests. The results from this volume of interest were thresholded using the false discovery rate theory, with  $q = 0.05$ .

## **RESULTS**

### **Analysis of Behavioral Changes**

An initial chi-square analysis showed that the Instrumental and Control groups did not differ in gender distribution ( $p > 0.1$ ). Initial analyses of variance (ANOVA) showed that the groups did not differ in vocabulary scores at baseline ( $p > 0.1$ ), replicating the results initially reported in Norton et al. (2005). The groups did differ in SES, with the Instrumental group (mean 5.1 points, SD 0.63) having a higher average SES than the Control group (mean 4.47 points, SD 0.87). The two groups also differed slightly in age at baseline (Time 1), with the Instrumental group (mean 6.32 years, SD 0.82) only about two weeks older than the Control group (mean 5.90 years, SD 0.54). Although this age

difference only approached significance ( $p=0.1$ ), we chose to be conservative and covaried age along with SES in our subsequent analyses.

A multiple analysis of covariance (MANCOVA), covarying age and SES, was conducted to determine that there were no pre-existing group differences at Time 1 on either near or far transfer outcomes. Missing values were replaced by the series' mean (2.42 % of all values). The MANCOVA revealed no significant overall difference between groups, Wilks' Lambda = .85,  $F(8, 20) = .44$ ,  $p=0.88$ . Follow-up univariate tests also indicated that the two groups did not differ on any of the outcomes (all  $p>.1$ ). Furthermore, the groups did not differ in interval length (in months) between baseline (Time 1) and Time 2 testing ( $p > .1$ )

To determine whether the Instrumental group progressed more than the Control group on any of the outcomes between Times 1 and 2, another MANCOVA was carried out using the behavioral difference scores (performance difference from Time 1 to 2) as our dependent variable, and age at baseline and SES as our covariates. Missing values were replaced by the series' mean (for 6.85% of all values). As predicted, there was a significant overall difference in the behavioral difference scores between the two groups, Wilks' Lambda = .50,  $F(8, 20) = 2.55$ ,  $p = .04$ , partial  $\eta^2=0.51$ . Univariate tests revealed differences in the two near transfer outcomes (motor and melody/rhythm tests) but not in any far transfer outcomes.

On the finger motor sequencing test, the Instrumental group significantly outperformed the Control group in terms of the right hand motor performance improvement over time,  $F(1, 27) = 7.25$ ,  $p = .01$ , partial  $\eta^2 = .21$ , and the difference between groups approached significance for the left hand,  $F(1, 27) =$

3.81,  $p = .06$ , partial  $\eta^2 = .12$ . The Instrumental group also significantly outperformed the Control group in improvement on the custom-made Melodic/Rhythmic Discrimination Test Battery,  $F(1, 27) = 13.20$ ,  $p < .01$ , partial  $\eta^2 = .33$ . No between-group differences in improvement over time (Time 1 to 2) were found for the far transfer measures of Block Design, Vocabulary, Object Assembly, Raven's Progressive Matrices and Auditory Analysis (all  $p > .1$ ).

### **Analysis of Brain Changes**

With regard to between-group brain differences, we did not see any differences between groups at Time 1. However, Instrumental children did show significantly different brain deformation changes (greater relative voxel size) over the 15 months (Time 2 scan at 15 months minus Time 1 scan at 0 months) as compared to Controls in motor areas, such as bilateral precentral gyri (motor hand area, Figure 1a), corpus callosum (4th and 5th segment, Figure 2a), and bilateral cerebellum (lobes V/VI, (Schmahmann et al., 1999), Figure 3a, b), as well as in bilateral auditory regions in the superior temporal gyri (anterior and lateral to primary auditory cortex, Figure 4a, b). Some significant brain deformation differences were also found outside auditory and motor brain areas. Musicians showed areas of greater relative voxel size in bilateral somatosensory regions in post-central gyri, right inferior temporal gyrus, left supramarginal gyrus, bilateral fronto-lateral and frontomesial regions and a left posterior peri-cingulate region. In comparison, fewer significant areas of lesser relative voxel size were found, including in right middle occipital, left

inferior frontal, right middle temporal, right superior frontal and left anterior cingulate regions.

### **Correlations between Brain and Behavioral Changes**

Brain deformation changes in motor-related brain areas including the right precentral gyrus, corpus callosum and left cerebellum were predicted by left-hand motor test improvement scores. To illustrate the relationship between brain morphometry and behavior, we plotted the longitudinal deformation change over 15 months in terms of relative voxel size for each child as a function of his or her behavioral difference score on the left-hand motor sequencing test at the most significant (peak) voxel in each of these areas. The relative voxel size significantly increased with increasing left-hand motor improvement score at peak voxels in the right precentral gyrus (Figure 1b), corpus callosum (Figure 2b), and left cerebellum (Figure 3c), but not in the auditory regions. Brain deformations in bilateral auditory areas in the superior temporal gyri (Figure 4c, d) and in the cerebellum (Figure 3d,e) were predicted by Melodic/Rhythmic Discrimination Test improvement. Brain deformations in the primary motor regions were not predicted by Melodic/Rhythmic Discrimination Test Battery improvement, and brain deformations in bilateral auditory regions as well as in the cerebellum were not predicted by motor improvement scores. No other significant correlations were found between brain deformations and either near or far transfer behavioral measures.

### **DISCUSSION**

In the present study, we demonstrated regional structural brain plasticity in the developing brain that occurred with only 15 months of instrumental musical training in early childhood. Structural brain changes in auditory and motor areas – of critical importance for instrumental music training - correlated with behavioral improvements on motor and auditory-musical tests. This study is the first longitudinal investigation to directly correlate brain structure and behavioral changes over time in the developing brain.

The lack of brain and behavioral differences between the Instrumental and Control children at baseline (prior to any music training) is consistent with previous findings from a larger sample that included the present subset of children tested here (Norton et al., 2005). These findings support the view that brain differences seen in adult musicians relative to non-musicians are more likely to be the product of intensive music training than pre-existing biological predictors of musicality (Norton et al., 2005; Schlaug et al., 2005). Children who played and practiced a musical instrument showed greater improvements in motor ability (as measured by the finger dexterity in both left and right hands) and in auditory melodic and rhythmic discrimination skills. Contrary to previous findings however (Rauscher et al., 1997 and 2000; Chan et al., 1998; Vaughn, 2000; Ho et al., 2003; Schellenberg, 2004), children who studied an instrument for 15 months did not progress more in visual-spatial and verbal transfer domain outcomes than children who did not receive instrumental training. We propose three reasons why 15 months of instrumental music training may not have been sufficient to result in far transfer: (1) 15 months of instrumental lessons may be too short a period of time (*duration* explanation); (2) children in our Instrumental

group may have practiced too little (*intensity* explanation); or (3) a larger sample may be required to demonstrate far transfer (*power* explanation).

The present findings of structural brain changes in response to 15 months of instrumental music training are consistent with previous findings of training-induced structural brain differences in adults in various contexts (Draganski et al., 2004; Draganski and May, 2008). More specifically, the brain deformation differences found in motor and auditory brain regions are consistent with structural brain differences found between adult musicians and adult non-musicians in the precentral gyri (Gaser and Schlaug, 2003b), corpus callosum (Schlaug et al., 1995; Ozturk et al., 2002; Schmithorst and Wilke, 2002; Lee et al., 2003), cerebellum (Schmithorst and Wilke, 2002; Gaser and Schlaug, 2003b; Hutchinson et al., 2003) and auditory regions (Schneider et al., 2002; Gaser and Schlaug, 2003b; Bermudez and Zatorre, 2005).

The brain-behavioral correlations found here in motor and auditory brain regions for performance on motor and auditory (melodic/rhythmic) tests show that different motor and auditory behavioral functions (both musically relevant) appear to be driving the group differences in separate predicted brain regions. These results are important from a functional perspective since these brain regions are known to be of critical importance in instrumental music performance and auditory processing. For example, the primary motor and cerebellar areas play a critical role in motor planning, execution, and control of bimanual sequential finger movements as well as motor learning (Karni et al., 1995; Grodd et al., 2001). The correlation found between the brain deformation measures and the motor test at the corpus callosum is consistent with the fact

that the peak voxel lies in the 4th and 5th segment of the corpus callosum (Witelson, 1989) (also called midbody) which contains fibers connecting primary sensorimotor cortex (Wahl et al., 2007). Moreover, it has been suggested that intense bimanual motor training of musicians could play an important role in the determination of callosal fiber composition and size ( Schlaug et al., 1995). Lastly, the correlation found between the brain deformation measures and the Melody/Rhythmic Test Battery in auditory regions and the cerebellum is consistent with functional brain mapping studies that have found activity changes using auditory-musical tests in similar auditory regions (Zatorre et al., 2002) and cerebellum (Griffiths et al., 1999; Parsons, 2001; Gaab and Schlaug, 2003).

While structural brain differences were expected in motor and auditory brain areas, unexpected significant brain deformation differences were also found in various frontal, temporal and occipital regions. However, none of these unexpected deformation changes were correlated with motor or auditory test performance changes. While we do not currently have an interpretation for some of these unexpected brain findings since they did not correlate with the auditory and motor behaviors, the left posterior peri-cingulate region warrants additional discussion since it showed a highly significant peak deformation difference. This region lies in the vicinity of Brodmann area 31 in the transition between posterior cingulate and occipital cortex and is involved in the integration of sensory (mostly visual) information and the limbic system. Such integration is involved in learning to read musical notation and relating music to its emotional content. The relative voxel size increases in frontomesial regions

(anterior cingulate and pre-SMA) also stands out, although no obvious relationship with changes in motor and auditory performance was seen for this region. Overall, these findings indicate that plasticity can occur in brain regions that control primary functions important for playing a musical instrument, and also in brain regions that might be responsible for the kind of multimodal sensorimotor integration likely to underlie the instrumental learning. None of these unexpected brain deformation differences mentioned above were correlated with behavioral performance changes in any of the far transfer domains. This may indicate that brain structural changes in association areas and multimodal integration regions may develop before the emergence of significant behavioral / cognitive changes in far transfer domains.

While we have discussed the functional significance of the brain-behavioral structural changes, the underlying structural properties of the results are not trivial to explain. The brain deformation techniques used here are key to localize brain size/shape changes over time, but are not able to inform us on micro-structural nature of these changes. Overall, instrumental children showed greater relative voxel size expansion compared to Controls over the 15 months, and fewer areas of voxel size contraction. A voxel expansion or contraction may reflect increased or decreased gray or white matter due to neural reorganization / pruning or increased / decreased brain connectivity. Evidence from animal models investigating the effects of long-term learning and practice of complex motor skills (Anderson et al., 2002) on brain structure may shed light on the structural neural basis of the brain structural changes seen here. Several groups have demonstrated micro-structural brain changes as a function

of long-term motor learning, including an increased number of synapses and glial cells, increased density of capillaries in primary motor cortex and the cerebellum, and new brain cells in the hippocampus after long-term motor training in adult rats (Black et al., 1990; Isaacs et al., 1992; Anderson et al., 1994; Kleim et al., 1996; Kempermann et al., 1997; Anderson et al., 2002). The sum of these micro-structural changes could amount to structural differences that are detectable on a macro-structural level such as those observed in the present study (see Anderson et al., 2002; Bangert & Schlaug, 2006). It is possible that the specific and continuous engagement of a unimodal and multimodal sensorimotor network, and the induced changes in this network across a musician's career, may provide the neural basis for some of the sensorimotor and cognitive enhancements attributed to musical training. Future, even higher resolution morphometric investigations with more direct measures of gray and white matter will be key to develop a better understanding of the underlying nature of the brain deformation differences found here.

In summary, our findings show for the first time that musical training over only 15 months in early childhood leads to structural brain changes that diverge from typical brain development. Regional training-induced structural brain changes were found in musically-relevant regions that were driven by musically-relevant behavioral tests. The fact there were no structural brain differences found between groups prior to the onset of musical training strengthens our conclusions that the differential development of these brain regions is induced by instrumental practice rather than pre-existing biological

predictors of musicality. These results provide new evidence for training-induced structural brain plasticity in early childhood. These findings of structural plasticity in the young brain suggest that long-term intervention programs can facilitate neuroplasticity in children. Such an intervention could be of particular relevance to children with developmental disorders and to adults with neurological diseases.

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**Figure legends:****Figure 1:**

Longitudinal group brain deformation differences and brain-behavioral correlations in primary motor area.

The brain image (a horizontal slice) shows areas of significant difference in relative voxel size over 15 months in Instrumental (n=15) versus Control (n=16) children in terms of a *t*-statistical color map superimposed on an average MR image of all children (n=31). The yellow arrow points to the right primary motor region (precentral gyrus). A voxel with a relative voxel size of 1 indicates no brain deformation change from Time 1, values greater than 1 indicate voxel expansion, whereas values less than 1 indicate voxel contraction. For example, a value of 1.1 at voxel X indicates a 10% expansion from Time 1, whereas 0.9 indicates a 10% contraction (this also applies to Figures 2-4). To illustrate the group differences, the relative voxel size (expressed as the mean by the horizontal dark black line, 25% and 75% quartiles, errors bars as standard deviations, and points as outliers) is plotted for each group at the most significant (peak) voxel in the right (x=40, y=-7, z=57; *t*=4.2, *P*=0.0003) (plot a) precentral gyrus. The significant positive correlation of relative voxel size with behavioral difference scores (from Time 1 to 2) of each child on the left-hand motor test that was found at the peak voxel in the right precentral gyrus is shown in plot 1b.

**Figure 2:**

Longitudinal group brain deformation differences and brain-behavioral correlations in the corpus callosum.

The brain image (a sagittal slice) shows areas of significant difference in relative voxel size over 15 months in Instrumental (n=15) versus Control (n=16) children in terms of a t statistical color map superimposed on an average MR image of all children (n=31). The yellow arrow points to the corpus callosum (4<sup>th</sup> and 5<sup>th</sup> segment or midbody). To illustrate the group differences, the relative voxel size (expressed as the mean by the horizontal dark black line, 25% and 75% quartiles, errors bars as standard deviations) is plotted for each group at the most significant (peak) voxel in the corpus callosum (x=14, y=-24, z=30;  $t=5.2$ ,  $P=0.00002$ ) (plot a). The significant positive correlations of relative voxel size with behavioral difference scores (from Time 1 to 2) of each child is shown for the left-hand motor test at the peak voxel in the corpus callosum (plot b).

**Figure 3:**

Longitudinal group brain deformation differences and brain-behavioral correlations in the cerebellum.

The brain image (a horizontal slice) shows areas of significant difference in relative voxel size over 15 months in Instrumental (n=15) versus Control (n=16) children in terms of a t statistical color map superimposed on an average MRI image of all children (n=31). The yellow arrows point to the left and right cerebellum (lobes V and VI). To illustrate the group differences, the relative voxel size (expressed as the mean by the horizontal dark black line, 25% and 75% quartiles, errors bars as standard deviations, and points as outliers) is plotted for each group at the most significant (peak) voxel in the left (x=-18, y=-53, z=-33;  $t=4.5$ ,  $P=0.0001$ ) (plot a), and right (x=29, y=-56, z=-36;  $t=4.7$ ,

$P=0.00009$ ) (plot b) cerebellum. The significant positive correlations of relative voxel size with behavioral difference scores (from Time 1 to 2) of each child is shown for the left-hand motor test at the peak voxel in the left cerebellum (plot c), and for the Melody/Rhythm test at the peak voxel in the left (plot d) and right cerebellum (plot e).

**Figure 4:**

Longitudinal group brain deformation differences and brain-behavioral correlations in auditory areas.

The brain image (a horizontal slice) shows areas of significant difference in relative voxel size over 15 months in Instrumental ( $n=15$ ) versus Control ( $n=16$ ) children in terms of a  $t$  statistical color map superimposed on an average MRI image of all children ( $n=31$ ). The yellow arrows point to the left and right auditory regions corresponding to the superior temporal gyri (STG). To illustrate the group differences, the relative voxel size (expressed as the mean by the horizontal dark black line, 25% and 75% quartiles, errors bars as standard deviations, and points as outliers) is plotted for each group at the most significant (peak) voxel in the left ( $x=-49$ ,  $y=-9$ ,  $z=7$ ;  $t=3.5$ ,  $P=0.001$ ) (plot a), and right ( $x=55$ ,  $y=-8$ ,  $z=10$ ;  $t=4.9$ ,  $P=0.00004$ ) (plot b) STG. The significant positive correlations of relative voxel size with behavioral difference scores (from Time 1 to 2) of each child is shown for the Melody/Rhythm Test at the peak voxel in the left (plot c) and right (plot d) STG.

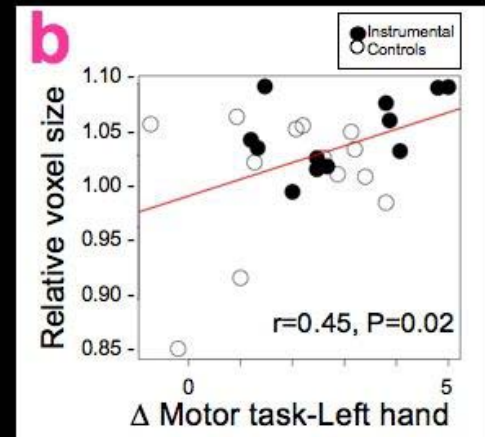
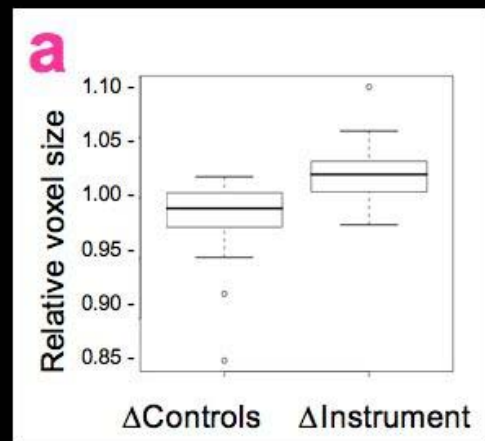
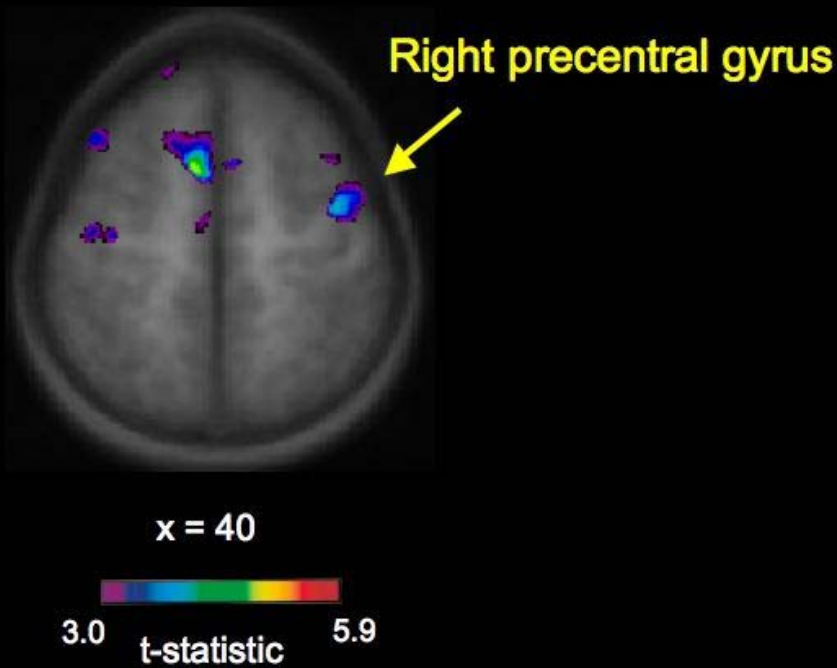
**Table 1: Subject characteristics**

| <b>Characteristics</b>         | <b>Instrumentals (n=15)</b> | <b>Controls (n=16)</b> |
|--------------------------------|-----------------------------|------------------------|
| Age at start of study (SD)     | 6.32 (0.82) years           | 5.90 (0.54) years      |
| Time from MRI scan 1 to 2 (SD) | 15.60 (3.30) months         | 14.80 (3.80) months    |
| Socio-economic-standard*       | 5.10 (0.60)                 | 4.60 (0.80)            |
| Gender                         | 9 females; 6 males          | 7 females; 9 males     |

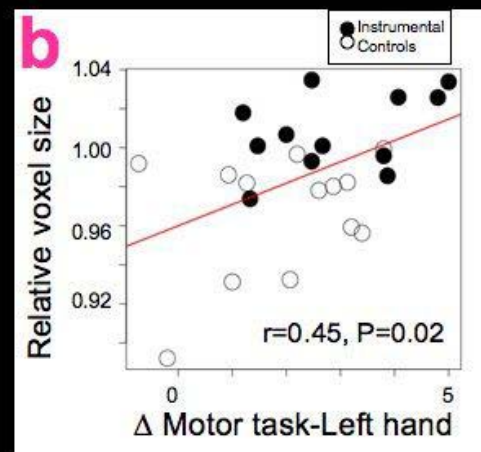
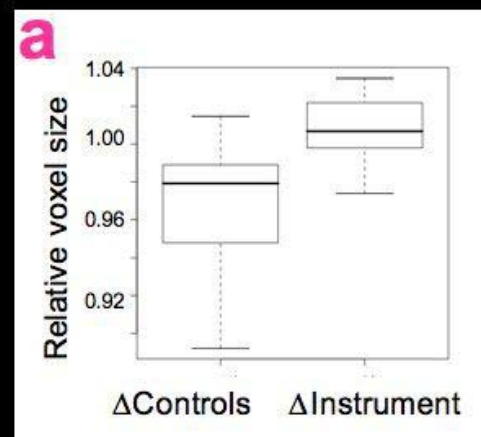
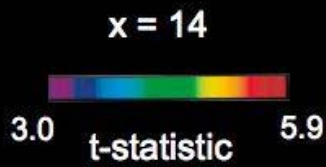
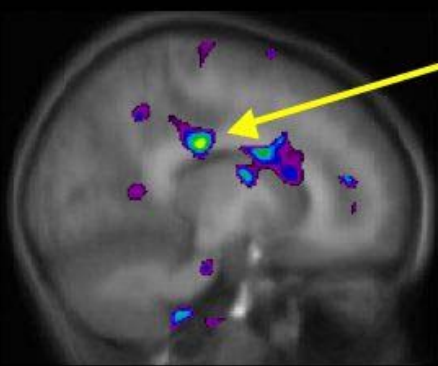
SD=standard deviation

\*Socio-economic standard was defined on a 6-point scale, with a score of 1, reflecting that the children's parents had some high school education, to a score of 6, reflecting that parents had a doctoral degree (see Norton et al., 2005).

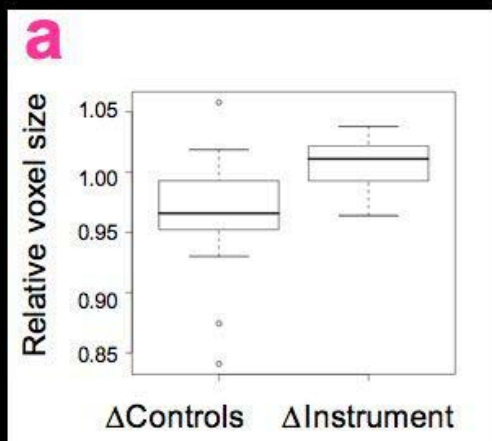
# Primary motor area (Instrument > Controls)



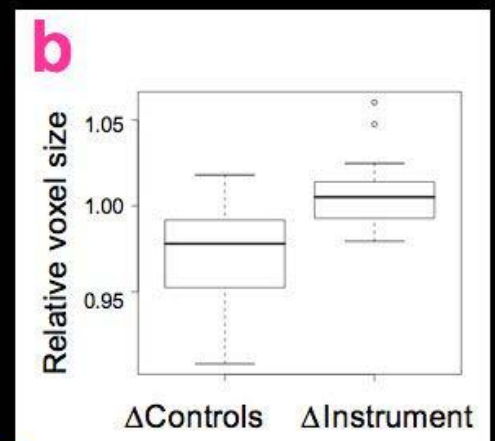
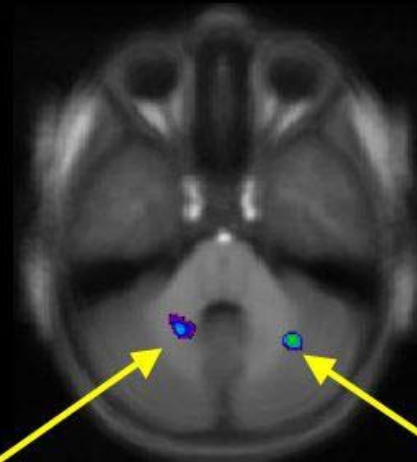
# Corpus callosum (Instrument > Controls)



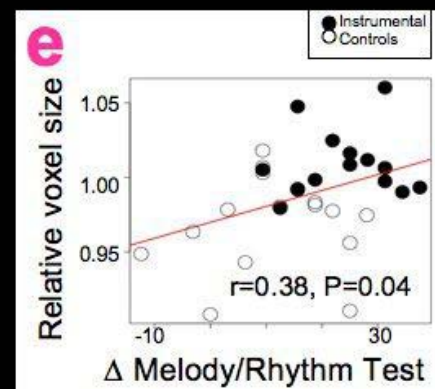
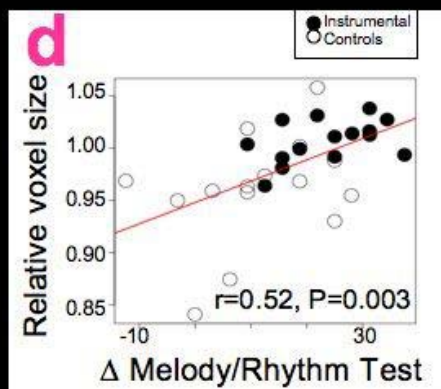
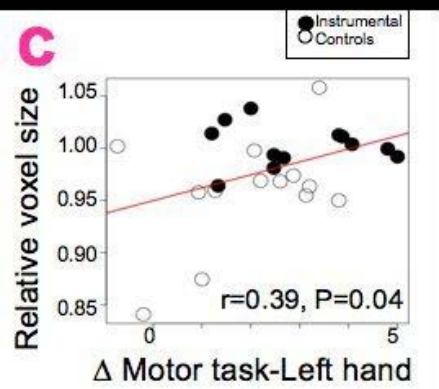
# Cerebellum (Instrument > Controls)



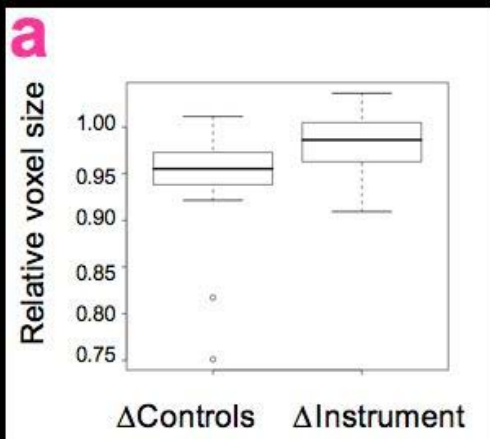
Left cerebellum



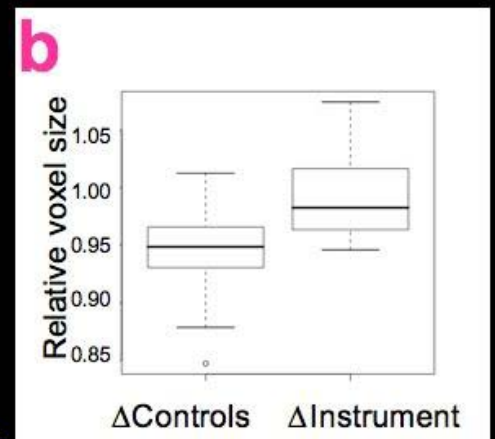
Right cerebellum



# Auditory areas (Instrument > Controls)



Left STG



Right STG

