Title: Brain plasticity reflects specialized cognitive development induced by musical training

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Abstract

Learning a musical instrument requires a long period of training and might induce structural and functional changes in the brain. Previous studies have shown brain plasticity resulting from training with a musical instrument. However, these studies did not distinguish the effects on brain plasticity of specific musical instruments as they examined the brain of musicians who had learned a single musical instrument/genre and did not control for confounding factors, such as common or interactive effects involved in music training. To address this research gap, the present work investigated musicians who had experience with both a piano
and a wind instrument, e.g., flute, trumpet, clarinet etc. By examining the difference between the two musical instruments in the same subject, we avoided the effects common to all musical instruments and the confounding factors. Therefore, we identified several high-tier brain areas displaying a brain plasticity specific to each musical instrument. Our findings show that learning a musical instrument might result in the development of high cognitive functions reflecting the skills/abilities unique to the instrument played.

**Keywords**

Brain plasticity / Cognitive development / Musical instruments / Musical training / VBM
Introduction

Learning to play a musical instrument requires a long period of training and might induce structural and functional changes in the human brain. Musicians usually learn over many years the physical and cognitive skills needed for playing the instrument including the required body movements, reading musical scores and understanding music through listening. The physical skills can induce brain plasticity, namely, structural and functional changes reflecting the abilities specific to each musical instrument. Similarly, the perceptive or cognitive skills generate structural and functional changes reflecting the specialized musical perception, cognition, and personal traits acquired through learning to play a musical instrument. Several behavioral studies have reported plasticity in the brain in relation to musical training. For instance, musicians trained with the keyboard, string instruments, or wind instruments acquired specific psychological traits according to the learning method or the type of instrument (Mihajlovski 2013). Previous work also demonstrated that structural and functional MRI can be used to measure the brain plasticity related to the type of musical instrument, the physical movements required to play the musical instrument, the perception of the sounds of the instrument, and the cognitive functions involved in the development of the personal traits (Bengtsson et al. 2007; Garcea et al. 2017).

Structural MRI studies revealed significant volumetric differences in the auditory area (Vaquero et al. 2016) and the white matter (WM), including the longitudinal fasciculus, which is close to gray matter (GM) areas, between musicians and nonmusicians (Giacosa et al. 2016). Structural changes in somatosensory areas related to the hands or fingers were reported in keyboard players, whereas structural modifications in mouth-related brain areas were observed in wind instrument players (Gebel et al. 2013; Choi et al. 2015). In functional MRI (fMRI) studies, a robust activation of various brain regions, including the primary motor area and high cognitive areas, was associated with music playing. Significant variations in the functional response were
observed in the auditory and motor areas after piano training (Engel et al. 2012), and a significant change in the functional connectivity of the frontoparietal network was measured during a musical performance (Meister et al. 2004). Additionally, resting-state fMRI (rs-fMRI) studies have shown a functional plasticity related to musical training in the parietal opercular auditory–sensorimotor network (Tanaka and Kirino 2018) and in insula-based functional networks (Zamorano et al. 2017, 2019).

Although brain plasticity has been associated with learning to play a musical instrument, studies so far have examined the plasticity related to one musical instrument or genre or to a group of instruments. Therefore, the brain plasticity reflecting the unique attributes of each musical instrument has not been investigated. The functional characteristics of the musical categories can be represented in different brain regions. Some brain regions control functions common to several categories or related to music playing in general, whereas other areas are regulating processes unique to each musical instrument. For example, the processes related to the visual function are robustly mapped to different brain areas such as the fusiform face area, visual word form area, and lateral occipital complex, which are activated by faces, words, and objects but show a stronger activation by the preferred stimuli (Spiridon and Kanwisher 2002; Kronbichler et al. 2004; Eger et al. 2008). Similarly, working memory tasks are represented in several brain regions, which are more strongly activated by a specific stimulus (Ragland et al. 2002; Chee and Choo 2004; Mu et al. 2005). Musical activities such as singing and playing a musical instrument are represented in several brain regions, which are simultaneously activated (Reznik et al. 2014; Whitehead and Armony 2018). Most fMRI study designs used to investigate the brain activation specific to a task are based on the hypothesis that the commonality between similar tasks can be eliminated by subtraction, resulting in the measurement of the effect specific to one task. Hence, two or more tasks are implemented in the stimulation paradigm to examine
task specific effects (Amaro and Barker 2006). The same rationale can be applied to rs-fMRI studies. Indeed, the rs-fMRI data from a subject having two or more musical experiences can provide information about the brain function specific to each musical instrument by applying the subtraction method and consequently eliminating the commonality among multiple musical experiences and the unmeasurable confounding factors.

Thus, to examine the brain plasticity specific to a unique musical instrument, we studied a group of musicians who were trained with a piano and a wind instrument. We chose those instruments since they are relatively commonly played and were reported to induce the development of different personality traits (Kemp 1981; Bell and Cresswell 1984; Mihajlovski 2013). We identified brain regions presenting plasticity in response to specifically the piano or the wind instrument.

Materials and Methods

Subjects

In total, 34 participants (all female, aged 20.7 ± 1.4 years) without a history of neurological disease or any other medical conditions participated in this study. All participants were right-handed and registered in the same college. All participants provided written informed consent and all experiments were approved by the Institutional Review Board of Tohoku Fukushi University.

Three participants were excluded from the analysis due to uncertainty in their memory related to their musical training. Of the remaining 31 participants who participated in this study, 14 were defined as the nontrained group and 17 were defined as the trained group, which had 10 or more training years in the total of the two musical instruments (piano and wind instrument). Six of the 17 participants in the trained group had less than one year of training in the piano or wind
instrument. Therefore, 11 participants had long-term training in both the piano and wind instruments. A detailed description of training years in the piano and wind instrument is shown in Supplementary Table S1.

**MRI acquisition**

Participants were scanned using a 3T investigational MRI scanner (Skyra-fit) with a default 20-channel head coil. Three-dimensional whole-brain high-resolution T1-weighted (T1w) images were acquired using the magnetization prepared rapid acquisition with gradient echo (MRRAGE) sequence with the following parameters: repetition time = 1900 ms; echo time = 2.52 ms; flip angle = 80°; number of slices = 192; slice thickness = 1 mm; matrix = 256 × 256; in-plane voxel resolution = 1 × 1 mm². rs-functional images were obtained using a gradient echo single-shot echo-planar image sequence with the following parameters: matrix = 64 × 64; repetition time = 1,000 ms; echo time = 24 ms; in-plane resolution = 3.4 × 3.4 mm²; slice thickness = 3.4 mm; the number of slices = 34 with no gap; slice orientation along AC-PC; the number of volumes = 480.

**Preprocessing of functional and structural MRI data**

rs-fMRI data were preprocessed by DPABI (Yan et al. 2016). The preprocessing included slice-scan time correction, 3D motion correction, nuisance regression, temporal filtering, spatial filtering. For the motion correction, the Friston 24-parameter model was used to correct head motion effects. Nuisance regression was performed using the CSF signal and the motion parameters. For temporal filtering, a bandpass filter with the passband of 0.01 to 0.1 Hz was used. For spatial filtering FWHM of 4 mm was used. The preprocessed functional images were co-registered with the corresponding structural images and spatially normalized to standard
coordinate space, Montreal Neurological Institute (MNI) space. The structural images were processed using ANTs (http://stnava.github.io/ANTs/) for customized VBM analysis (Supplementary Fig. S1). Firstly, all native T1w images were skull-stripped and spatially normalized to MNI space using an in-house script, including brain extraction and nonlinear registration based on ANTs built-in algorithms. Secondly, the brain extracted images were segmented into three different brain tissues, namely cerebral spinal fluid, gray matter (GM), and white matter (WM), using the ANTs brain segmentation method script (antsAtroposN4.sh). Thirdly, segmented GM and WM binary images were registered to MNI space using the acquired nonlinear transformation information acquired in the first step. Fourthly, the registered GM and WM images were registered to the MNI space tissue probability map using nonlinear transformation of ANTs. Finally, the normalized GM and WM images were modulated to ensure that the volumes of GM and WM were preserved during nonlinear spatial normalization. The modulated images were smoothed with an 8 mm full-width at half maximum kernel.

Statistical analysis

GM and WM VBM were compared between the trained and nontrained groups using a two-sample t-test. The age and global volume, including GM and WM volumes, were used as covariates. The statistical maps were compared between groups using 10,000 permutations with threshold-free cluster enhancement (TFCE) (p < 0.05) (Smith and Nichols 2009) for multiple comparison correction.

Regression analysis of resting-state fMRI data with musical training years

A correlation matrix was then constructed between the time series from the automated anatomical atlas 3 (AAL3) regions of interest (ROIs) and those from the ROIs of the GM VBM
difference. Significant correlation coefficients were selected using the criteria $p < 0.01$ and $r > 0.2$. A linear regression analysis with 5,000 permutations was conducted between the significant coefficients and musical training years for the piano and wind instruments using R version 3.6.3 (R Core Team, 2018).

In addition, we conducted a multiple regression analysis to distinguish secondary effects of specific musical instrument training to evaluate specific musical instrument dependent training year effects on the human brain.

**Regression analysis of white matter VBM values with musical training years**

A linear regression analysis with 5,000 permutations for the ROIs of the Johns Hopkins University (JHU) atlas was conducted between WM VBM values and musical training years of wind or keyboard musical instruments by R version 3.6.3 (R Core Team, 2018).

**Results**

The GM VBM of the trained and nontrained groups were compared to identify ROIs involved in musical training. ROIs in the bilateral insular cortex showed a greater GM volume in musically trained individuals compared with that in the nontrained group ($p < 0.05$, corrected) (Fig. 1A). No significant ROIs specific for the piano or wind instrument were identified.

The insular cortex is considered a hub of functional connectivity between areas related to musical training. Therefore, the identified ROIs were used as seed ROIs for the correlation analysis with the AAL3 parcellation regions in rs-fMRI (Zamorano et al. 2017, 2019).

The functional connectivity was assessed by calculating the correlation between the seed ROIs and other brain areas of the AAL3 parcellated regions using the ROI rs-fMRI data (time courses). The association between connection edges (an edge is defined as the correlation
value between the time courses of two ROIs, meaning that two ROIs are connected by the strength of their correlation value) and the years of experience playing wind instruments or the piano was evaluated by multiple regression analysis. The identification of ROIs associated exclusively with the duration of training with a wind instrument or the piano was possible because the times spent training with those instruments were not significantly correlated ($r = 0.03$, $p = 0.8$).

The multiple regression analysis showed a significant negative association between the level of experience playing the piano and the functional connectivity in the right precentral, the left and right Rolandic, the right Heschl’s gyrus, and the right superior temporal regions. A significant negative association between the extent of training with a wind instrument and the right putamen, right ventral posterior lateral thalamus, right ventral lateral thalamus, and right intralaminar thalamus was also found. By contrast, the functional connectivity values between these areas and the insular cortex were all positive (Fig. 2, Table 1).

The trained group had a higher WM volume in the right inferior longitudinal fasciculus compared with the nontrained group ($p < 0.05$, corrected) (Fig. 1B). The GM VBM analysis was followed by multiple regression analysis of the changes in rs-fMRI time courses with the duration of training with a wind instrument or the piano. However, the functional connectivity was not examined for WM VBM because rs-fMRI signal changes were typically small in WM. Instead, we conducted a multiple regression analysis of WM VBM changes with the extent of experience playing the piano or wind instruments because each WM ROI was a white matter tract and the WM VBM could be interpreted as reflecting a connectivity.

Multiple regression analysis of WM ROI variations with the duration of training with a wind instrument or the piano revealed that most of the ROIs of the JHU atlas were associated with piano training duration, whereas the others were linked to the length of the training with wind instruments as shown in Fig. 3 and Table 2.
Discussion

Musical training induces brain plasticity that is specific to the type of musical instrument, reflecting the unique characteristics of the playing techniques. We aimed to examine the existence of a brain plasticity reflecting the unique characteristics of a musical instrument by measuring the brain structures and functions of musicians trained with both the piano and wind instruments. We identified plasticity in several high-tier brain areas representing training with the piano or wind instruments, which shows that learning to play a musical instrument can promote the development of cognitive functions related to the unique abilities acquired by playing a specific instrument.

The functional roles of the brain regions identified can be inferred from previous neuroimaging studies. We identified five brain regions specifically related to piano or wind instrument training and involved in the development of personality traits: 1) the superior temporal gyrus is related to agreeableness (Li et al. 2017), conscientiousness, extraversion (Riccelli et al. 2017), and happiness (Vieira et al. 2017); 2) the precentral gyrus is linked to agreeableness (Riccelli et al. 2017); 3) the Rolandic operculum is involved in apathy, depression, anxiety (Sutoko et al. 2020), and happiness (Vieira et al. 2017); 4) the thalamus is an integral part of the emotional salience network, emotion modulation network, and cognitive/executive network; and 5) the putamen is associated with mood, motivation, impulsive processing, and the regulation of movement (Koolschijn et al. 2009; Lu et al. 2016; Yamamura et al. 2016; Luo et al. 2019).

The superior temporal gyrus, Heschl’s gyrus, and Rolandic operculum were specifically activated by the piano training (Peng et al. 2014) and are part of the auditory–verbal module, a network representing high cognitive functions displayed by piano players (Mihajlovski 2013). Wind instrument training was specifically related to the thalamus and putamen, which are
included in a network module called the affective processing module (Peng et al. 2014). The thalamus and putamen are also involved in motor control. Playing the piano and wind instruments requires sensory–motor control of body parts, including the tongue and lips. However, it is unlikely that the thalamus and putamen activation specific for the wind instruments was associated with motor function because the thalamus and putamen were not segmentalized in such details in the template. Thus, it is conceivable that the functional regions identified in this study are involved in higher cognitive functions. The different roles of the brain regions associated with the piano or wind instruments are consistent with previous behavioral studies showing that piano players had higher verbal IQ scores than wind instrument players, whereas the latter tended to be more effective (Jacobsen et al. 2006; Dor-Ziderman et al. 2013). It was also reported that piano players had a weaker ego and a stronger self-consciousness compared with players of other musical instruments, which supports the development of specific personality traits depending on the musical instrument played (Kemp 1981; Bell and Cresswell 1984; Mihajlovski 2013).

We identified structural differences in the insular cortex in both hemispheres between the trained and nontrained groups. The insular cortex is critical for musical training as it is a multifunctional area involved in multimodal sensory and emotional processing (Bianchi et al. 2017; Wang et al. 2019). Previous studies have reported that the insular cortex is a hub connecting other brain areas, including high-tier cognitive areas (Zamorano et al. 2019). Our data suggest that the insular cortex is involved in the processing of emotions induced by musical training, as brain plasticity in the insular cortex measured in piano and wind instrument players was not specific to the type of musical instrument. This is consistent with previous studies reporting a significant difference in the insular cortex between musicians and nonmusicians (Zamorano et al. 2017; Wang et al. 2019).
Little is known about the functional roles of the WM ROIs identified in association with piano or wind instrument training. They may be related to differences in the playing methods between the piano and wind instruments, such as the differences in the body movements, the sounds (including the volume, ton, and tune) produced by the instrument, or in the personality traits. Playing and practicing the piano can induce microstructural changes in the superior longitudinal fasciculus (Engel et al. 2014). The corpus callosum has been linked to verbal and intellectual abilities (Loui et al. 2019). Additionally, some studies have shown that structural changes in the corpus callosum or corona radiata are strongly related to traits such as social synesthesia (Rouw and Scholte 2007; Simner et al. 2016).

Overall, the brain plasticity observed in the present study can be interpreted as the result of the training with the piano or a wind instrument. Moreover, high cognitive functions, such as the development of personality traits, affected by the plasticity might be specific to the musical instrument.

The significant negative association between musical training with the piano or wind instruments and functional connectivity means that the connectivity between the hub area of the insular cortex and the other brain regions decreases as the training period is getting longer because the connectivity between the brain regions was positively correlated. This suggests that the functional plasticity occurred to achieve efficient functional connectivity during musical training. Previous work on brain plasticity showed a decrease in the brain volume or neuronal activation with the progress of the skill training (deCharms et al. 2005; Sampaio-Baptista et al. 2014; Best et al. 2015; Clark et al. 2017).

There are several limitations in this study. First, the sample size was small. We aimed to examine the brain plasticity induced by the musical training with one out of two instruments. Therefore, we enrolled musicians trained with two musical instruments, the piano and a wind
instrument. This strict condition was a limitation for recruiting participants. However, despite the limited sample size, we were able to identify regions undergoing significant brain plasticity induced specifically by the piano or wind instrument training. Second, we also did not collect behavioral data and relied on previous neuroimaging studies to indirectly infer the functional roles of the brain regions identified in this study.

Despite these limitations, our study provides novel evidence of brain plasticity induced by musical instrument training.

In conclusion, our study is the first to identify brain plasticity specifically reflecting the acquisition of personality traits induced by piano or wind instrument training. This finding suggests that long-term musical training results in the development of psychological traits unique to the musical instrument, which is reflected by changes in the brain structure and function.

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Table 1. Description of gray matter regions identified as having significant association of the functional connectivity between localized insular cortices and AAL3 ROIs with the training years of the piano or the wind instruments. ‘_R’ and ‘_L’ indicate brain regions in right and left hemispheres, respectively.

| VBM_ROIs | Instrument | AAL3 Index | AAL3 ROIs | p-value | adj.R  | Direction |
|----------|------------|------------|-----------|---------|--------|-----------|
| 2        | Precentral_R | 0.036      | 0.28      | -0.021  |
| 13       | Rolandic_Oper_L | 0.008      | 0.435     | -0.024  |
| Insular_R | Piano     | 14         | Rolandic_Oper_R | 0.021  | 0.324  | -0.022    |
| 84       | Heschl_R   | 0.034      | 0.346     | -0.024  |
| 85       | Temporal_Sup_L | 0.037      | 0.348     | -0.023  |
| 78       | Putamen_R  | 0.017      | 0.381     | -0.044  |
| Insular_L | Wind    | 128        | Thal_VL_R | 0.019  | 0.415  | -0.072    |
| 130      | Thal_VPL_R | 0.035      | 0.344     | -0.05   |
| 132      | Thal_IL_R  | 0.038      | 0.325     | -0.048  |
Table 2. Description of white matter regions identified as having significant association of the WM VBM ROIs with the training years of the piano or the wind instruments.

| Instrument | JHU Index | JHU ROIs | p-value | adj.R | Direction |
|------------|-----------|----------|---------|------|-----------|
| Piano      | 3         | Genu of corpus callosum | 0.001  | 0.657 | 0.015     |
| Piano      | 4         | Body of corpus callosum | 0.004  | 0.542 | 0.012     |
| Piano      | 5         | Splenium of corpus callosum | 0.001  | 0.746 | 0.013     |
| Piano      | 6         | Fornix (column and body of fornix) | 0.045  | 0.288 | 0.006     |
| Piano      | 23        | Anterior corona radiata R | 0.004  | 0.46  | 0.012     |
| Piano      | 24        | Anterior corona radiata L | 0.024  | 0.374 | 0.011     |
| Piano      | 25        | Superior corona radiata R | 0.034  | 0.328 | 0.009     |
| Piano      | 28        | Posterior corona radiata L | 0.042  | 0.306 | 0.009     |
| Piano      | 29        | Posterior thalamic radiation (include optic radiation) R | 0.014  | 0.386 | 0.007     |
| Piano      | 30        | Posterior thalamic radiation (include optic radiation) L | 0.011  | 0.415 | 0.008     |
| Piano      | 32        | Sagittal stratum (include inferior longitudinal fasciculus and inferior fronto-occipital fasciculus) L | 0.012  | 0.406 | 0.011     |
| Piano      | 35        | Cingulum (cingulate gyrus) R | 0.002  | 0.519 | 0.009     |
| Piano      | 38        | Cingulum (hippocampus) L | 0.011  | 0.488 | 0.005     |
| Piano      | 39        | Fornix (cres) / Stria terminalis R | 0.037  | 0.329 | 0.007     |
| Piano      | 40        | Fornix (cres) / Stria terminalis L | 0.041  | 0.304 | 0.007     |
| Piano      | 41        | Superior longitudinal fasciculus R | 0.041  | 0.306 | 0.008     |
| Wind       | 9         | Medial lemniscus R | 0.045  | 0.299 | 0.017     |
| Wind       | 13        | Superior cerebellar pedunde R | 0.018  | 0.404 | 0.018     |
| Wind       | 14        | Superior cerebellar pedunde L | 0.024  | 0.366 | 0.017     |
| Wind       | 37        | Cingulum (hippocampus) R | 0.027  | 0.394 | 0.011     |
Captions to figures

Figure 1. (A) Right and left Insular cortices localized by the comparison of the trained and nontrained groups. (B) White matter regions localized by the comparison of the trained and nontrained groups.

Figure 2. Brain regions identified as having significant association of functional connectivity between localized Insular cortices and AAL3 ROIs with the training years of the piano or the wind instruments. (A) Brain regions that showed a significant association with piano instrument
training years. Sky, green, yellow, and orange colored regions indicate precentral gyrus, Rolandic operculum, Heschl’s gyrus, superior temporal gyrus, respectively. (B) Brain regions that showed a significant association with wind instrument training years. Sky, orange, yellow, and green colored regions indicate putamen, ventral lateral thalamus, ventral posterolateral thalamus, and intralaminar thalamus, respectively.

Figure 3. Brain regions identified as having significant association of WM VBM in ROIs of JHU atlas with the training years of the piano or the wind instruments. (A) Sky, green, orange, cyan, red, yellow, and pink colored regions indicate corpus callosum, fornix, corona radiata, posterior thalamic radiation, sagittal stratum, cingulum, and superior longitudinal fasciculus, respectively. (B) Green, sky, and yellow colored regions indicate medial lemniscus, superior cerebellar peduncle, and cingulum, respectively.