

Gray matter density and white matter integrity in pianists' brain: A combined structural and diffusion tensor MRI study

Ying Han^{a,d}, Hong Yang^{b,c}, Ya-Ting Lv^a, Chao-Zhe Zhu^a, Yong He^a, He-Han Tang^b, Qi-Yong Gong^b, Yue-Jia Luo^a, Yu-Feng Zang^{a,*}, Qi Dong^a

^a State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, China

^b Huaxi MR Research Center (HMRC), Department of Radiology, West China Hospital of Sichuan University, China

^c Department of Radiology, The First Affiliated Hospital, School of Medicine, Zhejiang University, China

^d Department of Neurology, Xuanwu Hospital, Capital Medical University, China

ARTICLE INFO

Article history:

Received 8 April 2008

Received in revised form 23 May 2008

Accepted 21 July 2008

Keywords:

Magnetic resonance imaging

Diffusion tensor imaging

Voxel-based morphometry

Gray matter density

White matter integrity

ABSTRACT

The current study combined structural magnetic resonance imaging (sMRI) and diffusion tensor MRI (DT-MRI) to investigate both gray matter density (GMD) and white matter integrity (WMI) in 18 pianists and 21 age-matched non-musicians. The pianists began their piano training at a mean age of 12. Voxel-based morphometry of the sMRI data showed that the pianists had higher GMD in the left primary sensorimotor cortex and right cerebellum. Voxel-based analysis of the DT-MRI data showed that pianists had higher fractional anisotropy (FA) (indicating higher WMI) in the right posterior limb of the internal capsule. The sMRI and DT-MRI results indicate that both the GMD and WMI of pianists may exhibit movement-related increases during adolescence or even early adulthood compared with non-musicians.

© 2008 Elsevier Ireland Ltd. All rights reserved.

Professional piano playing requires extensive and long-term training of finger movement, auditory perception and visual perception. Therefore, pianists are a useful group in which to study the neural mechanisms of long-term training. Magnetic resonance imaging (MRI) is a tool most commonly used for non-invasive study of the anatomy and function of the musicians' brain. Modern MRI consists of multiple modalities, including structural MRI (sMRI), diffusion tensor MRI (DT-MRI) and functional MRI (fMRI). sMRI can be used to measure the cortical gray matter density (GMD) or concentration, as well as white matter volume. With an index named fractional anisotropy (FA, ranged 0–1), DT-MRI can assess the degree of myelination, integrity or organization of white matter.

sMRI can provide high resolution, high contrast and whole brain anatomical images. Researchers can then manually draw some regions of interest (ROIs) and compare the volumes of these ROIs between musician and control groups. Such a ROI-based method has been used in most of the previous sMRI studies on musicians. For example, the anterior corpus callosum was found to be significantly larger in musicians than in non-musicians [16,12]. However,

there is usually no clear border between cortical gray matter and white matter; therefore, to measure the cortical thickness or GMD by manual drawing is labor-intensive and time-consuming. In contrast to this manual ROI-based method, voxel-based morphometry (VBM) is an automated technique for measurement of GMD in each voxel of the entire brain [21,3] and has minimal user bias [14]. There have been a few studies in which VBM has been used to compare GMD in a voxel-wise manner between musicians and non-musicians [19,10,17,6]. However, only two studies consistently reported increased GMD in the primary sensorimotor cortex and cerebellum of musicians [10,17].

DT-MRI is a crucial method for measuring the in vivo integrity of directionally organized neural fibers. To date, there have only been two DT-MRI studies in which voxel-based analysis was performed on the FA maps of musicians and non-musicians. Schmithorst and Wilke [18] compared the FA values between five musicians and six non-musicians. They found changes in FA in widespread brain regions of musicians, including higher FA in the genu of the corpus callosum and lower FA in the bilateral internal capsule. Bengtsson et al. [5] studied eight pianists and eight non-musicians, and showed that the right posterior limb of internal capsule (PLIC) was the only region showing significantly greater FA in pianists than in non-musicians. A strong positive correlation was found between the FA in the right PLIC and the mean time of practicing during childhood (<age of 11) [5]. The findings from the two studies are

* Corresponding author at: State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, No. 19, Xin Jie Kou Wai Da Jie, Beijing 100875, China. Tel.: +86 10 58801023; fax: +86 10 58801023.

E-mail addresses: zangyf@263.net, zangyf@gmail.com (Y.-F. Zang).

quite inconsistent, even showing contrary results in the internal capsule. Therefore, further evidence should be provided.

Combination of sMRI and DT-MRI could reveal simultaneous changes in the GMD and white matter integrity (WMI). Such a combination has been previously used in studies of brain diseases [22,20]; however, it has not been reported in musician MRI studies so far. The current study aimed to investigate the differences in GMD and WMI between pianists and non-musicians by combining sMRI and DT-MRI techniques. Two groups of subjects, pianists and non-musicians were included. There were 19 pianists (19–28 years old, with a mean and S.D. of 22.6 ± 2.6 years; 7 males) in the pianists' group. They were college students of or graduated from a local conservatory school, and were recruited through personal contacts. All of them majored in piano. One pianist was excluded due to large head motion (see data analysis); therefore 18 pianists were left. They began to learn playing the piano at the age of 5.5–15 (12.2 ± 3.2) years old, and had had an average of 10.4 ± 4.2 years of piano training by the day of MRI scanning. The control subjects ($n = 21$, 18–30 years old, with a mean and S.D. of 22.4 ± 2.6 years; 9 males) were medical students or faculty members from the West China Hospital. They had never experienced formal music training. The subjects in both groups were right-handed Han Chinese, and had no history of neurological or psychiatric disorders. All subjects gave their informed consent before scanning. The current study was approved by the Ethic Review Board of the State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University.

The MRI data were acquired at Huaxi MR Research Center of West China Hospital using a 3T GE scanner equipped with an eight-channel coil. After localizer scanning, three fMRI sessions were performed, with a total time of approximately 24 min. The fMRI data were not used in the current study; therefore, the scanning parameters for fMRI sessions are omitted here. DT-MRI data were acquired with the following parameters: TR = 10 s, TE = 70.8 ms, $b = 1000 \text{ s/mm}^2$, matrix = 128×128 , field of view (FOV) = 240 mm, 32 gradient directions together with one no-gradient weighted scanning (B0), 31 axial slices, thickness/gap = 3/0 mm. SMRI data (that is, 3D-T1 MRI data) were obtained using spoiled gradient-recalled sequence (SPGR) with the following parameters: TR = 8.528 ms, TE = 3.4 ms, matrix size = 512×512 , FOV = 240 mm, 156 axial slices, thickness/gap = 1/0 mm.

The 3D structural images were analyzed using SPM2 (<http://www.fil.ion.ucl.ac.uk/spm>). The individual 3D images were first spatially normalized to the MNI space by using a non-linear transformation, and then were re-sampled to $1 \text{ mm} \times 1 \text{ mm} \times 1 \text{ mm}$. The intracranial tissue was further segmented into gray matter, white matter and cerebrospinal fluid (CSF). Finally, the gray matter maps were spatially smoothed (full width at half maximum (FWHM) = 8 mm) for further VBM analysis.

The 33 DT-MRI volumes (1 B0 volume and 32 gradient volumes) of each subject were concatenated using AFNI software [9] and then were visually inspected in a cinematic way. One pianist was found to have prominent head motion. This subject's data (including sMRI data) were excluded from further analysis. Eddy current correction and FA calculation were performed using the fMRI of the brain (FMRIB) software library's (FSL's) Diffusion Toolkit (FDT) (www.fmrib.ox.ac.uk/fsl) [4]. The individual FA image was manually co-registered to his/her 3D image via B0 image. Then, the FA maps were spatially normalized to MNI template using the transformation matrix generated in the aforementioned spatial normalization procedure, re-sampled to $1 \text{ mm} \times 1 \text{ mm} \times 1 \text{ mm}$ and spatially smoothed (FWHM = 8 mm).

To remove voxels of non-interest, averaged GMD and FA maps were produced across all subjects, and then a threshold value of 0.2 for both of the averaged GMD and FA maps was used. A GMD mask and FA mask were obtained. Within the corresponding masks,

Table 1

Gray matter density (GMD) and FA differences between the two groups

	Area	Volume (mm ³)	Peak coordinate (x, y, z)	BA
GMD				
Musician > non-musician				
L	SMC	314	-31, -11, 74	6
R	Crbl	282	6, -76, -39	
Non-musician > musician				
R	OFC	1065	10, 37, -29	11
L	ACC	230	-12, 27, 24	32
FA				
Musician > non-musician				
L	IFG	497	-30, 31, -9	47
R	PLIC	285	-12, -7, 5	
R	MB	132	11, -23, -8	

ACC, anterior cingulate cortex; Crbl, cerebellum; IFG, inferior frontal gyrus; MB, midbrain; OFC, orbital frontal cortex; PLIC, posterior limb of internal capsule; SMC, sensorimotor cortex; L, left; R, right; BA, Brodmann area.

two-sample *t*-tests were performed in a voxel-wise manner to compare the GMD and FA between the pianists and controls. Clusters with voxels' minimum $|t| > 3.574$ ($p < 0.001$, uncorrected) and with volumes $> 100 \text{ mm}^3$ were considered to show significant difference between groups and were superimposed on the averaged 3D map across all subjects.

To explore the potential relationships between the demographic data (total years and the age of beginning of piano training, respectively) and the imaging indices (GMD and FA, respectively), a correlation analysis was performed for pianists. The peak voxel and its 26 nearest neighboring voxels were selected within the ROIs exhibiting significant GMD or FA differences between the two groups. Averaged GMD and FA values across the 27 voxels were obtained for each individual; then, linear correlation analysis was performed.

Compared with non-musicians, pianists showed significantly higher GMD in the left sensorimotor cortex and right cerebellum, and showed significantly lower GMD in the right orbital frontal gyrus and left anterior cingulate cortex (Table 1 and Fig. 1). Pianists showed higher FA in the right PLIC, the brain stem, and left inferior frontal gyrus (IFG). Pianists had no brain regions showing lower FA than controls (Table 1 and Fig. 1).

Within the pianists' group, no significant correlation ($p > 0.05$) was found between the demographic data (total years and the age of the commencement of piano training) and the imaging indices (GMD and FA).

There have been at least five studies [14,19,10,17,6] using VBM to investigate the gray matter volume in a voxel-wise manner across the entire brains of musicians. However, the results of these five previous studies were inconsistent. For example, greater gray matter volume in musicians than non-musicians was found in the left Heschl gyrus in one study [10], but in the right Heschl gyrus in another study [6]. Two other studies failed to find significant between-group differences in the Heschl gyrus [19,17]. The only consistent result was that two of these studies found increased gray matter in the bilateral primary sensorimotor cortex and bilateral cerebellum of musicians [10,17]. The current study found increased gray matter in the left sensorimotor cortex and right cerebellum of pianists. This result was, to a large extent, consistent with those of the two compatible previous studies [10,17], indicating that long-term piano practicing may lead to gray matter increases in movement-related brain areas. In addition to the increased GMD in the pianists' group, the current study also found decreased GMD in pianists in the anterior cingulate cortex and in the right orbital frontal cortex. Decreased gray matter in musicians has not been previously reported. A proper interpretation of such decreased

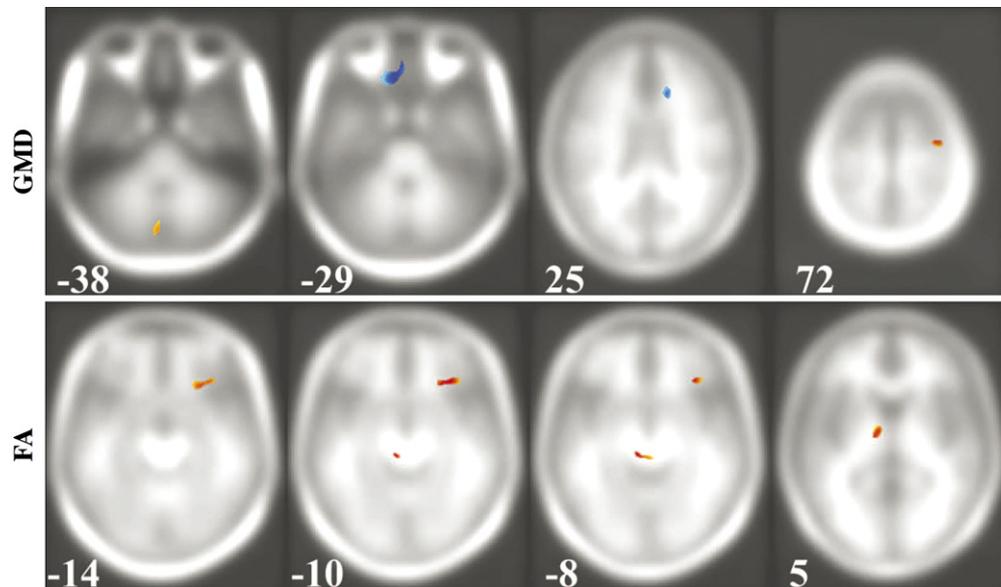


Fig. 1. The differences in gray matter density (upper row) and FA (lower row) between pianists and non-musicians ($|t| > 3.574$, $p < 0.001$, uncorrected) were overlaid on the averaged 3D images across all subjects. The z-coordinates correspond to those in Table 1. Red and yellow color indicates greater values in pianists than non-musician; blue indicates the opposite. Left in the figure denotes right in the brain. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

GMD remains difficult. It might be due to the pianists engaging in fewer activities unrelated to music training than non-musicians.

The current study found that the pianists showed higher FA in the right PLIC, left IFG, and the midbrain (Table 1 and Fig. 1). The PLIC carries the fibers from the primary motor cortex to the spinal cord. The current result of higher FA in pianists than in non-musicians in the right PLIC was highly consistent with that reported by Bengtsson et al. [5]. That study found a significant correlation between FA values in the right PLIC and practicing time during childhood, but not that during adolescence or adulthood [5], suggesting that childhood training is critical for white matter plasticity in the right PLIC. The mean age of the commencement of piano training in the current study was 12 years (and there were only two pianists who began their piano training before 7 years of age), much later than that in the study of Bengtsson et al. [5] in which all subjects began piano playing before 7 years of age. Developmental study has found that FA may undergo an age-related increase and reach a plateau during the late teens or twenties [11]. The current finding suggests that higher FA in the right PLIC may be related to extensive sequential motor learning during adolescence or even early adulthood, although the piano players recruited in the current study began their piano training later than those recruited in previous studies [5].

We also found higher FA in the white matter in the left IFG (near Broca's area, Fig. 1) in pianists than non-musicians. It has been indicated that musicians have greater GMD in Broca's area than non-musicians [19]. Although the current study did not find increased GMD in the pianists, the higher FA in the left IFG might also support shared neural substrates of underpinning expressive output of music and language [19].

A few concerns should be addressed. Compared with previous DT-MRI studies on musicians [18,5], although the current study used a relatively large sample (40 subjects), the statistical power was not very high. For example, Bengtsson et al. [5] recruited only 16 subjects (eight pianists and eight non-musicians), but they found group differences at a threshold of $p < 0.000$ and $t > 4.34$ ($p < 0.001$ and $t > 3.574$ for the current study). This discrepancy may be partly due to the fact that the age of the commencement of piano training

was late (mean age = 12 years old) for the pianists in the current study. Moreover, some detailed information of the pianists, for example, the absolute pitch, their level of piano performance, and their total hours of piano playing were not recorded. It has been indicated that the FA of white matter tracts (for example, the pyramidal tract and corpus callosum) connecting movement-related areas correlates with some motor performance parameters in healthy subjects [7,15] or patients with movement disorders [8,13]. In future studies, it would be important and interesting to investigate the effects of these factors.

Taken together, the results of the current study found that pianists showed increased GMD in the left sensorimotor cortex and the right cerebellum, and showed increased white matter integrity in the right PLIC. These results indicate that long-term piano practicing may lead to gray matter and white matter adaptation in movement-related regions. Such gray matter and white matter changes may reflect numbers of synapses, volume of glia, or increased myelination and diameter of axons [5,1,2]. Further studies may focus on the relationship between the change in gray matter and that in white matter (white matter volume as well as FA) by using both VBM and fiber tracking techniques.

Acknowledgements

This study was supported by the Natural Science Foundation of China (30470575, 30625024, 30728017, 30530290 and 30621130074), an SRFDP grant from SEM (Grant No. 20060610073), the National Basic Research Program of China (973 Program No.: 2007CB512305/1), and the National High Technology Program of China (863 Program No.: 2007AA02Z430). The authors would like to thank Mr. LI Chun-Xiao for his help in recruiting the pianists.

References

- [1] B.J. Anderson, X. Lim, A.A. Alcantaram, K.R. Isaacs, J.E. Black, W.T. Greenough, Glial hypertrophy is associated with synaptogenesis following motor-skill learning, but not with angiogenesis following exercise, *Glia* 11 (1994) 73–80.

- [2] B.J. Anderson, P.B. Eckburg, K.I. Relucio, Alterations in the thickness of motor cortical subregions after motor-skill learning and exercise, *Learn. Mem.* 9 (2002) 1–9.
- [3] J. Ashburner, K.J. Friston, Voxel-based morphometry—the methods, *Neuroimage* 11 (2000) 805–821.
- [4] T.E. Behrens, H. Johansen-Berg, M.W. Woolrich, S.M. Smith, C.A. Wheeler-Kingshott, P.A. Boulby, G.J. Barker, E.L. Sillery, K. Sheehan, O. Ciccarelli, A.J. Thompson, J.M. Brady, P.M. Matthews, Non-invasive mapping of connections between human thalamus and cortex using diffusion imaging, *Nat. Neurosci.* 6 (2003) 750–757.
- [5] S.L. Bengtsson, Z. Nagy, S. Skare, L. Forsman, H. Forssberg, F. Ullén, Extensive piano practicing has regionally specific effects on white matter development, *Nat. Neurosci.* 8 (2005) 1148–1150.
- [6] P. Bermudez, R.J. Zatorre, Differences in gray matter between musicians and nonmusicians, *Ann. NY Acad. Sci.* 1060 (2005) 395–399.
- [7] S. Böhr, D. Güllmar, R. Knab, J.R. Reichenbach, O.W. Witte, J. Haueisen, Fractional anisotropy correlates with auditory simple reaction time performance, *Brain Res.* 1186 (2007) 194–202.
- [8] L. Bonzano, A. Tacchino, L. Roccatagliata, G. Abbruzzese, G.L. Mancardi, M. Bove, Callosal contributions to simultaneous bimanual finger movements, *J. Neurosci.* 28 (2008) 3227–3233.
- [9] R.W. Cox, AFNI: software for analysis and visualization of functional magnetic resonance neuroimages, *Comput. Biomed. Res.* 29 (1996) 162–173.
- [10] C. Gaser, G. Schlaug, Brain structures differ between musicians and non-musicians, *J. Neurosci.* 23 (2003) 9240–9245.
- [11] C. Lebel, L. Walker, A. Leemans, L. Phillips, C. Beaulieu, Microstructural maturation of the human brain from childhood to adulthood, *Neuroimage* 40 (2008) 1044–1055.
- [12] D.J. Lee, Y. Chen, G. Schlaug, Corpus callosum: musician and gender effects, *NeuroReport* 14 (2003) 205–209.
- [13] N.A. Ludeman, J.I. Berman, Y.W. Wu, R. Jeremy, J. Kornak, A.I. Bartha, A.J. Barkovich, D.M. Ferriero, R.G. Henry, O.A. Glenn, Diffusion tensor imaging of the pyramidal tracts in infants with motor dysfunction, *Neurology* (2008), doi:10.1212/01.wnl.0000304084.59964.e2.
- [14] E. Luders, C. Gaser, L. Jancke, G. Schlaug, A voxel-based approach to gray matter asymmetries, *Neuroimage* 22 (2004) 656–664.
- [15] R.L. Muetzel, P.F. Collins, B.A.M. Mueller, A. Schissel, K.O. Lim, M. Luciana, The development of corpus callosum microstructure and associations with bimanual task performance in healthy adolescents, *Neuroimage* 39 (2008) 1918–1925.
- [16] G. Schlaug, L. Jancke, Y. Huang, H. Steinmetz, In vivo evidence of structural brain asymmetry in musicians, *Science* 267 (1995) 699–701.
- [17] G. Schlaug, A. Norton, K. Overy, E. Winner, Effects of music training on the child's brain and cognitive development, *Ann. NY Acad. Sci.* 1060 (2005) 219–230.
- [18] V.J. Schmithorst, M. Wilke, Differences in white matter architecture between musicians and non-musicians: a diffusion tensor imaging study, *Neurosci. Lett.* 321 (2002) 57–60.
- [19] V. Sluming, T. Barrick, M. Howard, E. Cezayirli, A. Mayes, N. Roberts, Voxel-based morphometry reveals increased gray matter density in Broca's area in male symphony orchestra musicians, *Neuroimage* 17 (2002) 1613–1622.
- [20] D. Sydykova, R. Stahl, O. Dietrich, M. Ewers, M.F. Reiser, S.O. Schoenberg, H.J. Möller, H. Hampel, S.J. Teipel, Fiber connections between the cerebral cortex and the corpus callosum in Alzheimer's disease: a diffusion tensor imaging and voxel-based morphometry study, *Cereb. Cortex* 17 (2007) 2276–2282.
- [21] I.C. Wright, P.K. McGuire, J.B. Poline, J.M. Travers, R.M. Murray, C.D. Frith, R.S. Frackowiak, K.J. Friston, A voxel-based method for the statistical analysis of gray and white matter density applied to schizophrenia, *Neuroimage* 2 (1995) 244–252.
- [22] S. Xie, J.X. Xiao, G.L. Gong, Y.F. Zang, Y.H. Wang, H.K. Wu, X.X. Jiang, Voxel-based detection of white matter abnormalities in mild Alzheimer disease, *Neurology* 66 (2006) 1845–1849.