Sensorimotor skills and focal dystonia are linked to putaminal grey-matter volume in pianists

Oliver Granert,¹ Martin Peller,¹,² Hans-Christian Jabusch,³,⁴ Eckart Altenmüller,⁴ Hartwig Roman Siebner¹,²,⁵

ABSTRACT

Background Focal hand dystonia has been associated with morphometric changes and distorted somatotopic representations in the putamen.

Objective The authors used voxel-based morphometry (VBM) to identify regions in the putamen where grey-matter volume is associated with musician’s dystonia (MD) or the skill level of piano playing in professional pianists.

Methods In 11 pianists with MD affecting the right hand and 12 healthy pianists without dystonia, the authors performed high-resolution T1-weighted MRI of the brain. The authors also measured the temporal variability of key strokes during scale playing with the right hand to characterise the individual skill level of piano playing. Statistical comparisons of the normalised and smoothed grey-matter maps were performed to test for dystonia and performance-related structural changes in the putamen.

Results During scale playing, the timing of consecutive key strokes was more variable in MD patients than in non-dystonic pianists. Regional grey-matter volume in the middle part of left and right putamen increased with timing variability during piano playing in pianists with and without MD. Between-group comparisons revealed that MD patients had a larger grey-matter volume in the right middle putamen compared with healthy musicians.

Conclusion In highly trained pianists with and without MD, the volume of the associative motor territory in the middle putamen reflects both the skill level of piano playing and the presence of dystonia. While a smaller volume is associated with better timing skills, a relative expansion is correlated with the presence of focal task-specific hand dystonia.

INTRODUCTION

Musician’s hand dystonia (MD) is a task-specific form of focal dystonia. Affected patients show dystonic muscle activity in the upper limb while playing a musical instrument. This includes cocontractions of agonist and antagonist muscles and overflow of motor activity to muscles that are normally not involved in a given movement.¹ Current concepts assign the basal ganglia a central role in the pathophysiology of dystonia.² ³ In healthy individuals, the sensorimotor cortico-striato-thalamo-cortical circuits are involved in learning motor sequences and increasing automaticity over practice.⁴–⁶ It has been supposed that dysfunctional sensorimotor integration in these circuits is a major pathophysiological factor in task-specific hand dystonia such as MD or writer’s cramp.⁷ ⁸

Several morphometric studies have used structural MRI to investigate whether primary focal dystonia is associated with structural changes in basal ganglia.⁹–¹³ These studies have revealed inconsistent results. Some studies found structural changes in the putamen,¹⁰ ¹⁵ globus pallidus internus (GPI)¹¹ or ventralstriatum¹² in patients with primary focal dystonia. Yet a large morphometric MRI study including 31 patients with writer’s cramp and five patients with MD failed to demonstrate consistent morphometric changes in the basal ganglia.⁹

Voxel-based morphometry (VBM) based on high-resolution structural MRI is a well-established method to identify interindividual variations in regional brain structure related to interindividual differences in a given brain function as well as to pinpoint regional changes in brain structure associated with different disease states.¹⁴ ¹⁵ Several longitudinal VBM studies have shown regional increases in grey matter (GM) volume after prolonged periods of intensive training (ie, training of juggling or preparing for a medical exam) in cortical areas that were subserving the trained brain function.¹⁶–¹⁸

In contrast to training related volume changes in the cortex, a recent VBM study with adult left-handed individuals who were forced to adopt right-handedness for handwriting at school showed a reduction in GM volume in the middle putamen.¹⁹ This region corresponds to the motor associative territory of the striatum. Converted subjects with at least one left-handed first-degree relative showed a correlation between the acquired right-hand advantage for writing and the reduction in putaminal volume. These findings suggest that a smaller volume in the middle putamen may be associated with a higher degree of proficiency in highly trained subjects. Conversely, a larger putaminal volume might increase the risk for dysfunctional maladaptive plasticity, increasing the risk for dystonia.

Here, we used VBM to test for volumetric differences in the associative motor territory of the putamen between pianists with and without MD. We hypothesised that the middle putamen is enlarged in MD pianists relative to pianists without MD. We further expected the volume of the middle putamen to correlate inversely with the skill level of piano playing in healthy pianists and in those with MD.

METHODS

Participants
Eleven pianists with MD and 12 healthy pianists participated in the study. Demographic data are...
given in table 1. All participants were right-handed and were expert pianists with a total life practice time of more than 10 000 h. Handedness was assessed as self-declared handdness based on hand preference in selected activities referred to in the Edinburgh Handedness Inventory.20 None of the participants had any history of neurological disease other than focal hand dystonia. The participants gave written informed consent prior to MRI scanning. The study was in accordance with the declaration of Helsinki and had been approved by the ethics committee of the Christian-Albrechts-University.

All pianists with MD displayed task-specific dystonia of the right hand when playing the piano, but not at rest or during other manual tasks. The diagnosis of MD was established by neurological examination and visual inspection while patients were playing the piano. The clinical course and the absence of additional clinical, biochemical or MRI abnormalities were compatible with primary dystonia. The duration of MD ranged from 1 to 25 years (median 10.9 years). Botulinum toxin treatment of four patients was interrupted at least 5 months prior to the participation in the study. Demographic data, details about MD and information on pianistic expertise as assessed by a researcher-developed musical biography questionnaire are given in table 1.

### Performance measure during scale playing

Motor performance during piano playing was assessed by MIDI-based scale analysis according to a previously published protocol.31 All participants played sequences of 10 to 15 C major scales over two octaves in both playing directions, inward and outward, with the right hand, on a digital piano (KAWAI MP-8). Scales were played using the conventional C major fingering: 1, 2, 3, 1, 2, 3, 4, 1, 2, 3, 1, 2, 3, 4, 5 (fingers 1–5 refer to thumb, index, middle, ring and little finger, respectively). The tempo of scale playing was paced by a metronome (desired interonset interval: 125 ms). Scales were saved as MIDI files on a PC connected to the piano. In each participant, interonset intervals (IOI) were analysed using custom-made software. For each participant, the variability of IOIs (mSDIOI) was selected for further analysis. The MAX-mSDIOI parameter has been described as a reliable, valid and precise indicator of the skill level in healthy pianists as well as of motor impairment in pianists with MD.21

### MRI data acquisition and image pre-processing

All participants were scanned on a 3 T Trio system (Siemens, Erlangen, Germany). We used a T1-weighted FLASH 3D sequence (repetition time (TR)=15 ms, echo time (TE)=4.92 ms, flip angle=25, 192 slices, slice thickness=1 mm, matrix: 256×256 mm) with an isotropic resolution of 1×1×1 mm.

The structural MRI data were analysed using the VBM5 toolbox VI.13 (Structural Brain Mapping Group, Department of Psychiatry, University of Jena; http://dbm.neuro.uni-jena.de/vbm). The toolbox is integrated in the statistical parametric mapping (SPM) software (SPM5, Wellcome Department of Imaging Neuroscience, Institute of Neurology, UCL, London; http://www.fil.ion.ucl.ac.uk/spm) and operates in a MATLAB environment. The images were segmented using the a priori tissue probability maps delivered with SPM. In addition to the standard VBM processing, a Hidden Markov Random Field model was applied to reduce noise in the segmentation. Resulting GM density maps were modulated by the Jacobian determinants as derived from deformation parameters used for spatial normalisation. Modulated result images were then smoothed using an isotropic Gaussian kernel of 10 mm full width at half-maximum to satisfy the subsequent statistical analysis.

### Statistical analysis

Mann–Whitney U tests were computed to test for group differences in age, total GM volume, pianistic expertise and motor performance. Gender distributions between both groups were compared using the Fisher exact tests. Spearman rank correlations were calculated to detect associations between variables. The two-tailed level of statistical significance was set at p<0.05. This statistical analysis was carried out using SPSS Version 17.0.

Regional differences in the normalised GM maps were analysed with SPM5 software using a full-factorial design and additional covariates. A design matrix was defined in the framework of a generalised linear model with six independent variables. Two variables of the model specified group membership. Two further variables modelled age and total GM volume. These covariates were inserted to account for subject specific variations of the local GM estimates caused by individual age and brain-volume differences between the subjects. Finally, individual MAX-mSDIOI values were included as covariate to model individual variations in the temporal precision of piano playing. The covariate was inserted separately for pianists with and without MD. This separation allowed us to test for differences in the correlation between motor performance and local GM volume between the two groups. In the general linear model, all covariates were centred to their overall mean to avoid offset and interference effects. In particular, the adjustment to the group means compensated for the differences in mean MAX-mSDIOI between MD patients and healthy musicians, removing possible interference with the group factor in the statistical model.

We performed separate one-tailed t tests by specifying appropriate t-contrasts within SPM5 to identify regions in the brain where the GM structure is related to MD or the motor performance level in scale playing. The first pair of contrasts was defined to detect local differences in GM between the two groups. The second pair detected positive and negative correlations between regional GM and the intersubject variation in motor performance as captured by the MAX-mSDIOI. Finally, two contrasts were specified to find regions in the brain where the strength of the correlation between GM and motor performance differs between musicians with and without MD.

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### Table 1

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Age range</th>
<th>Musician’s dystonia onset (age)</th>
<th>Affected fingers</th>
<th>Start keyboard playing (age)</th>
<th>Playing time (h/year)</th>
<th>No of yearly concerts</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>40–50</td>
<td>27</td>
<td>4; 5</td>
<td>7</td>
<td>690</td>
<td>3</td>
</tr>
<tr>
<td>02</td>
<td>40–50</td>
<td>27</td>
<td>4; 5</td>
<td>7</td>
<td>329</td>
<td>1</td>
</tr>
<tr>
<td>03</td>
<td>30–40</td>
<td>31</td>
<td>4; 5</td>
<td>9</td>
<td>738</td>
<td>1</td>
</tr>
<tr>
<td>04</td>
<td>40–50</td>
<td>34</td>
<td>4; 5</td>
<td>6</td>
<td>811</td>
<td>2</td>
</tr>
<tr>
<td>05</td>
<td>60–70</td>
<td>40</td>
<td>3; 4; 5</td>
<td>11</td>
<td>880</td>
<td>2</td>
</tr>
<tr>
<td>06</td>
<td>70–80</td>
<td>60</td>
<td>4; 9</td>
<td>4</td>
<td>411</td>
<td>0</td>
</tr>
<tr>
<td>07</td>
<td>30–40</td>
<td>24</td>
<td>3</td>
<td>4</td>
<td>1722</td>
<td>5</td>
</tr>
<tr>
<td>08</td>
<td>40–50</td>
<td>40</td>
<td>2; 6</td>
<td>6</td>
<td>891</td>
<td>4</td>
</tr>
<tr>
<td>09</td>
<td>50–60</td>
<td>50</td>
<td>4; 7</td>
<td>7</td>
<td>799</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>50–60</td>
<td>30</td>
<td>3</td>
<td>7</td>
<td>1612</td>
<td>12</td>
</tr>
<tr>
<td>11</td>
<td>30–40</td>
<td>34</td>
<td>2; 5</td>
<td>5</td>
<td>1667</td>
<td>36</td>
</tr>
</tbody>
</table>
The putamen was defined as the primary volume of interest (VOI) because previous neuroimaging studies reported changes in GM structure and function in patients with focal dystonia,34 10 and the putamen is the primary receiving structure from the motor and pre-motor cortex.22 The VOI was defined bilaterally (left and right) by mask images generated by the WFU-Pick Atlas toolbox.23 Within the putaminal VOI, we applied small volume correction (SVC) to correct for multiple comparisons using the familywise error (FWE) method (p_{SVC/FWE} < 0.05). Voxels showing a difference of p_{unc} <\ 0.01 (uncorrected) in the putaminal VOI are reported as statistical trends.

For all other brain regions, FWE correction for multiple comparisons considered all voxels in the brain (p_{FWE} < 0.05). Outside the putaminal VOI, voxels showing a change in GM volume at an uncorrected p value of \leq 0.001 are reported as trend changes to inform future morphometric MRI studies.

In addition to the single model analysis, we compared the goodness of fit between the full model described so far and the same model without the two MAX-mSDIOI variables using the difference of the deviance statistic.24 The corresponding F-statistics were calculated based on the residual sum of squares images (ResSS.img) provided by SPM for both models.

**RESULTs**

**Group characteristics**

There were no differences between the two groups regarding the distribution of age, gender, total GM volume and musical expertise as measured by the mean playing time per year, the number of years of playing a keyboard instrument or the total life practice time (table 2). As expected, the timing of scale playing was more variable in patients with MD relative to healthy musicians. Patients with MD showed higher MAX-mSDIOI values (W = 11, p = 0.0002, table 2).

**Dystonia-related differences in GM structure**

The middle portion of the right putamen showed an increase in GM volume in pianists with MD relative to healthy pianists (peak increase at x, y, z = 23, −1, 1; Z-score = 3.66; cluster extent = 807 voxels; p_{SVC/FWE} = 0.036; figure 1A). The cluster of significant voxels in the right putamen extended into the region of the right globus pallidus and may therefore also be an indicator for an increased local GM volume in this region. When applying a more liberal statistical threshold of p_{unc} < 0.01 to search for trend changes in the basal ganglia of the left hemisphere, we observed a similar trend towards a regional GM volume increase in the left middle putamen p_{unc} = 0.008 (T = 2.67). Further analysis of this trend revealed that the numerical mean difference in the left middle putamen between groups was comparable with the homologous part in the right putamen. However, the Cls reported by SPM were slightly higher in the left hemisphere (figure 1B). This observation leads us to analyse the error variances at the two peak locations in the statistical map separately for each group and hemisphere. Here we found that the error variances of the fitted model were approximately twice as high on the left hemisphere in the MD group as compared with the volume estimates on the right side in both groups and on the left side in the healthy group. This increased interindividual variation in left putaminal volume in the patient group suggests the existence of structural differences in the left putamen of MD patients that were not explained by our statistical model. It also explained why the increase in GM volume in the left middle putamen in patients did not reach statistical significance relative to healthy controls, although the mean increase in putaminal volume was similar in both hemispheres. Overall, the regional GM volumes were

### Table 2: Group characteristics of the patients with musician’s dystonia and healthy pianists without musician’s dystonia

<table>
<thead>
<tr>
<th></th>
<th>Pianists with musician’s dystonia</th>
<th>Healthy pianists</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43 (28−73)</td>
<td>41.5 (29−60)</td>
<td>0.756</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>9/2</td>
<td>1/1</td>
<td>0.590</td>
</tr>
<tr>
<td>Duration of keyboard instrument playing (years)</td>
<td>36 (24−64)</td>
<td>35.5 (23−49)</td>
<td>0.579</td>
</tr>
<tr>
<td>Total life practice time (h)</td>
<td>36 708 (17 715−74 146)</td>
<td>41 684 (15 089−143 544)</td>
<td>0.880</td>
</tr>
<tr>
<td>Average playing time per year (h)</td>
<td>811 (411−1722)</td>
<td>1041 (419−2929)</td>
<td>0.786</td>
</tr>
<tr>
<td>MAX-mSDIOI (ms)</td>
<td>21.5 (13.9−24.4)</td>
<td>11.9 (5.5−18.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Total grey-matter volume (cm³)</td>
<td>700 (633−823)</td>
<td>738 (602−833)</td>
<td>0.902</td>
</tr>
<tr>
<td>Total white-matter volume (cm³)</td>
<td>514 (415−587)</td>
<td>518 (438−626)</td>
<td>0.758</td>
</tr>
<tr>
<td>Total volume of the cerebral spinal fluid (cm³)</td>
<td>592 (460−685)</td>
<td>604 (419−836)</td>
<td>0.608</td>
</tr>
</tbody>
</table>

Except for gender, group data are given as median and total range. The level of significance was calculated by a two-tailed Fisher exact test (gender) or Mann−Whitney U test (all other variables). As expected, there was a significant group difference for temporal variability of scale playing as indexed by MAX-mSD interonset intervals (IOD).

**Figure 1** Group estimates at the peak locations of the statistical map in the left and right putamen and the globus pallidus. (A) Spatial distribution of voxels in the putamen showing an increased grey-matter (GM) volume in the MD group compared with controls (for visualisation purposes, a statistical threshold of uncorrected p (p_{unc}) of < 0.01 was used). (B) Differences in regional grey-matter volume on both hemispheres with equal sizes. Different error variances (as indicated by slightly larger CIs on the left hemisphere) lead to smaller (non-significant) statistical estimates.
greater in the left than in the right middle putamen in both groups (Figure 1B).

Several cortical regions showed relative increases or decreases in GM volume in patients with MD compared with healthy pianists (Table 3). However, none of these regional changes in the cortical volume survived a whole-brain correction for multiple comparisons.

**Relationship between GM volume and motor performance**

Pianists with and without dystonia showed a linear relationship between the temporal variability of piano playing (as indexed by individual MAX-mSDIOI) and putaminal GM volume (Figure 2, Table 3). The higher the temporal variability of consecutive piano strokes as indicated by the individual MAX-mSDIOI, the larger was the GM volume in the middle portion of the left putamen (peak at x, y, z = 30, 2, 5; Z-score = 4.2; cluster extent = 1285 voxels; pSVC/FWE = 0.006). There was a similar trend for the right putamen (peak at x, y, z = 22, 2, 3; Z-score = 3.5; cluster extent = 565 voxels; pSVC/FWE = 0.058). In other words, the better the temporal precision of piano playing, the smaller was the volume in the middle part of the putamen. The strength of the linear relationship between temporal precision and

**Table 3** Peak locations of clusters determined at a statistical threshold of uncorrected p < 0.001

<table>
<thead>
<tr>
<th>Region</th>
<th>Peak coordinate</th>
<th>Cluster extent (voxel)</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dystonia-related increases in grey matter (musician’s dystonia patients &gt; healthy musicians)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right putamen (middle portion)*</td>
<td>23</td>
<td>807</td>
<td>3.66</td>
</tr>
<tr>
<td>Right posterior cingulate cortex</td>
<td>7</td>
<td>490</td>
<td>3.8</td>
</tr>
<tr>
<td>Left precuneus</td>
<td>-12</td>
<td>424</td>
<td>4.3</td>
</tr>
<tr>
<td>Left posterior cingulate cortex</td>
<td>-5</td>
<td>145</td>
<td>3.4</td>
</tr>
<tr>
<td>Dystonia-related decreases in grey matter (musician’s dystonia patients &lt; healthy musicians)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right cerebellum crus1</td>
<td>43</td>
<td>410</td>
<td>4.0</td>
</tr>
<tr>
<td>Left inferior temporal cortex</td>
<td>-50</td>
<td>130</td>
<td>3.6</td>
</tr>
<tr>
<td>Left middle occipital gyrus</td>
<td>-30</td>
<td>123</td>
<td>4.0</td>
</tr>
<tr>
<td>Left inferior occipital gyrus</td>
<td>-38</td>
<td>106</td>
<td>3.6</td>
</tr>
<tr>
<td>Linear increase in regional grey-matter volume with piano-playing skill level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left putamen (middle portion)*</td>
<td>-30</td>
<td>1285</td>
<td>4.2</td>
</tr>
<tr>
<td>Right putamen (middle portion)</td>
<td>22</td>
<td>565</td>
<td>3.5</td>
</tr>
<tr>
<td>Left inferior temporal gyrus</td>
<td>-43</td>
<td>490</td>
<td>3.9</td>
</tr>
<tr>
<td>Right dorsal premotor cortex</td>
<td>24</td>
<td>178</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Regions are sorted by type and cluster extent. Stereotactic coordinates (Montreal Neurological Institute (MNI) space) and Z-scores correspond to regional peak voxels in the statistical map. *Significant findings in the putaminal volume of interest after small volume correction for multiple comparisons (familywise error p < 0.05) are shown in bold.

**Figure 2** (A) Statistical parametric maps (threshold at uncorrected p (p_{unc}) of < 0.001) showing clusters of voxels where regional grey-matter volume increased with the temporal variability of scale playing (as indexed by MAX-mSD-IOI). (B) Left panel: projection of the statistical parametric map (p_{unc} < 0.001) showing significant positive correlations between grey-matter volume and temporal variability in scale playing (as indexed by MAX-mSDIOI). Right panel: individual estimates of the regional grey-matter volume (y-axis) plotted against the individual MAX-mSD IOI reflecting the temporal variability of key strokes during scale playing (x-axis). The grey-matter volume estimates were extracted from the two voxels in the right and left putamen showing the strongest linear increase in grey-matter volume and the behavioural measure. Local grey-matter estimates are adjusted for age and total grey matter according to the parameters determined by the generalised linear model estimated by the SPM5 software. Individual values are plotted separately for pianists with pianist’s cramp (red) and healthy pianists without dystonia (green). The solid line represents the estimated linear relation between regional grey-matter volume and temporal variability in scale playing. The dotted horizontal line gives the group mean for the estimated regional grey-matter volume.
putaminal GM did not differ between the two groups, indicating that a low temporal precision during scale playing was associated with a larger relative volume of the putamen, irrespectively of the presence of dystonia.

At the cortical level, the right dorsal premotor cortex and left inferior temporal gyrus showed a statistical trend towards an increase in regional cortical GM volume with a higher temporal precision of piano playing (table 3).

**Statistical model comparisons**

The statistical comparisons between the model with and without the MAX-mSD_{mSD} scores showed significant improvements in the goodness of fit in the putamen on both hemispheres when using the full statistical model. The statistical estimates of the model comparisons were \( F_{2,17} = 12.05 \), \( p_{\text{unc}} = 0.0006 \) at the peak location of the group comparison \((x, y, z) = (23, -1, 1)\) in the right putamen, and we found similar improvements of the extended model to the two peak location of the GM versus and skill correlation \( F_{2,17} = 18.03 \), \( p_{\text{unc}} = 0.0001 \) at peak \((x, y, z) = (-30, 2, 5)\) in the left putamen and \( F_{2,17} = 11.63 \), \( p_{\text{unc}} = 0.0007 \) at peak \((x, y, z) = (22, 2, 3)\) in the right putamen. A graphical representation of the statistical map of the comparisons is shown in figure 3 to give an overview of the spatial extension of the pattern.

Furthermore, we observed that the reduced model, which did not include the behavioural data, failed to show the dystonia-related structural changes in the putamen detected by the full model.

**DISCUSSION**

Our study revealed three main findings. First, patients with pianist’s cramp showed an expansion in regional GM volume in the right middle putamen and the right globus pallidus relative to healthy musicians. Second, in agreement with other reports, the interindividual variability in motor performance correlated with interindividual variations of putaminal GM volume in both pianists with and without MD. The more variable the timing of key strokes during piano playing, the greater the volume became in the middle part of the putamen. We conclude that the middle part of the putamen reflects both disease status and skill level in professional pianists.

The posterior putamen receives inputs from primary sensorimotor cortex and supports executive aspects of movements such as movement rate, whereas the middle portion of the putamen receives input from the premotor cortex and processes planning aspects of motor control. A similar rostro-caudal segregation has been shown with invasive recordings in the striatum of monkeys when they learnt sequential hand movements (figure 4). Learning of sequences was associated with neural activity in more anterior parts of the putamen, while the execution of well-learnt sequences was associated with activity in more posterior parts.

In our study, the magnitude of motor skills and the presence of dystonia had a structural correlate in the anterior planning territory rather than in the posterior ‘executive’ territory of the putamen, emphasising the importance of this part of the basal ganglia for skilled motor control.

Although the localisations of these findings conform to previous findings, the exact localisations may vary because of methodological limitations of the VBM method. The regional
GM maps have to be smoothed before the statistical analysis, and it has recently been shown that the posterior part of putamen is sometimes misclassified as white matter when using the T1 imaging protocol. Therefore, our negative finding with respect to the posterior putamen needs to be interpreted with caution.

**Increase in putaminal volume in musician’s hand dystonia**

Pianists with MD showed a well-defined increase in putaminal volume in the right hemisphere with a similar trend in the homotopic region of the left putamen. Since both groups were carefully matched, the observed differences cannot be attributed to between-group difference in age, gender, total GM volume and musical expertise. Our findings significantly extend previous MRI studies of structural basal ganglia changes in focal hand dystonia, because the structural difference in putaminal GM only emerged in an extended statistical model that integrated the group-centred data on temporal variability in piano playing. A reduced model which did not include the behavioural data failed to show any dystonia-related structural changes in the putamen. This observation has important implications for morphometric MRI studies showing that the inclusion of behavioural variables that account for interindividual variations in skill level may increase the sensitivity of structural MRI to detect disease-related sources of anatomical variance in the human brain.

The dystonia-related increase in putaminal volume may constitute an invariant structural trait of pianist’s cramp. Alternatively, it is possible that the categorical increase in regional GM volume in the right putamen in dystonic pianists is related to the overall reduction in piano skill level in dystonic patients as opposed to healthy musicians. Since we assessed the sensorimotor skill level during piano playing which was affected by dystonia, we cannot disentangle how much the dystonic status per se or disease-related impairment in skillful piano playing contributed to the local increase in mid-putaminal volume in patients with pianist cramp. Future studies have to clarify this issue, for instance by assessing sensorimotor skills in tasks that are not affected by task-specific dystonia.

The observed increase in putaminal volume in pianists with MD is in good agreement with a volumetric study reporting a bilateral increase in total putaminal volume in 13 adults with cranial or hand dystonia relative to age- and sex-matched healthy controls. However, a VBM study found an increase in GM volume in right GPi but not in the putamen in 10 patients with idiopathic cervical dystonia. Yet another VBM study including nine patients with focal dystonia and healthy controls found reduced GM volume in the putamen in the group with dystonia. A possible explanation for the discrepancies among studies is that different forms of focal dystonia have been studied, and all studies were conducted with relatively small sample sizes. In addition, more consistent results might have been obtained if statistical analysis had accounted for interindividual differences in motor skills. In our study, analysis of the error variances revealed higher variances for the left hemisphere in the putamen of the MD group, suggesting that the dystonia-related volumetric changes were still not fully explained by our current models.

An explanation for a possible right-hemispheric preponderance can be found in a study with writer’s cramp patients, another task-specific hand dystonia, where the contingent negative variation as a physiological index of sensorimotor integration showed an interhemispheric asymmetry with larger amplitudes on the right. The preponderant changes in right putamen might be related to well-known hemispheric asymmetries in sensorimotor integration. The right precentral cortex has been implicated in mapping extrapersonal space onto personal space during response mapping, and the right prefrontal cortex has been linked to specific working-memory functions such as item memory, which depends on the precise spatial relations among item features or components.

Functional neuroimaging also revealed a right-hemispheric lateralisation for emotional processing. The functional lateralisation to the right hemisphere might be particularly relevant for skilful piano playing and, thus, may account for the preponderant right-hemispheric expression of structural change in putamen in professional musicians. On the other hand, analogous changes were observed as a trend in the homologous territory of the left putamen, suggesting that the structural changes were not strictly lateralised. This is in good agreement with a previous fMRI study in writer’s cramp showing an excessive bilateral activation of the putamen during a tactile grating discrimination task.

**Relationship between motor performance and putaminal volume**

The increased temporal variability in scale playing in pianists with MD indicates impaired sensorimotor integration causing a decrease in movement-to-movement regularity. Interestingly, the interindividual variation in motor performances correlated with interindividual volume variations in middle putamen. Since the inverse relationship between the temporal regularity of piano playing and putaminal volume was found in both groups, we infer that this function—structure relationship generalises beyond specific disease states. In other words, the higher the skill level of piano playing in professional pianists, the smaller the volume of the right mid-putamen, regardless of whether dystonia was present or not. Our observation ties in with the findings that were obtained in a recent VBM study on professional ballet dancers. In that study, professional ballet dancers demonstrated a reduction in putaminal GM density compared with control subjects. Adult left-handed individuals who were forced to adopt right-handedness for handwriting at school also show a reduction in GM volume in the middle putamen. Based on these observations, one might speculate that chronically trained individuals with a high proficiency level in a specific motor skill may show a reduction in GM in the putamen because the high skill level makes the putamen less important to control their movements.

A relative increase in basal ganglia volume has been reported in other conditions. In patients with schizophrenia, structural MRI studies have consistently shown that treatment with typical antipsychotics increase the GM volume of the basal ganglia whereas non-medicated patients with schizophrenia appear to have smaller global putamen volumes than controls. The presence of a non-manifesting heterozygous mutation in the Parkin or PINK1 gene is associated with a bilateral increase in GM volume in the posterior putamen and in the GPi which correlates with the relative presynaptic nigrostriatal dysfunction as revealed by F-DOPA PET imaging.

Most of these findings suggest that dysfunctional states of the basal ganglia may result in an increase in regional volume. This pattern is opposite to the function—structure relationship at the cortical level where regional increases in regional GM have been associated with better performance in distinct cognitive domains. For example, the posterior hippocampus of London taxi drivers is greater than in age-matched controls, and the individual sizes correlate positively with the time spent for taxi driving. A relative expansion in cortical GM has been...
documented in the temporoparietal junction region during the course of learning to juggle.16 Most relevant to the present study, extensive lifelong training in keyboard playing was positively correlated with GM volume in several cortical regions including inferior temporal gyrus, precentral gyrus or Heschl’s gyrus.38 39

These structural MRI studies consistently show that achieving a high performance level in a given skill is generally associated with relative increases in regional GM in cortical regions subserving that task.

This, and our findings, begs the question as to why the basal ganglia deviate from this ‘the more volume, the higher the level of skill’ rule. Several models of basal ganglia emphasise the funneling function of the corticobasal ganglia-thalamocortical loops which facilitates the relevant cortical inputs while suppressing irrelevant ones.40 41 A dysfunction in the basal ganglia that reduces the funneling properties would cause overall increases in noisy neuronal activity. This increased but inefficient regional neural activity might be a mechanism that drives the local increases in putaminal GM volume in dystonic musicians.

In fact, there is some evidence for increased but inefficient neural processing in the basal ganglia of patients with focal dystonia. Using functional MRI, excessive basal ganglia activation has been described in focal hand dystonia with motor42 and sensory tasks.32 In one study, excessive activation persisted even when patients stopped performing a manual tapping task.42 In patients suffering from right-hand dystonia, functional MRI revealed a distorted somatotopic representation of foot, hand and face movements in the contralateral left putamen, and the duration of illness correlated with the somatotopical distortion in the putamen.8

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REFERENCES

29. Slotnick SD, Moo LR. Prefrontal cortex hemispheric specialization for categorical and coordinate visual spatial memory. Neuropsychology 2006; 44:1560–8.
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