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ORIGINAL ARTICLE

Musical training intensity yields opposite effects on grey matter density in cognitive versus sensorimotor networks

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Abstract Using optimized voxel-based morphometry, we performed grey matter density analyses on 59 age-, sex- and intelligence-matched young adults with three distinct, progressive levels of musical training intensity or expertise. Structural brain adaptations in musicians have been repeatedly demonstrated in areas involved in auditory perception and motor skills. However, musical activities are not confined to auditory perception and motor performance, but are entangled with higher-order cognitive processes. In consequence, neuronal systems involved in such higher-order processing may also be shaped by experience-driven plasticity. We modelled expertise as a three-level regressor to study possible linear relationships of expertise with grey matter density. The key finding of this study resides in a functional dissimilarity between areas exhibiting increase versus decrease of grey matter as a function of musical expertise. Grey matter density increased with expertise in areas known for their involvement in higher-order cognitive processing: right fusiform gyrus (visual pattern recognition), right mid orbital gyrus (tonal sensitivity), left inferior frontal gyrus (syntactic processing, executive function, working memory), left intraparietal sulcus (visuo-motor coordination) and bilateral posterior cerebellar Crus II (executive function, working memory) and in auditory processing: left Heschl's gyrus. Conversely, grey matter density decreased with expertise in bilateral perirolandic and striatal areas that are related to sensorimotor function, possibly reflecting high automation of motor skills. Moreover, a multiple regression analysis evidenced that grey matter density in the right mid orbital area and the inferior frontal gyrus predicted accuracy in detecting fine-grained incongruities in tonal music.

Keywords Musical training · Voxel-based morphometry · Grey matter density · Plasticity · Cognition · Sensorimotor function

Introduction

Plasticity of the brain, its ability to structurally and functionally adapt in response to environmental demands, relies importantly on the nature and intensity of its use (Blakemore and Frith 2005).

Musical expertise is a rising star amongst topics investigating experience-driven brain plasticity (Pantev and

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Herholz 2011; Wan and Schlaug 2010; Jancke 2009) for two reasons. First because mastering a musical instrument fosters a panoply of intricately linked sensorimotor (Zatorre et al. 2007; Schneider et al. 2002) and higher-order cognitive functions (Oechslin et al. 2012; Schulze et al. 2011; Sluming et al. 2007). Second because musical expertise levels vary continuously from people solely exposed passively to musical stimuli in their environment, to highly trained expert performers.

The latter aspect has not been investigated extensively in neuroscience research on musicians' brain plasticity. Hence, the major interest of the present study resides in the fact that we studied whole-head grey matter differences as a function of three strictly controlled, distinct and progressive levels of musical expertise. In contrast to musicians versus non-musicians comparisons, including an intermediate level of proficiency allows identifying brain regions that are susceptible to progressive experience-driven neural adaptations.

Grey matter structural differences between the brains of musicians and non-musicians are known to manifest inter alia in the cerebellum (Hutchinson et al. 2003; Schlaug et al. 1995), primary auditory cortex (Schneider et al. 2002, 2005; Bermudez and Zatorre 2005), and primary and associative motor areas (Gaser and Schlaug 2003; Schlaug 2001; Hyde et al. 2009). Such structural adaptations appear to be intimately related to functional adaptations (Schneider et al. 2002; Zatorre et al. 2012).

As already stated, musical perception and execution are not limited to auditory processing and sensorimotor function, but also involve higher-order cognitive, mnemonic and attentional mechanisms (Janata et al. 2002b; Oechslin et al. 2012). Processing of musical syntax requires profound knowledge and comprehension of musical structure as well as keeping track of the short- and long-term musical context (Oechslin et al. 2012). Expert musicians encode, manipulate, and retrieve information differently compared to non-experts (Williamon et al. 2002). Musicians demonstrated faster updating of auditory and visual working memory representations compared to non-musicians (George and Coch 2011). Instrumental performance also relies strongly on attentional focus (Janata et al. 2002b; Williamon et al. 2002). Therefore, experience-driven brain plasticity may not only modulate central auditory and motor processing but also neuronal systems involved in higher-order processing. Advantages with respect to higher-order cognitive functioning as a consequence of musical expertise have been shown previously for verbal working memory (Chan et al. 1998), executive control (Bialystok and Depape 2009), linguistic perception abilities (Moreno et al. 2009) and spatio-temporal reasoning (Rauscher et al. 1997).

Structural neuroplasticity seems to follow the law "more skill, more grey matter" (Gaser and Schlaug 2003; Sluming et al. 2002; Draganski et al. 2004; Hyde et al. 2009). However, new evidence exists that training and ensuing expertise sometimes induce local decrease of cortical volume (Granert et al. 2011; Hanggi et al. 2010). Skill acquisition provokes synaptic enhancement in frequently used connections that are strengthened whereas infrequently used connections are eliminated through pruning (Kanai and Rees 2011; Zatorre et al. 2012). In ballet dancers (Hanggi et al. 2010) as well as skilled pianists (Granert et al. 2011), striatal volume decreased with increasing motor function efficiency.

Given this background, we searched here for both positive and negative structural neural correlates reflecting stepwise increase in musical expertise. We performed regression analyses on whole-head grey matter density as a function of musical training intensity in three groups of young adults (non-musicians, amateur and professional "expert" pianists) matched for sex, age, age of training onset and fluid intelligence. We could verify the progressive increase in musical expertise of the groups by means of behavioural data from a recent functional MRI study (Oechslin et al. 2012) in which the same groups of subjects participated. The in-scanner task consisted in detection of refined multi-level musical transgressions.

According to the above-mentioned findings, we expected to observe progressive changes in grey matter density as a consequence of musical training in auditory and motor function related brain areas as well as in regions hosting universal functions of working memory and attention. We merely anticipated increases, but expected to possibly replicate findings reporting reduction of grey matter density with increasing musical skill in striatal areas. Because both musician groups were classically schooled pianists, we also anticipated some instrument-specific adaptations.

We could also establish relationships between grey matter density data from the current study, and behavioural in-scanner and fMRI results from the same group of participants (Oechslin et al. 2012). Zatorre et al. (2012) recently emphasized that brain function and structure are dynamically linked and advocated that searching for network-level patterns in anatomical structures is plausible. We hypothesized that grey matter density in areas involved in higher-order cognitive processing may predict behavioural results of music syntactic processing.

Methods

Participants

Fifty-nine volunteers gave written informed consent to take part in this experiment and received financial compensation. All participants were right-handed according to the

Edinburgh Inventory (Oldfield 1971), reported normal hearing and presented no history of neurological illnesses. The protocol was approved by the local ethics committee.

Groups consisted of 20 professional pianists (experts; 24.5 ± 4.5 years; 10 women), 20 amateur pianists (amateurs; 22.2 ± 3.1 years; 11 women) and 19 non-musicians (non-musicians; 24.0 ± 4.5 years; 9 women). The groups were matched for gender and age (one-way ANOVA on age $F_{2,56} = 2.2$, $p = 0.12$). No significant group differences existed for fluid intelligence (Raven's Advanced Progressive Matrices Set II; Raven et al. 2003; $F_{2,58} = 1.2$, $p = 0.31$). One supplementary non-musician was removed from the analysis, because of a data acquisition artefact. Experts were mainly advanced conservatory students but also established artists or teachers, who received their training at the Conservatoires of Geneva, Lausanne, Paris and Zurich. Almost all non-musicians and amateurs were students at the Universities of Geneva and Lausanne. Two exceptions occurred, one non-musician was a young university professor, and the youngest amateur was still in secondary education (final year). Inclusion/exclusion criteria were the following: non-musicians should not have received any extracurricular musical education and never have practised a musical instrument; piano practice of amateurs should never have exceeded 10 h training per week and their musical practice should have been continuous from childhood until the moment of testing; the latter condition of course also applied to the experts.

Musicians (amateurs and experts) should have started their piano practice at the age of ten at the latest. Amateurs started studying the piano at 7.0 ± 1.4 years, experts at 6.2 ± 1.9 years; age at beginning of practice was not significantly different between the two musician groups ($t_{38} = 1.5$, $p = 0.19$). By means of a questionnaire we assessed individual training intensity in different age brackets (in years: 6–8, 8–10, 10–12, 12–14, 14–16, 16–18, 18–25). For the first two periods (6–8, 8–10) we found no significant differences in reported training intensity between amateurs and experts, whereas the subsequent periods revealed a pattern of consistently increasing training lag of amateurs compared to experts (Table 1).

Table 1 Training intensities of amateur and expert pianists reported in mean (±SD) number of hours/week (h/w) within consecutive age brackets

Training intensity			
Age bracket	A (h/w)	E (h/w)	*t* values
6–8	3.0 (±1.9)	3.1 (±1.7)	t_{26}: 1.1
8–10	3.5 (±0.5)	4.2 (±0.5)	t_{38}: 1.1
10–12	4.0 (±2.3)	6.5 (±4.3)	t_{38}: 2.7*
12–14	4.7 (±2.6)	9.0 (±5.3)	t_{38}: 3.3**
14–16	5.3 (±3.2)	14.8 (±7.7)	t_{38}: 5.1***
16–18	4.7 (±2.2)	19.9 (±9.3)	t_{38}: 7.1***
18–25	4.8 (±2.6)	30.7 (±8.5)	t_{38}: 12.4***

Groups were not yet complete in the first age bracket

Differences were assessed by *t* tests (two-tailed) for each bracket, asterisks indicate level of significance: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

All subjects also participated in an fMRI study reported in Oechslin et al. (2012). This in-scanner behavioural task is described at the end of this Methods session in "Behavioural measures". The results from this task allowed verifying the progressive increase in musical expertise of the groups.

Data acquisition and analysis

We recorded a T1-weighted 3-D gradient-echo structural image for each individual (MPRAGE, TE = 2.27 ms, TR = 1900 ms, flip angle = 9°, FOV = 256 × 256 mm, slice thickness = 1 mm, inversion time (TI) = 900 ms, voxel size = 1 × 1 × 1 mm, intensity correction with Prescan Normalize) on a 3-tesla MRI scanner (Siemens TIM-TRIO, Erlangen, Germany). Data analysis was performed with statistical parametric mapping software (SPM8, Welcome Department of Imaging Neuroscience, London, UK).

The pre-processing pipeline for the voxel-based morphometry (VBM) analyses comprised the following steps. Brain tissue was segmented into grey matter (GM), white matter (WM) and cerebrospinal fluid (CSF) using the new segment procedure of SPM8. This tool represents an improved version of the default unified segmentation method (Ashburner and Friston 2005). Images were transformed nonlinearly to standard MNI space using the diffeomorphic registration algorithm (DARTEL) implemented in SPM8 (Ashburner 2007). GM probability maps were then "modulated" by the Jacobian determinants of the deformations to account for local compression and expansion due to linear and non-linear transformations (Good et al. 2001). In a final step, modulated GM probability maps were smoothed with an isotropic Gaussian kernel of 8-mm full width at half maximum (FWHM).

Based on behavioural results from exactly the same participants in a musical expectation violation detection test (Oechslin et al. 2012) in which amateurs demonstrated an intermediate level of performance between experts and non-musicians, we modelled musical expertise as a three-level regressor (non-musicians = 1; amateurs = 2; experts = 3) to study possible linear relationships between musical expertise and grey matter density (GMD). We corrected for differences in total intra cranial volume (sum of GM, WM and CSF, computed with the SPM extension easy volume) and age, integrating covariate vectors for these two variables into the regression model (Ridgway et al. 2008). In order to include only relatively homogeneous voxels, and to exclude possible edge effects around the grey and white matter borders, we excluded all voxels with GMD values below 0.2 of the maximum value. We then performed a linear regression analysis (Analysis I) on GMD with the expertise vector as predictor and studied positive (GMD increase) and negative (GMD decrease) effects of expertise.

Subsequently, we extracted mean first eigenvariates (EVs) for all brain clusters exhibiting significant positive or negative effects of expertise (outcome of Analysis I) for each individual. The extraction of these EVs from the GMD values of the significant clusters was computed independently, and not adjusted to the linear regression model of Analysis I. EVs were extracted with SPM8 by means of singular value decomposition; they provide one GMD value for each cluster for each individual. SPM extracts the EVs for a cluster, rather than the mean values, because the former are more robust and resistant to heterogeneity of response distribution within all voxels of a cluster. We used these EVs to determine, which of these brain clusters were the best predictors for two different behavioural measures, via multiple linear regression analyses (Analysis II) separately for positive and negative effects of expertise. The behavioural task that yielded both behavioural measures is described below. A multiple regression analysis determines which predictors among several best predict a certain variable and thus enables the ranking of predictors according to their relative predictive influence on that variable.

Behavioural measures

We used two behavioural measures as dependent variables for Analysis II collected from the same participant group (Oechslin et al. 2012) during an event-related sparse temporal sampling ("silent") fMRI protocol, optimal for the presentation of auditory stimuli (Hall et al. 1999). Thirty original polyphone expressive musical stimuli[1] were presented in pseudo-randomized order at three levels of syntactical transgression at musical closure: regular, subtly transgressed and apparently transgressed endings. An example of a stimulus at all transgression levels is provided in the supplementary material, as well as musical scores and corresponding sound files.

Participant's appraisals consisted in expressing whether end formulas (cadences) were correct, yes or no, by means of button presses. From these binary results we computed d-prime values (Macmillan and Creelman 1997) for, respectively, the appraisals of subtly (T^{sub}) and apparently (T^{app}) transgressed musical end formulas (see "Results"; Table 2). The d-prime index is a statistic derived from signal detection theory (Macmillan and Creelman 1997) and provides an index of rater sensitivity: higher d-prime values indicate that the transgressed ending was better detected.

For details on the experimental task and materials, and for details on the fMRI study as well as complete results please see Oechslin et al. (2012).

Results

Behavioural results (Oechslin et al. 2012)

An ANOVA on d-prime values (see Table 2) with the factors expertise (3, between) and transgression (2, within) yielded significant main effects for expertise and transgression, as well as significant interaction between the two factors: expertise: $F_{56.2} = 51.4$, $p < 0.001$; transgression: $F_{56.1} = 210$, $p < 0.001$; expertise × transgression $F_{56.2} = 13.6$, $p < 0.001$ (data from Oechslin et al. 2012; cf. "In scanner behavioural results").

In order to verify the intermediate position of the amateurs for these behavioural results, a test consisting of two combined difference contrasts (non-musicians = −1, amateurs = 1, experts = 0 and non-musicians = −0, amateurs = −1, experts = 1) confirmed the intermediate position of the amateurs both for T^{sub} ($F_{56,2} = 51.9$, $p < 0.001$) and T^{app} ($F_{56,2} = 39.2$, $p < 0.001$). Figure 1 illustrates the intermediate position of the amateurs for d-prime for T^{sub}, T^{app} and for mean d-prime of both transgressions.

VBM results

Anatomical labels were assigned according to cytoarchitectonic probabilities using the SPM anatomy toolbox (Eickhoff et al. 2007).

Table 2 Mean d-prime values (±SD) or rater sensitivity of non-musicians (N), amateurs (A) and experts (E) for subtle transgressions (T^{sub}) and apparent transgressions (T^{app}) of end-formulas in expressive music

Rater sensitivity	Expertise		
	N ($n = 19$)	A ($n = 20$)	E ($n = 20$)
d-prime T^{sub} (mean ± SD)	0.4 ± 0.7	1.2 ± 0.8	3.0 ± 0.9
d-prime T^{app} (mean ± SD)	1.4 ± 1.2	3.5 ± 1.2	4.2 ± 0.6
Mean d-prime $T^{sub} - T^{app}$ (mean ± SD)	0.9 ± 0.9	2.3 ± 0.9	3.6 ± 0.7

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[1] The compositions were electronic versions of specifically composed string quartets with a duration of approximately 10 s. The musical pieces were prepared with the "Sibelius" software (Avid Technology, Inc.) and "Logic Pro" (Apple Inc.); instrumental timbres were implemented using the "Garritan Personal Orchestra" (Garritan).

Analysis I

The linear regression analysis (Analysis I) on GMD with expertise (non-musicians = 1; amateurs = 2; experts = 3) as predictor, corrected for age and total intracranial volume, executed with SPM8 yielded the following results (Fig. 2).

Positive effects of expertise

A positive effect of expertise implies here a stepwise increase in GMD as a function of the three degrees of expertise and thus that GMD was highest in professional musicians or experts, intermediate in amateur musicians, and lowest in non-musicians (red clusters in Fig. 2). All brain clusters with such significant stepwise increase are summarized in Table 3. Statistical significance was threshold at $p < 0.001$ (unc.) and only clusters with a minimum of 30 voxels were retained.

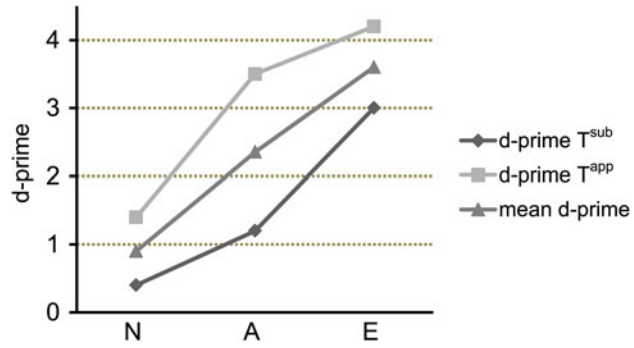

Fig. 1 Mean d-prime values for responses to end-formulas in expressive music of non-musicians (N), amateurs (A) and experts (E) for subtle transgressions (T^{sub}) in *dark grey*, apparent transgressions (T^{app}) in *light grey* and mean d-prime for both transgressions in intermediate *grey*

At the initial threshold of $p < 0.001$ (unc.), there was no evidence of enhanced GMD in the primary auditory cortex/Heschl's gyrus. However, many important studies demonstrated grey matter volumetric increases in this area (Bermudez et al. 2009; Bermudez and Zatorre 2005; Gaser and Schlaug 2003; Schneider et al. 2002, 2005). In order to verify whether our regression model could show stepwise increase in GMD in auditory cortices as a function of expertise, we executed supplementary regression analyses, using the same three-level regressor, in two regions of interest: the left and right superior temporal gyri, now with a more liberal threshold of $p < 0.005$ (unc.) and again a minimum cluster size of 30 voxels. The regions of interest were extracted using the AAL atlas (automated anatomical labelling (Tzourio-Mazoyer et al. 2002), via the Pickatlas toolbox implemented in SPM8.

Positive effects (Table 3) in cortical areas exhibited, respectively, in a small cluster in the medial posterior part of the right fusiform gyrus (peak effect), in the right mid (medial) orbital gyrus, in the left inferior frontal gyrus (this cluster extends from the pars triangularis into more medial regions in the anterior insula; see Fig. 2d.4.) and in the left inferior parietal lobule, more precisely in the grey matter of the anterior intraparietal sulcus.

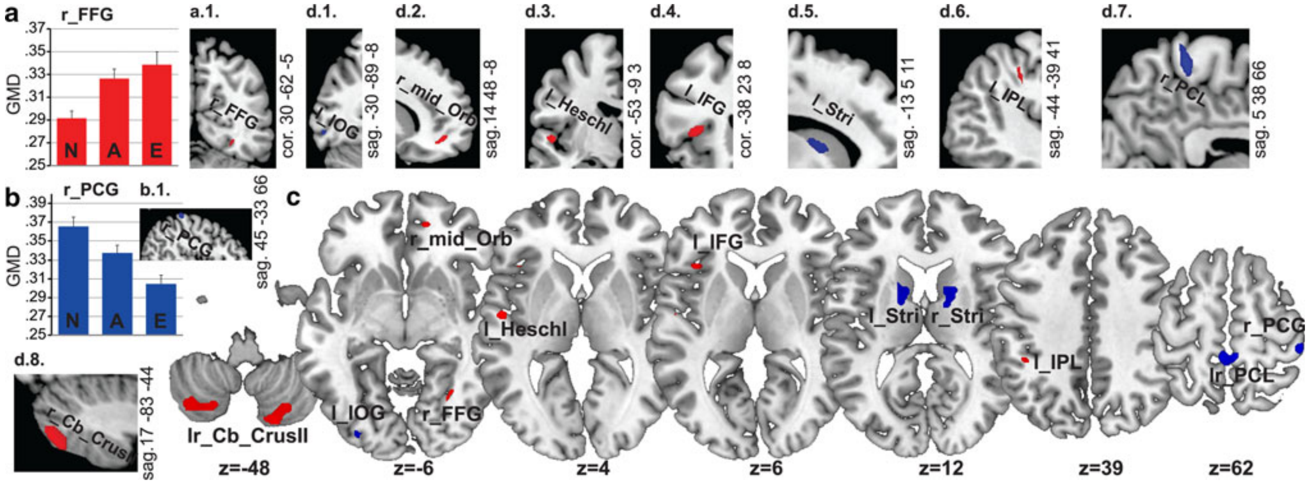

Fig. 2 Brain clusters with significant positive (*red*) and negative (*blue*) effects of expertise on GMD ($p < 0.001$, unc., $k = 30$; only for l_Heschl $p < 0.005$, unc., $k = 30$). **a** Positive peak effect in r_FFG, *a.1.*, detailed view of r_FFG in coronal orientation. **b** Negative peak effect in r_PCG. *b.1.*, detailed view of r_PCG in sagittal orientation. **c** All other positive and negative effects of expertise shown on axial slides at seven different z levels. **d**.*1.–8.* Detailed views of all other areas showing positive and negative effects of expertise. MRI coordinates and orientations are provided vertically. Orientations: *cor.* coronal, *sag.* sagittal. Positive effects: r_FFG, right fusiform gyrus; r_mid_Orb, right mid orbital gyrus; r_Cb_CrusII, right cerebellum Crus II; l_IFG, left inferior frontal gyrus; l_IPL, left inferior parietal lobule; l_Cb_CrusII, left cerebellum Crus II; l_Heschl, left Heschl's gyrus. Negative effects: r_PCG, right postcentral gyrus; l_PCL, left paracentral lobule; r_Stri, right striatum; l_IOG, left inferior occipital gyrus; l_Stri, left striatum

Table 3 Significant clusters with increased GMD as a function of expertise, identified by a regression analysis (Analysis I) corrected for intracranial volume and age

Regions	Voxels	T_{max}	Z_{max}	MNI coord. peak voxel		
r_FFG	35	4.05	3.77	30	−62	−5
r_mid_Orb	74	3.87	3.62	14	48	−8
r_Cb_CrusII	537	3.83	3.59	17	−83	−44
l_IFG	83	3.82	3.58	−38	23	8
l_IPL	49	3.66	3.45	−44	−39	41
l_Cb_CrusII	388	3.66	3.44	−35	−68	−47
l_Heschl	81	3.03	2.90	−53	−9	3

Anatomical labels (MNI coordinates of peak voxels) are provided. Expertise was defined as a 3-level regressor (non-musicians = 1, amateurs = 2; experts = 3). Only clusters with a minimum of 30 voxels were retained

Statistical significance was threshold at $p < 0.001$ (unc.). The last cluster in Heschl's gyrus was threshold at $p < 0.005$ (unc.)

r_FFG right fusiform gyrus, *r_mid_Orb* right mid orbital gyrus, *r_Cb_CrusII* right cerebellum Crus II, *l_IFG* left inferior frontal gyrus, *l_IPL* left Inferior parietal lobule, *l_Cb_CrusII* left cerebellum Crus II, *l_Heschl* left Heschl's gyrus

Table 4 Significant clusters with decreased GMD as a function of expertise, identified by a regression analysis (Analysis I) corrected for intracranial volume and age

Regions	Voxels	T_{max}	Z_{max}	MNI coord. peak voxel		
r_PCG	120	4.92	4.46	48	−33	66
l_Prec/l_PCL	432	4.35	4.02	−5	−41	66
r_Prec/r_PCL				5	−38	66
r_Stri	235	3.92	3.66	18	5	9
l_IOG	40	3.79	3.56	−30	−89	−8
l_Stri	237	3.52	3.33	−15	5	11

Anatomical labels (MNI coordinates of peak voxels) are provided. Expertise was defined as a 3-level regressor (non-musicians = 1, amateurs = 2; experts = 3). Only clusters with a minimum of 30 voxels were retained

Statistical significance was threshold at $p < 0.001$ (unc.)

r_PCG right postcentral gyrus, *l_Prec* left precuneus/l_PCL left paracentral lobule, *r_Stri* right striatum, *l_IOG* left inferior occipital gyrus, *l_Stri* left striatum

Positive effects in cerebellar areas manifested in large bilateral clusters in the posterior lobe, in Crus II of Lobule VIIa.

The supplementary region of interest analysis in the left and right superior temporal gyrus yielded significant results in the left primary auditory cortex, namely in the anterior lateral area of Heschl's gyrus or Te 1.2 (Morosan et al. 2001).

Negative effects of expertise

A negative effect of expertise implies here a stepwise decrease in GMD following the three degrees of musical expertise and thus that GMD was lowest in experts, intermediate in amateur musicians, and highest in non-musicians (blue clusters in Fig. 2). All brain clusters with such significant stepwise decrease are summarized in Table 4.

Negative effects manifested, respectively, in the right postcentral gyrus (peak effect), in bilateral precuneus/paracentral lobule, left inferior occipital gyrus and bilateral striatal areas.

The peak voxel was found in the right postcentral gyrus (assigned to sensory area 1 according to Eickhoff et al. 2007). The bilateral paracentral clusters reached, in their most rostral and medial extents, the borders of the precuneus, and more anteriorly the paracentral lobules (assigned to area M1-4a according to Eickhoff et al. 2007). These regions are situated on the junction between the most anterior part of the precuneus and the primary motor cortex (M1). The precuneus and M1 are adjacent (on both sides of the central sulcus) in the most medial part of the brain.

The bilateral striatal clusters encompassed parts of the caudate nucleus, the borders of the putamen, as well as grey matter tissue stripes within white matter regions in between those two nuclei (see Fig. 2c, d.5.). These grey matter strands, at the origin of the name of this region, cannot be appreciated on MRI templates, but can be clearly visualized in sections of the human brain at the level of a coronal plane passing through the anterior commissure (Duvernoy 1991, pp. 226–227). All brain areas that showed positive and negative effects of expertise are depicted encompassing their peak voxels in Fig. 2c, more extensive representation of significant voxels is provided in Fig. 2d.1.–8. for all brain clusters.

Analysis II

For each participant, we extracted one mean first eigenvariate (EV) for each brain cluster that gave rise to significant increase or decrease of GMD as a function of expertise in Analysis I. These EVs were implemented in multiple regressions analyses as predictors for behavioural results, respectively, for d-prime of T^{sub} (subtle syntactic transgression) and T^{app} (apparent syntactic transgression; see "Methods" section), separately for positive and negative effects of expertise.

Residuals were normally distributed for all regression equations. One outlier in the expert group was excluded from the analyses. The results from both multiple regression analyses for T^{sub} and T^{app} for areas manifesting positive effects of expertise are provided in Table 5. Both multiple regression equations were highly significant (top lines of Table 5), so all brain clusters together predicted the behavioural outcomes (d-prime for T^{sup} and T^{app}, respectively) very well. For T^{sub}, two individual brain clusters within the model predicted the behavioural outcome significantly: the right mid orbital gyrus and left inferior frontal gyrus (i.e. pars triangularis and anterior insula). In these areas, increased GMD resulted in significantly better detection of T^{sub}. For T^{app} not one individual cluster predicted behaviour significantly; however, the right mid orbital gyrus reached marginal significance. Results from both multiple regression analyses for, respectively, T^{sub} and T^{app} for areas manifesting negative effects of expertise are provided in Table 6. Again both equations were highly significant (top lines of Table 6). At the level of individual regions, only the left inferior occipital gyrus predicted the behavioural outcome of both T^{sub} and T^{app}. For this area, less GMD resulted in better performance.

Discussion

The key finding of this study resides in the observed functional dissimilarity between areas showing increase versus decrease of grey matter density (GMD) as a function of musical expertise. Progressive increase of GMD as a consequence of expertise manifested in several cortical areas known to be involved in higher-order cognitive processing, primary auditory processing and in bilateral posterior cerebellar areas also implicated in cognitive behaviour. Increase in GMD as a function of musical expertise in the fusiform gyrus and in posterior cerebellar areas has not been evidenced before.

Table 5 Results of two multiple regression analyses with as predictors all significant brain clusters with positive effect of expertise (outcome Analysis I, cf. Table 3) for (a) dependent variable d-prime T^{sub} (subtle transgression) and (b) dependent variable d-prime of T^{app} (apparent transgression)

Predictor	Beta	SEM (beta)	t (50)
(a) Regression summary for dependent variable T^{sub}; $F_{7,50} = 5.12$***; $R^2 = 0.39$			
r_FFG	0.24	0.12	1.94
r_mid_Orb	**0.28**	**0.11**	**2.46***
r_Cb_CrusII	0.18	0.17	1.05
l_IFG	**0.28**	**0.12**	**2.32***
l_IPL	0.14	0.12	1.19
l_Cb_CrusII	−0.07	0.18	−0.39
l_Heschl	0.16	0.12	1.34
(b) Regression summary for dependent variable T^{app}; $F_{7,50} = 3.80$**; $R^2 = 0.35$			
r_FFG	0.16	0.13	1.27
r_mid_Orb	0.23	0.12	1.91^{o}
r_Cb_CrusII	0.22	0.18	1.20
l_IFG	0.17	0.13	1.34
l_IPL	0.18	0.12	1.41
l_Cb_CrusII	0.03	0.19	0.16
l_Heschl	0.11	0.13	0.85

In the top panels the results for the full regression equations are reported. Below beta coefficients, standard error of mean (SEM) for beta coefficients and corresponding t values for the individual predictors are reported

Dependent variable T^{sub} d-prime subtle transgression; *SEM* standard error of mean

Significant results are plotted in bold font

Asterisks indicate level of significance: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$, ^{o} $p < 0.07$

Table 6 Results of two multiple regression analyses with as predictors all significant brain clusters with negative effect of expertise (outcome Analysis I, cf. Table 4) for (a) dependent variable d-prime T^{sub} (subtle transgression) and (b) dependent variable d-prime of T^{app} (apparent transgression)

Predictor	Beta	SEM (beta)	t (53)
(a) Regression summary for dependent variable T^{sub}; $F_{5,52} = 6.61$***; $R^2 = 0.39$			
r_PCG	−0.16	0.13	−1.23
lr_Prec/PCL	−0.10	0.13	−0.72
r_Stri	−0.19	0.21	−0.90
l_OG	**−0.37**	**0.12**	**−3.17****
l_Stri	−0.13	0.22	−0.62
(b) Regression summary for dependent variable T^{app}; $F_{5,52} = 8.14$***; $R^2 = 0.44$			
r_PCG	−0.19	0.13	−1.52
lr_Prec	−0.16	0.13	−1.30
rStri	−0.07	0.21	−0.35
l_IOG	**−0.45**	**0.11**	**−4.00*****
l_Stri	−0.13	0.21	−0.63

In the top panels the results for the full regression equations are reported. Below beta coefficients, standard error of mean (SEM) for beta coefficients and corresponding t values for the individual predictors are reported

Dependent variable T^{sub} d-prime subtle transgression, *SEM* standard error of mean

Significant results are plotted in bold font

Asterisks indicate level of significance: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

In contrast, decreases were found principally in sensorimotor function related areas. Reduction of GMD exhibited in perirolandic cortical areas and subcortical areas in the striatum, possibly induced by ruling out of non-pertinent movement and proprioceptive feedback relative to piano performance, resulting in greater efficiency and automation, thus increasing virtuosity. Such cortical and subcortical sensorimotor function related GMD reduction adds a new perspective on cerebral reorganisation with increasing motor skill.

We suggest that these findings are the consequence of our well-defined group categorizations that allowed observing progressive changes of GMD with stepwise increasing expertise as a consequence of specific training.

The homogeneity of all groups used here and more specifically the similarity of training experiences shared by the two pianist groups may have induced the revelation of more refined differences. Diverse training experiences might have masked these findings.

Analysis I

Positive effects of expertise

The peak effect was found in the right fusiform gyrus (FFG), known for its implication in symbolic processing through visual form recognition (Koutstaal et al. 2001). Lesion studies (Leff et al. 2001) as well as functional imaging (Price and Mechelli 2005) evidenced that the left posterior FFG plays an important role in reading. Prime-target pairs of orthographically related words produced a neural priming effect in the left FFG that decreased if the prime-target pairs were semantically related (Price and Mechelli 2005). This result suggests that the FFG not just stores visual word forms but rather acts as an interface between visual form information and higher-order stimulus characteristics such as associated sound and meaning (Devlin et al. 2006). This function is not specific to text reading, but may be engaged in the processing of any meaningful visual stimulus (Devlin et al. 2006), and prone to plastic changes. Musically untrained adults who learned to read music and play the piano over a period of 3 months showed learning-related functional changes in the fusiform gyrus (Stewart 2005). Musicians trained from early childhood relied more on the left posterior fusiform gyrus for mathematical processing (addition and subtraction of fractions) than non-musicians (Schmithorst and Holland 2004). The fact that we found right-sided increase in GMD can be explained by the fact that the right cerebral hemisphere may retain more specific visual form information than the left, which may store more abstract lexical-semantic representations (Koutstaal et al. 2001). A music expert directly links music notation to sound (Behmer and Jantzen 2011). In conclusion, we suggest that the increase in GMD in the right fusiform area with increasing expertise may reflect the acquisition of abstract musical score representations and their sound associations through progressive training. Among instrumentalists' scores, those of pianists are among the most complex.

The second cortical effect manifested in an area in the right mid orbital gyrus. No consensus seems to exist concerning the specific functions of this area. It is reported to be involved in self-referential judgement (Denny et al. 2012), in cognitive control of emotion (Ochsner et al. 2009), in metamemory (prediction of memory success, Do Lam et al. 2012) and in tracking of tonality in western tonal music (Janata et al. 2002a). It is also presumed to be part of the default network (Kim 2012) that is active during most internally oriented mental activities. We would like to adopt the interpretation by Petr Janata (Janata et al. 2002a; Janata 2005) concerning the function of this area as a "nexus of cognitive, affective and mnesic processing", with a specific sensitivity for the tracking of changes in tonality in western tonal music. That such an area develops its GMD with intensive musical training seems plausible, specifically in pianists that play polyphonic music all the time. Analysis II underpinned this presumption, as GMD in this area best predicted the detection of syntactical transgressions in tonal music.

Another important cortical effect was increased GMD in the left inferior frontal gyrus in a cluster extending from the pars triangularis into the anterior insula. Possible explanations for GMD enhancement in this area are twofold. In the first place both pars triangularis and anterior insula are well known for their role in syntactic processing of language and music (Friederici 2002; Koelsch et al. 2001; Nan and Friederici 2012; Tillmann et al. 2006). In analogy, grey matter volume increase in Broca's area (pars opercularis) could be evidenced via VBM in professional male orchestra musicians (Sluming et al. 2002). Secondly, increase of grey matter volume in these regions could also reflect enhanced general cognitive function in musicians, encompassing processes such as top-down attention and working memory (Janata et al. 2002b; Schulze et al. 2011). In conjunction with this, anterior insula activation can express stimulus driven perceptual demand (Sterzer and Kleinschmidt 2010). In a visual 3-back working memory task with letters (Oechslin et al. 2012), in which the same participant group as in the current experiment participated, the expert musicians outperformed the two other groups. This is not surprising, as attentional and working memory loads are high during musical performance. To summarize, increased GMD in the inferior frontal cortex with expertise may thus represent experience-driven brain adaptation allowing musicians to optimally retain and interpret complex auditory stimuli, in highly demanding attentional contexts such as on stage musical performance.

Moreover, in our associated fMRI study, (Oechslin et al. 2012) bilateral anterior insulae (ant_INS) were activated differentially as a function of expertise and degree of syntactical transgression (interaction effect expertise x transgression). In Fig. 3, the overlap of these functional and the here analyzed structural results in the left hemisphere are shown. In the fMRI study, subtle transgressions (T^{sub}) activated the ant_INS more strongly with increasing expertise; apparent transgressions (T^{app}) induced the opposite effect. For details on the contrasts used in this fMRI study we refer to the original communication (Oechslin et al. 2012). This result suggests that local

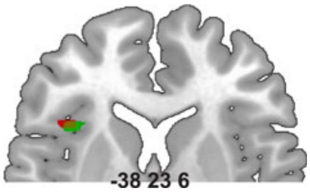

Fig. 3 Overlap of functional results (in *green*; interaction expertise × transgression) from Oechslin et al. (2012) and structural results of the present study (in *red*) in the left inferior frontal cortex. The MRI coordinate is provided

structure of grey matter as assessed by voxel-based morphometry is intimately linked to cognitive behaviour as shown before (Kanai and Rees 2011; Schneider et al. 2002).

Then, increased cortical density was observed in the left anterior intraparietal sulcus (IPS), whose functions are related to perceptual motor coordination (Simon et al. 2002). An increase in grey matter density in the left posterior IPS could be demonstrated using VBM in a longitudinal study on the plastic effects of juggling training (Draganski et al. 2004). Accordingly, although inferior parietal areas were activated during both real and imagined piano performance, the IPS exhibited significantly stronger BOLD responses during music performance compared to imagined musical behaviour (Meister et al. 2004). Furthermore, the IPS has been identified as a critical structure for note reading (Schön et al. 2002; Stewart et al. 2003). Therefore, both visuo-motor coordination (hand-keyboard) during performance and music score reading or “translating” music notation into sound may have contributed to the gradual expansion of GMD with expertise in this area.

The supplementary regression analyses in left and right superior temporal lobes demonstrated increase of GMD with expertise in the left primary auditory cortex, more precisely in the anterior lateral area of Heschl’s gyrus or Te1.2 (temporal cortical area 1.2; Morosan et al. 2001; Eickhoff et al. 2007). The observation that GMD increases with musical aptitude in the primary auditory cortex confirms the literature on enhanced grey matter volume in the primary auditory cortices of musicians (Bermudez et al. 2009; Bermudez and Zatorre 2005; Gaser and Schlaug 2003; Schneider et al. 2002, 2005), and can be easily explained by musical practice. In a population of non-musicians, amateur musicians and professional musicians, Schneider et al. (2002) evidenced bilateral increases in grey matter in Heschl’s gyrus with increasing musical aptitude that could be associated with stepwise differences in strength of MEG responses to sinusoidal tones. Gaser and Schlaug (2003) and the current study found exclusively left-sided enhancement. These left-sided findings do not tally well with the literature proposing that right auditory cortex may subserve fine grained pitch (frequency) processing, specifically of musical stimuli (Zatorre et al. 2002). Several studies report bilateral or right-sided enhancement of grey matter in musicians in this area (Bermudez et al. 2009; Bermudez and Zatorre 2005; Schneider et al. 2002). It is possible that our regression model comprising two groups of pianists with different levels of expertise accounts for this left-sided observation. Instrumentalists that play percussive instruments (piano, trumpet, drums etc.), so-called “fundamental pitch listeners” showed enhanced grey matter volume in left Heschl’s gyrus (Schneider et al. 2005), which is sensitive to rapid temporal processing (Zatorre et al. 2002). Gaser and Schlaug (2003) also examined exclusively keyboard players.

Bilateral cerebellar cortex exhibited massive increase of GMD with expertise in bilateral Crus II of lobule VIIa. Traditionally the cerebellum has been associated to motor function (Ito 2002). This seems a plausible explanation in the present context: increased GMD with increasing pianistic virtuosity. Nevertheless, a thorough reading of recent literature on cerebellar function rejects this point of view. Distinct loops exist between cerebellum and cortex for, respectively, cognitive and motor function. Functional neuroimaging in combination with diffusion-weighted MRI (Salmi et al. 2009) revealed that the posterior cerebellum (Crus I and II), which is connected to lateral prefrontal areas, was activated by cognitive load increase in a nonverbal auditory memory task; in contrast, the anterior cerebellum (lobules V/VI), known to be involved in sensorimotor function, was not. An analysis on resting state functional connectivity observed the same dissociation: a primary sensorimotor zone (lobules V, VI and VIII) could be distinguished from a supramodal zone (lobules VIIa, Crus I, and II). The cortical connectivity of the supramodal zone was driven by areas of frontal and parietal cortex that are not directly involved in sensorimotor functioning (O’Reilly et al. 2010). A meta-analysis (53 studies) on cerebellar function concluded that language and executive tasks activated regions of Crus I and lobule VII supposed to be engaged in prefrontal-cerebellar loops (Stoodley and Schmahmann 2009); these authors thus also suggest an anterior sensorimotor versus posterior cognitive/emotional dichotomy in the cerebellum. We conclude that the increased GMD in bilateral Crus II observed here, thus, reflects improved working memory and executive function. As stated with respect to the inferior frontal cortex increase above, attention and working memory loads are high during musical performance.

Negative effects of expertise

We observed a decrease of GMD in sensorimotor areas, in the right postcentral gyrus (sensory area 1; Eickhoff et al.

2007), bilateral paracentral lobule (comprising the precuneus and also M1-4a; Eickhoff et al. 2007) and bilateral striatum. M1-4a represents an area of secondary motor execution that actively participates in complex sensorimotor processing; its activation depends thus on a feedback system (Nakada et al. 2000). M1-4a even responds to sensory stimulation without involving in actual motion (Wilson et al. 2004). Conversely, M1-4p is rather involved in initiation of movement, and does not respond to sensory stimulation (Terumitsu et al. 2009). While learning to play an instrument; visual, proprioceptive and auditory feedbacks are essential, but with increasing skill, these external cues are no longer necessary (Krings et al. 2000), and can even become a nuisance and hamper smooth automatized sensorimotor function. Motor skill acquisition and mastery manifest according to principles of economy: chunking complex behaviour into compact units diminishes the number of degrees of freedom. With enhanced skill, fewer neurons are recruited for the same movements, which show a decrease in movement variability, and less effort is necessary for their execution, allowing musicians to progressively dedicate their attention to artistic goals rather than sensorimotor ones (Krings et al. 2000; Jancke et al. 2000). Finally, internally generated movement deriving from a forward model gives rise to motor-induced suppression of sensory cortical feedback (Aliu et al. 2009).

The striatum also follows this principle of parsimony. In professional ballet dancers a reduction in putaminal GMD compared with control subjects could be evidenced. Granert et al. (2011) also observed that the basal ganglia deviate from the rule “the more volume, the higher the level of skill”. Better timing of key stroke, characterising skill level of piano playing, could be associated with less grey matter volume in the putamen of pianists compared to healthy non-musician controls, whereas an increase of GMD manifested in pianists suffering from musician’s dystonia.[2] Apparently high movement skill reduces the importance of striatal movement control. Models describing this focusing of cortico-basal ganglia-thalamo-cortical loops that strengthen relevant cortical inputs while suppressing irrelevant ones have been described in the past (Mink 1996, 2003; Bar-Gad et al. 2003). Our study demonstrates a GMD decrease in the border region of the putamen, but more clearly in the caudate nucleus, as well as in their connections passing through the internal capsule. Chess experts, who also depend on quick automatized responses like expert musicians, also manifested a reduced volume in the caudate nucleus (Duan et al. 2012). This phenomenon also manifested in other board games and skills (Wan et al. 2011; Poldrack et al. 2005). In accordance, we show for the first time a stepwise GMD decrease in the caudate nucleus with musical aptitude.

Finally, the cluster in the left inferior occipital area that also displayed decrease in GMD with expertise is virtually the same that was found less activated in musicians in the right hemisphere, during math processing relative to non-musicians (Schmithorst and Holland 2004). Interestingly the same study found increased activation in the fusiform area. The authors explained the decreased activation in the inferior occipital area as a habituation effect, a practice effect shown before in the context of visuospatial working memory and stimulus repetition (Garavan et al. 2000; Koutstaal et al. 2001). We suppose that pianists, following intensive daily practice, rely on the fusiform gyrus for decoding complex musical scores and, therefore, recruit the secondary visual areas less, resulting in a decrease of GMD.

Analysis II

The first multiple regression analysis using all brain clusters with positive effects of expertise as predictors for T^{sub} (subtle transgression) revealed that the right mid orbital gyrus cluster best explained sensitivity (d-prime). This strengthens our hypothesis that this area is implicated in tracking of tonality (Janata et al. 2002a), a faculty that demands mnesic, cognitive and also affective processing. It is through changes of tonality that western classical composers induced affect over the centuries. This affective processing may manifest as a form of relevance detection, as is also suggested for the amygdala in certain contexts (Ousdal et al. 2008). We suggest that such relevance detectors play an important role in the dynamic context of stage performance and allow a professional to quickly adapt in incongruous musical situations due to individual or contextual errors (James et al. 2008). Second best in explaining sensitivity for T^{sub} was the left inferior frontal gyrus cluster. This result stresses the importance of this area for syntax processing, in conjunction with our functional imaging results (Oechslin et al. 2012). The latter study evidenced increase of activation with expertise in the bilateral anterior insulae for T^{sub} in an area that overlaps in the left hemisphere with positive effect of expertise of the current study (see Fig. 3). Detection of these subtle transgressions increased with expertise (see Fig. 1).

The second multiple regression analysis using all brain clusters with positive effects of expertise as predictors for T^{app} (apparent transgression) did not reveal any significant results for individual predictors. The right mid orbital gyrus cluster best explained sensitivity (d-prime) again, but this effect was only marginally significant.

The third and fourth regression analyses using all brain clusters with negative effects of expertise as predictors for,

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[2] Musician’s dystonia or focal dystonia is a neurological disorder that affects muscle control in specific often overtrained areas.

respectively, T^{sub} and T^{app} indicated that one area present among the predictors, the left inferior occipital gyrus, predicted accuracy significantly in a negative way: less GMD in this area correlated with higher d-prime values. This intriguing finding may be related to the increase of GMD in the right fusiform area with expertise. Complex score reading, essential for pianists, may progressively induce specific pattern recognition with increasing expertise in the right fusiform gyrus, consequently reducing involvement of more basic visual areas. Therefore, the reduction of GMD in occipital areas may indirectly reflect enhanced pattern recognition, subserving score reading but possibly also musical syntactical processing, operated in the fusiform gyrus.

Comparison to the literature

A similar study also using VBM showed different, but equally plausible results (Gaser and Schlaug 2003). These authors also acquired rapid acquisition gradient echo scans, with the same voxel sizes, although on a 1.5 T scanner versus a 3T scanner here. They also applied VBM; although not using Dartel tools, or New Segment that did not exist at the time, and used a larger smoothing kernel before applying statistics (12 FWHM vs. 8 FWHM here). They also investigated non-musicians, amateur and expert pianists, with groups of the same size, but only male participants. Statistical analyses were similar (three level expertise regressor), although different statistical thresholds and cluster sizes were applied. First, GMD increase in the cerebellum exhibited in anterior sensorimotor regions, whereas we found increase in posterior cerebellar areas linked to executive function. These differences in cerebellar areas may be explained by the presence of 50 % of women in our sample. Only in men, not in women, an increase of relative and absolute cerebellar volume has been observed between musicians and non-musicians (Schlaug 2001; Hutchinson et al. 2003). Therefore, the presence of women in our sample may have masked possible effects of musicianship in motor function related areas of the cerebellum as found in men by Gaser and Schlaug (2003). Like in the current study, left Heschl's gyrus, left inferior frontal gyrus and right medial frontal gyrus showed enhanced GMD with increased musical expertise. However, Gaser and Schlaug (2003) found strong GMD increase in perirolandic areas, whereas we found decrease. The explanation resides, in our opinion, in the choice of the participants, namely our highly controlled and unique inclusion/exclusion criteria that shed a new light on training-induced grey matter plasticity. We could verify by means of behavioural results that the amateur group was well situated between non-musicians and experts thus legitimating a linear model. In the above-mentioned study, the group of professional musicians practiced at least 1 h a day; in our expert group the mean was almost 5 h per day. Our amateurs practiced almost an hour per day (see Table 1). Therefore, the degree of automaticity and skill of motor performance in our musician groups was enhanced in all likelihood. Intensity of practice can be associated with degree of automaticity and associated with decreased activation in sensorimotor areas (Poldrack et al. 2005). Practice strongly influences long-term retention of motor skills (Dayan and Cohen 2011). A longitudinal study with a group of established expert pianists indicated that daily practice time exceeding 3.75 h or more induced an improvement in a specific motor skill. The authors concluded that even in established expert pianists, maintenance of motor skills is strongly influenced by current practice quantity (Jabusch et al. 2009). This observation can be generalized; amount of deliberate practice is closely related to performance level in musicians (Ericsson et al. 1993; Sloboda et al. 1996), chess players (Charness et al. 1996) and athletes (Starkes et al. 1996).

Limitations

A limitation of our study is that the macroscopic level of our analyses prevents us from drawing any conclusions on the nature of the underlying microscopic mechanisms. Moreover, the cross-sectional design prevents us from discriminating learning effects from genetic or epigenetic factors (Zatorre et al. 2012). Only longitudinal studies beginning in childhood can distinguish nature and nurture in a musician population.

Finally, our findings are restricted to the population studied here, namely classically schooled pianists.

Conclusion

The brain generates behaviour, and is in turn modified by the behaviour it produces (Pascual-Leone 2001). The present study yielded intriguing functional dissimilarity between areas exhibiting increase versus decrease of grey matter with musical expertise. A network of higher-order cognitive-function related areas increased in volume, whereas a network of sensorimotor function related areas showed decrease. Apparently, more resources are available for higher-order music processing with increasing expertise; in contrast the development of motor skill is accompanied by progressive ruling out of non-pertinent movement and sensory feedback relative to piano performance, resulting in greater efficiency and automation, thus increasing virtuosity.

We also established links between brain structure and function in our participants. In the first place GMD in the right mid orbital gyrus and the left inferior frontal gyrus (pars triangularis and anterior insula) significantly predicted accuracy in detecting fine-grained incongruities in tonal music. Second, an area in the inferior frontal cortex with increased GMD as a function of musical expertise overlapped anatomically with an activation cluster of a preceding functional study (Oechslin et al. 2012), in which the same participants detected musical incongruities. These results suggest that local structure of grey matter as assessed by voxel-based morphometry is intimately linked to cognitive behaviour.

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