Musical literacy shifts asymmetries in the ventral visual cortex

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ABSTRACT

The acquisition of literacy has a profound impact on the functional specialization and lateralization of the visual cortex. Due to the overall lateralization of the language network, specialization for printed words develops in the left occipitotemporal cortex, allegedly inducing a secondary shift of visual face processing to the right, in literate as compared to illiterate subjects. Applying the same logic to the acquisition of high-level musical literacy, we predicted that, in musicians as compared to non-musicians, occipitotemporal activations should show a leftward shift for music reading, and an additional rightward push for face perception. To test these predictions, professional musicians and non-musicians viewed pictures of musical notation, faces, words, tools and houses in the MRI, and laterality was assessed in the ventral stream combining ROI and voxel-based approaches. The results supported both predictions, and allowed to locate the leftward shift to the inferior temporal gyrus and the rightward shift to the fusiform cortex. Moreover, these laterality shifts generalized to categories other than music and faces. Finally, correlation measures across subjects did not support a causal link between the leftward and rightward shifts. Thus the acquisition of an additional perceptual expertise extensively modifies the laterality pattern in the visual system.

Introduction

The ventral visual stream hosts a set of regions preferentially responding to one category of objects more than to others. The Fusiform Face Area (FFA) responds preferentially to faces (Kanwisher et al., 1997), the Visual Word Form Area (VWFA) to strings of letters (Cohen et al., 2000), the Parahippocampal Place Area (PPA) to places and buildings (Epstein and Kanwisher, 1998), etc. Such category-selective areas vary in their distribution across the two hemispheres. Some of the homologous regions show similar profiles of object selectivity, as for instance the left- and right-hemispheric versions of the PPA. Yet, the overall symmetry of the ventral stream is broken for two major category-specific regions, the VWFA and the FFA, which show strong lateralization biases to the left (Cohen et al., 2002) and to the right (Rossion et al., 2012; Yovel et al., 2008), respectively. A rightward bias for faces exists already in 4-to-6-month-old infants (Heering and de Rossion, 2015), long before the acquisition of literacy (Le Grand et al., 2003). It has been suggested that an additional rightward push of face processing results from the later acquisition of literacy, possibly as a consequence of competition of the FFA with the newly developed left-hemispheric VWFA (Behrmann and Plaut, 2015; Dehaene et al., 2010, 2015). In the present study, we assess the impact on functional lateralization in the ventral stream of expertise for music reading, a form of perceptual expertise in many respects comparable to word reading.

The main cause of the asymmetry of visual regions is thought to be the asymmetry of distant networks to which they provide an input (Cai et al., 2008; Mahon and Caramazza, 2011; Pinel and Dehaene, 2010). This hypothesis has been mostly documented in the case of reading. Indeed, the VWFA collateralizes with language areas, particularly Broca's area and the posterior superior temporal sulcus (pSTS) (Cai et al., 2010, 2008; Pinel and Dehaene, 2010; Pinel et al., 2015; Van der Haegen et al., 2012). A similar process may be at play for the lateralization of the FFA, as a set of remote regions specifically activated during face processing are also right-lateralized (Rossion et al., 2012). In addition to this driving factor, the lateralization of ventral visual regions may be modulated by interactions among them, possibly involving competition for cortical space. Supporting evidence

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Table 1
Demographic information on the group of controls and professional musicians. Means and standard deviations are given for numerical variables. The third column indicates statistical difference between groups (using a chi-square test for the first row, and Wilcoxon rank sum tests for the others). In addition, there were no statistical differences between the ages when musicians learnt to read words and music (Wilcoxon signed rank test V=50.5, p=0.12), or between the ages when they started to practice and read music (V=54, p=0.95).

	Controls	Musicians	Group comparison
Number of women / men	9 / 11	10 / 10	χ^2 = 0.10, p = 0.75
Age (years)	30.9 (± 10.8)	32.8 (± 10.4)	W = 159.5, p = 0.28
Years of education	14.7 (± 1.8)	15.7 (± 1.9)	W = 134.5, p = 0.07
Age when learning to read words	5.2 (± 0.9)	4.9 (± 1.3)	W = 222, p = 0.54
Age when learning to read music		5.9 (± 2.9)	
Age when learning to play music		5.9 (± 2.2)	
Years of music practice		26.2 (± 9.6)	
Main instrument played	Violin (6), Piano / Keyboard (5), Oboe (3), Cello (3), Trumpet (1), Clarinet (1), Viola (1)		

comes from Dundas and colleagues who showed that left-hemifield preference for faces, an index of right-hemispheric dominance, emerges from childhood to adulthood, and is positively correlated with reading competence. This behavioral finding was paralleled by a right shift of the N170 potential evoked by faces. The link between lateralization for faces and words was further supported by the correlation observed in children between the N170 for faces over the RH and for words over the LH (Dundas et al., 2013, 2014). Congruent evidence also comes from the comparison of literate and illiterate adults. Illiterates fail to show the typical right-lateralization of the FFA (Dehaene et al., 2010), and reading proficiency correlates positively with the activation level in the right FFA, while it is negatively correlated with the activation to faces in the left VWFA (Dehaene et al., 2010, 2015). In addition, left handers lack on average both the left-lateralization of the VWFA (Van der Haegen et al., 2012) and the right-lateralization of the FFA (Bukowski et al., 2013) supporting the existence of a link between those two features. In left-handers, all face-selective areas other than the FFA show the same right-lateralization as in right-handers, suggesting that the atypical lateralization of the FFA might result from reduced competition with the VWFA within the visual cortex (Dundas et al., 2015). Finally, dyslexic children show both an hypoactivation of the VWFA in the left and of the FFA in the right hemisphere, as compared to normal readers (Monzalvo et al., 2012).

In exploring the impact that the acquisition of musical literacy may have on functional lateralization in the ventral visual cortex, we will consider the contribution of the two factors we just discussed, namely the lateralization of distant cortical networks, and the interaction between specialized ventral areas. More specifically, we derived two predictions from the above overview.

First, in the same way as the lateralization of distant language areas drive that of the VWFA in literate subjects, ventral activations to music stimuli should be biased by functional lateralization in distant regions involved in music expertise. Although the traditional view of an overall left-lateralization of expert musical abilities may be an oversimplification (Bever and Chiarello, 1974), various aspects of musical expertise do recruit predominantly left-hemispheric networks, unlike music processing in non-experts. This is the case for musical reading by professional musicians, which, compared to other visual stimuli and to musically naïve subjects, activates a left predominant fronto-parietal network (Mongelli et al., 2017). Accordingly, impairments of music reading results exclusively from left-hemispheric lesions (Hébert and Cuddy, 2006). A leftward asymmetry also prevails with auditory (Habibi et al., 2013; Matsui et al., 2013; Ono et al., 2011) and motor (Bangert et al., 2006; Pa and Hickok, 2008) components of musical expertise. Our first prediction was therefore that ventral activations to music stimuli should be left-lateralized in musicians, and more so than in musically naïve subjects.

Second, would the tuning of the visual cortex to music reading modify the lateralization of other category-selective regions, in the same way as the development of the VWFA shifts face-related activations to the right? Mongelli et al. (2017) showed that group-level

activations for music and words in the occipitotemporal cortex were largely overlapping. However, individual analyses revealed that activations for music peaked significantly posterior and lateral to activations for words, and had a larger volume in musicians than in controls. Thus, category-selective activations to music being close to activations to words, we predicted that they may interact similarly with neighboring areas. Specifically, our second prediction was that music reading should team up with word reading, resulting in a stronger right-hemispheric shift of face processing in professional musicians as compared to controls.

To assess these predictions, we studied the lateralization pattern of ventral activations in professional musicians and musically naïve controls, as they viewed five different categories of visual objects (words, faces, musical scores, houses, and tools). Changes in asymmetry were assessed both by using a laterality index over a ventral occipitotemporal region of interest (ROI), and by deriving asymmetry maps in order to preserve spatial resolution.

Material and methods

Participants

Twenty-one adult musicians (12 men) and 23 musically naïve controls (13 men) took part in the experiment. Both groups were matched in gender and age. All participants were right-handed according to the Edinburgh inventory (Oldfield, 1971). Musicians were either professional musicians or masters' students at one of the most prestigious music schools in France (CNSM, *Conservatoire de Musique et de Danse de Paris*). They varied in their type of musical practice, but they all started learning to read both words and music around the age of 5/6 years old (words: 4.9, music: 5.9, V=50.5, p > 0.1). One musician and three controls were found to be right lateralized for language (see below), and were excluded from further analyses, resulting in a final cohort of 20 musicians and 20 controls. Table 1 provides detailed information on the final cohort.

Stimuli

We used five categories of black and white pictures: faces, tools, houses, pairs of words, music scores (Fig. 1A). Each category contained 38 pictures. All stimuli were black line drawings on a white background. Faces, houses and tools were derived from highly contrasted gray-level photographs matched for size and overall luminance. Faces (17 females, 21 men) were front or slightly lateral views of non-famous people. Houses comprised outside pictures of houses and buildings. Tools were common hand-held household objects (e.g. knife, hair-dryer) presented in a normal orientation. The faces, tools, and houses images used here were used in previous studies in order to map category selectivity in the occipitotemporal cortex (Dehaene et al., 2010; Gaillard et al., 2006; Pegado et al., 2014; Pinel et al., 2015; Thirion et al., 2007). Music notation corresponded to one bar of
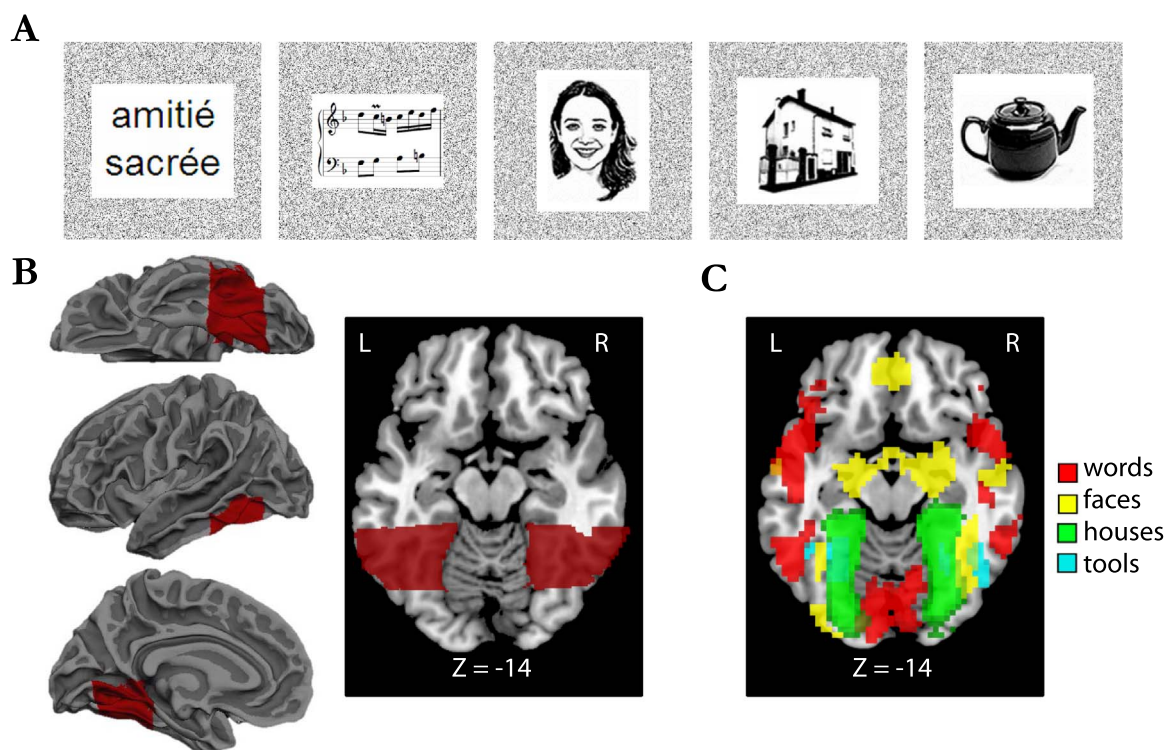
Fig. 1. A – Exemplar stimuli for each of the five categories presented: word pairs, music scores, faces, houses and tools. B – Mask of the ventral stream used for the computation of laterality indices (LIs) in the ROI-approach. C – Group activations for words, faces, houses and tools (controls and musicians together, voxel p < 0.001, cluster FWE p < 0.05, each category is contrasted to the other three categories).

classical piano music (G and F clefs), containing no alphabetic symbol. They were extracted from the "Mutopia project" database (http://www.mutopiaproject.org/), and selected from Mozart, Bach and Beethoven pieces. Pairs of words were semantically congruent adjective plus noun pairs (e.g. "*amitié sacrée*", "*sacred friendship*"), written in lower-case, both 6-letters long and of high lexical frequency (http://lexique.org). Music scores were 100 pixel wide × 71 pixel high, word pairs were 108 pixel wide×87 pixel high, faces were 86 pixel wide×108 pixel high, houses were 108 pixel wide×96 pixel high, tools were 107 pixel wide × 102 pixel high. All images were padded with random visual noise to reach a size of 300 × 300 pixels (7°×7° of visual angle).

Experimental design

Using E-Prime software, subjects were presented with an alternation of blocks of pictures and blocks of rest. They were asked to perform a repetition detection task, i.e. to press a button with their right thumb whenever a picture was identical to the previous one.

Each stimulation block included eight pictures from one category of stimuli (total duration: 8 s). Each trial consisted of a picture displayed for 600 ms, followed by a 400 ms blank screen. Repetitions occurred for 20% of trials (50% of blocks had 1 repetition, 33% had 2 and 17% had 3). During rest blocks (7.8 s) and inter-trial intervals, a central fixation cross remained present in order to minimize eye-movements. The experiment included 10 s of initial rest, followed by 30 blocks of pictures (six for each category) and 30 blocks of rest. Blocks were presented in pseudorandom order to maximize the variety of transitions between categories while avoiding repetition of the same condition in successive blocks.

Behavioral results

There was no difference between repetition detection (hit) rates between musicians and controls for all categories (mean hit rates per group and category higher than 93%) but music. Musicians were

more proficient than controls in detecting repetition with music scores (p = 0.025).

Full results are reported in Mongelli et al. (2017).

fMRI acquisition and analyses

We used a 3-Tesla MRI (Siemens Trio) with a 32-channel head coil, and a multiband echo-planar imaging sequence sensitive to brain oxygen-level-dependent (BOLD) contrast (54 contiguous axial slices, 2.5 mm isotropic voxels, in-plane matrix = 80 × 80; TR = 1160 ms; angle = 62°, TE = 25 ms). 420 volumes were acquired. The first four volumes were discarded to reach equilibrium. Five additional BOLD volumes with reverse phase encoding direction were also acquired. Functional images were realigned, treated with the FSL "topup" toolbox in order to correct EPI distortions due to B0 field inhomogeneity, normalized to the standard MNI brain space and spatially smoothed with an isotropic Gaussian filter (3 mm FWHM). A two-level analysis was then implemented in SPM8 software (http://www.fil.ion.ucl.ac.uk/spm/software/spm8/).

For each participant, data were high-pass filtered and modelled by regressors obtained by convolution of the five experimental conditions plus the button presses with the canonical SPM haemodynamic response function. Individual contrast images for the five types of stimuli minus rest were smoothed with an isotropic Gaussian filter (2 mm FWHM) to take into account between-subject differences in functional anatomy, and entered into a second-level whole-brain ANOVA with subjects as random factor, stimulus category as within-subject factor, and musical status as between-subject factor.

Univariate results both at the group and the individual levels were described in Mongelli et al. (2017).

Lateralization analyses

The lateralization of ventral stream activations to each category of visual stimuli, and the differences in lateralization between musicians

and controls were assessed using both an ROI approach, and a voxel-based approach.

Symmetrical MNI template

In order to allow for inter-hemispheric comparisons and correct for deformation biases induced by known structural asymmetries (Didelot et al., 2010), we derived a symmetrical anatomical template from the MNI template by successive iterations of flipping, coregistering and averaging. Specifically, we first flipped the MNI template along the x-axis, and summed the flipped and original MNI to create a symmetrical image (symMNI). We then coregistered the original MNI and flipped MNI images on symMNI, and averaged these two images creating cMNI. Finally, we flipped this last image, and computed the mean of cMNI and flipped cMNI to obtain the final symmetrical template (sMNI).

Laterality indices in a ventral ROI

Laterality Indices (LIs) were computed within an anatomical mask of the ventral stream using the LI toolbox in SPM8 (Wilke and Lidzba, 2007) for each individual and each contrast.

Mask. The mask of the ventral stream included the inferior occipital, inferior temporal, fusiform, lingual and parahippocampal gyri of both hemispheres from the AAL atlas (Tzourio-Mazoyer et al., 2002). The mask was truncated to keep only regions extending roughly between MNI y=−70 and y=−35, encompassing most of group-level activations to houses, music, words, and faces (Fig. 1). However, given that borders on the y-axis are not equivalent in MNI template, the mask of included gyri was transformed to our symmetrical MNI template (sMNI), truncated at sMNI y=−70 and −35 (included), and transformed back into MNI space.

Because we excluded from the mask lateral occipital cortex where category-specific activations for tools and objects lie, the mask is not appropriate to investigate the laterality of tool activations. Their asymmetry patterns will be reported but not discussed.

Computation of laterality indices. For a given contrast, LIs were computed for each individual based on the magnitude of signal change defined by the t-values, using the general formula for laterality indices:

$$LI = \frac{\sum activation_{left} - \sum activation_{right}}{\sum activation_{left} + \sum activation_{right}}$$

The LI toolbox was used with the default bootstrap option: for each individual and contrast, 10,000 LI indices were calculated over multiple statistical thresholds and by bootstrapping at each step (Wilke and Schmithorst, 2006). More specifically, at each threshold, one vector of t-values from the voxels surviving the threshold within the mask is obtained for each hemisphere (note that the number and location of voxels may differ between hemispheres). The two vectors are then bootstrapped separately 100 times to obtain 100 LIs based on the formula above. The first and last quartiles of these 100 LIs are trimmed. These indices (50 LIs per threshold) are then summarized across thresholds into an overall weighted bootstrapped LI. For each participant and for each contrast of interest, we thus obtained a robust laterality index ranging from −1 (complete lateralization to the right) to 1 (complete lateralization to the left).

The LI toolbox was used with the default bootstrapping option, entering the ROI described in the previous section as an inclusive mask, and with the default option to exclude all voxels within 5 mm of the midline from the computation of LIs (notably due to the smoothness of the data and blurring across hemispheres).

Because the obtained LIs were not normally distributed and had many outliers, we chose to perform non-parametric rank tests:

Wilcoxon rank sum tests to compare LIs between groups, Wilcoxon signed rank test to compare LIs within each group to zero, the Scheirer Ray Hare test for rank ANOVAs, and Kendall's τ to assess correlations. Statistics were performed in R (https://www.r-project.org), using the 'coin' library to obtain effect sizes for Wilcoxon tests (https://cran.r-project.org/web/packages/coin/index.html). Effect sizes for the Wilcoxon rank sum tests were obtained using Rosenthal's formula r=Z/√(N) where N is the total number of observations - here 40 (Rosenthal et al., 1994).

Exclusion of participants with atypical language lateralization. The LI toolbox was also used to identify participants atypically lateralized for language. LIs were obtained for the contrast of words minus the average of faces, houses, and tools, in a mask of Broca's area including the pars opercularis and triangularis of the Inferior Frontal Gyrus (IFG). Three control participants and one musician were identified as right lateralized (LI ≤ −0.25) and therefore excluded. LIs for other participants ranged from 0.17 to 0.93.

Voxel-based approach: asymmetry maps

In order to investigate the differences in lateralization in the ventral stream with higher spatial accuracy, we created asymmetry maps for each participant and each contrast in a symmetrical template, by subtracting the activity in the right hemisphere from the activity in the left hemisphere.

For each participant, we flipped the normalized anatomical image (original MNI space). We then computed the spatial transformations appropriate to align both the original and flipped anatomical images to the sMNI template. For each functional contrast of interest, we applied these transformations respectively to the functional contrast volume and to its flipped counterpart. Finally, for each contrast, we subtracted the flipped contrast from the original one in sMNI space to obtain an individual asymmetry map.

All transformations were performed using nonlinear registration in SPM8, using the default parameters. Specifically, a 8 mm-FWHM Gaussian spatial smoothing was applied to the source image, a first affine registration was computed using 12 parameters (affine regularization in ICBM space template), and followed by a nonlinear transformation (nonlinear frequency cutoff: 25, number of nonlinear iterations: 16, nonlinear regularization parameter: 1).

Asymmetry maps for each contrast were then entered in a second-level whole-brain ANOVA to investigate the separate voxelwise effects of musical literacy on the asymmetry of contrasts of interest. Subjects were entered as a random factor, stimulus category as a within-subject factor, and musical status (musician vs. control) as a between-subject factor.

Figures report asymmetry maps either in MNI space (slices), after transformation from the symmetrical MNI template to the original MNI template, or projected onto the FreeSurfer average brain surface (with an additional transformation to Freesurfer average brain). We chose to report MNI coordinates of asymmetry results using the MNI coordinates of a given peak in the left hemisphere. The conjunction analysis of differences between musicians and controls in asymmetry maps across all categories was performed in SPM (Friston et al., 2005). Unless stated otherwise, we used a voxelwise threshold of p < 0.001 with a clusterwise threshold of p < 0.05 with family-wise error (FWE) correction for multiple comparisons.

ROI vs. voxel-based approaches

We chose to use both the ROI and voxel-based approaches as they allow for a complementary investigation of asymmetries. The ROI approach has the advantage of summarizing the asymmetry of a given functional contrast as one single index over the ROI. It is resistant to issues of matching homologous voxels across cerebral hemispheres at

the individual level, and of matching anatomy across individuals. Additionally, iterations across statistical thresholds, as well as the bootstrapping of voxel values at each threshold, allows for the computation of robust indices, with a higher weighting of voxels with the highest levels of activations. On the opposite, the voxel-based approach allows for a much higher spatial resolution, but it is less powerful due to normalization issues and higher number of statistical comparisons. Also, a value is obtained in each voxel regardless of its functional relevance to the task.

Functional contrasts used in laterality analyses

The two laterality assessment methods were applied both to category-specific contrasts, comparing activations to one category versus the others, and to the activations of each category versus rest. Because of differences in musical expertise between groups, music was not included in the baseline in category-specific contrasts. Because of the high similarity of activations to musical notations and words, words were also removed from the baseline of the music-specific contrast. Category-specific contrasts hence consisted in: {words − (faces, houses, tools)}, {music − (faces, houses, tools)}, {faces − (words, houses, tools)}, {houses − (words, faces, tools)} and {tools − (words, faces, houses)}. They are further referred to as the word-, music-, face-, house- and tool- specific contrasts.

Results

Asymmetry of category-specific activations

To investigate differences between professional musicians and controls in the asymmetry of ventral visual activations, we first applied the ROI and voxel-based approaches to category-specific activations (activation to one category vs. the others), following the view of the ventral pathway as a set of regions with distinct category selectivity.

Laterality Indices

The analysis of LIs in the ventral ROI revealed typical patterns of lateralization in both groups (see Fig. 2). There was a strong leftward bias for words (controls: mean LI = 0.53, Wilcoxon signed rank tests: V=209, $p < 10^{-3}$; musicians: mean LI = 0.58, V = 209, $p < 10^{-3}$), and a rightward bias for faces (controls: mean LI = −0.27, V = 6, $p < 10^{-4}$; musicians: mean LI = −0.43, V = 5.5, $p < 10^{-3}$). For music, activations were left-lateralized in musicians (mean LI = 0.24, V = 192.5, p = 0.0016) but did not deviate from symmetry in controls (mean LI = −0.03, V = 89, p =
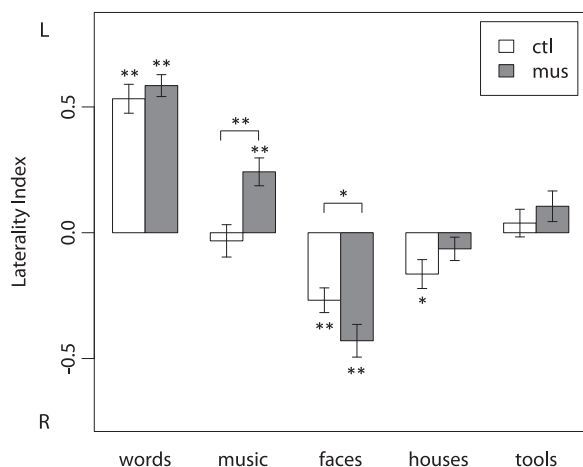
Fig. 2. : Laterality Indices of category-specific activations (each category minus the others) in the ventral stream ROI (mean ± s.e.m.) for controls (ctl, white bars) and musicians (mus, gray bars). Positive (resp. negative) indices reflect a left-hemispheric (resp. right-hemispheric) advantage. Musicians had left-lateralized music-specific activations, and more so than controls. Their face-specific activations were more right-lateralized. **: p < 0.01; *: p < 0.05.

0.56). House activations were right lateralized in controls (mean LI = −0.16, V = 36, p = 0.01) but not in musicians (mean LI = −0.06, V = 70.5, p = 0.20). There was no hemispheric bias for tool-specific activations in both groups (controls: p = 0.55, musicians: p = 0.10). The comparison of musicians and controls revealed a stronger leftward bias for music (Wilcoxon rank sum test: W = 95.5, effect size r = 0.45, p = 0.004) and a stronger rightward bias for faces (W = 279, r = 0.34, p = 0.03) in musicians. No group difference was observed for the lateralization of words (p = 0.34), houses (p = 0.15) and tools (p = 0.52). Thus, this first analysis supported both our predictions on the lateralization of music and faces processing.

Asymmetry maps

We then moved to the study of asymmetry maps for the same category-specific activations within the ventral region. In both musicians and controls, the voxel-based results were in good agreement with the LI indices presented before (Fig. 3, first two columns). For words, both groups showed extensive left-lateralization spanning the fusiform gyrus (FG), the occipito-temporal sulcus (OTS) and the inferior temporal gyrus (ITG), consistent with the typical left-lateralization of the visual word form system. For faces, both groups showed right-lateralization in the fusiform and OTS regions. For houses, there was also a marked right lateralization in both groups. For tools, a left-hemispheric advantage was observed for controls in lateral occipital cortex, but no significant asymmetry was found in musicians. Finally, asymmetry maps for musical notations showed a cluster with a leftward lateralization in both groups, extending from the OTS and ITG to the middle temporal gyrus (MTG).

On inspection, there was some suggestion of larger asymmetries in musicians than in controls for words and music to the left, and to the right for faces. However differences in asymmetry maps between groups did not reach significance for cluster size in the ventral pathway. At a lower voxelwise threshold (p < 0.01), we only found a fusiform cluster more right-lateralized for faces in musicians, which passed small volume correction for multiple comparison in the ventral ROI used for LIs (FDR q < 0.05; Fig. 3, third column and additional slice).

In summary, the analysis of category-specific ventral activations using laterality indices showed that activations to music were more left-lateralized, and that activations to faces were more right-lateralized in musicians than in controls. However, beyond suggesting that the right shift for faces originated in the fusiform region, voxelwise analyses did not show significant group differences. Moreover, the leftward shift of LIs for music in musicians was associated with a left shift in distant perisylvian areas (Fig. 4), including Broca's pars opercularis, the superior frontal gyrus and motor cortex, the postcentral and supramarginal gyri, as well as the intraparietal sulcus and the occipitoparietal junction. We also observed more left-lateralized word-specific activations in musicians in the posterior superior temporal sulcus (STS). There was no significant asymmetry difference between groups for the other visual categories, including faces.

Asymmetry of activations vs. rest

We next moved to the study of asymmetries using rest as a baseline common to all contrasts. This step is required, as the analysis of category-specific activations may miss group differences in asymmetry which are common to all or several categories of stimuli, and therefore subtracted by the baseline. This could explain the lack of significant group differences in the above analysis. Conversely, group differences derived from category-specific contrasts may in principle be contaminated by differences in the categories included in the baseline.

Laterality Indices

The ROI approach showed the same overall pattern of lateralization for activations vs. rest as with category-specific contrasts. Activations were left-lateralized for words in both groups (controls: mean LI =
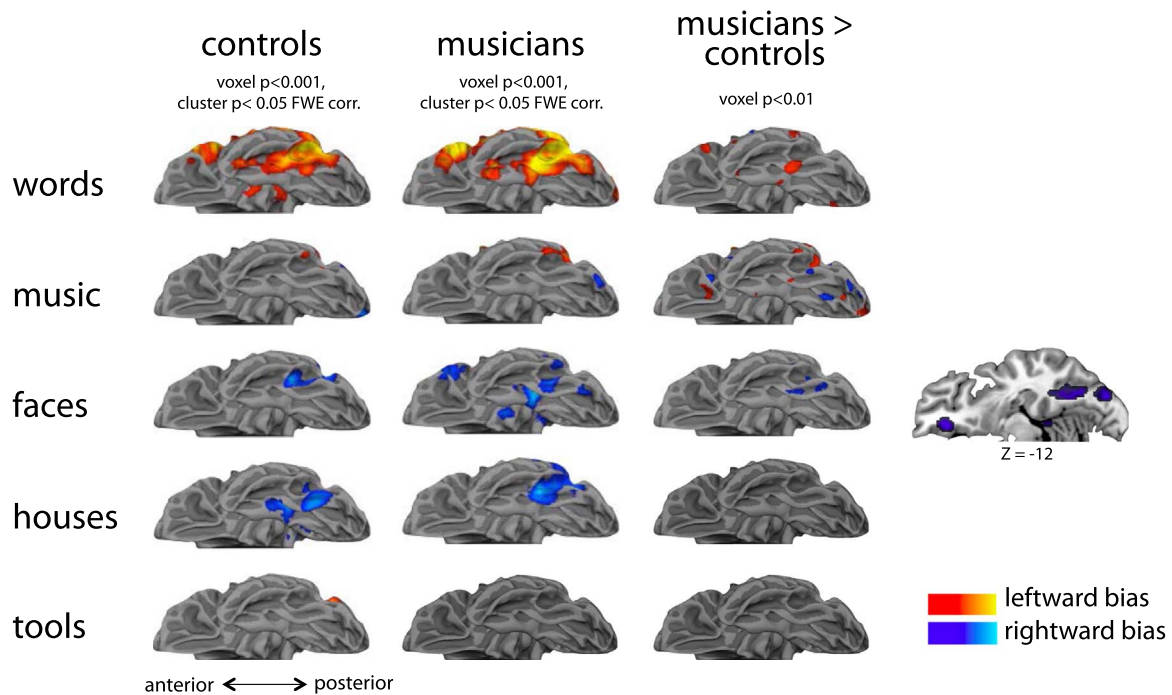
Fig. 3. : Asymmetry maps of category-specific activations (each category minus the others). Ventral surfaces are displayed for each category (rows), for controls (first column), musicians (second column) and musicians > controls (third column and additional slice). Hot and cool colors represent leftward and rightward asymmetry, respectively. Group differences were not significant, although uncorrected maps suggested marginally more left-lateralized activations for music and right-lateralized activations to faces, in musicians than controls.

0.20, Wilcoxon signed rank tests: V = 173, p = 0.012; musicians: mean LI = 0.38, V = 210, p < 10^{-4}); and right-lateralized for faces (controls: mean LI = −0.20, V = 10, p < 10^{-3}; musicians: mean LI = −0.15, V = 40.5, p = 0.017) (see Fig. 5). Controls had right-lateralized activations to music and houses (music: mean LI = −0.15, V = 25.5, p < 0.01; houses: mean LI = −0.20, V = 10, p < 10^{-3}), and a marginal rightward advantage for tools (mean LI = −0.10, V = 56.5, p = 0.073). No significant asymmetry was observed in musicians for these three categories (music: p = 0.21; houses: p = 0.37; tools: p = 0.48), and noticeably, music was the only non-word category to show a mean LI towards the left hemisphere.

The comparison of LIs between groups showed an overall leftward shift in musicians, revealed as a main effect of group in a rank ANOVA (Scheirer Ray Hare test: group: H = 16.4, p = 5.10^{-5}; contrast: H = 61.7, p < 10^{-6}). LIs were significantly more to the left in musicians than controls for words (Wilcoxon rank sum test: W = 111, effect size r = 0.38, p = 0.015) and for music (W = 95, r = 0.45, p = 0.004), marginally

more to the left for both houses (W = 129, r = 0.30, p = 0.055) and tools (W = 134, r = 0.28, p = 0.075), but there was no difference for faces (p = 0.38). While the interaction term between category and group was not significant in the Scheirer Ray Hare test (H = 1.6, p = 0.81; rank ANOVAs are generally considered too weak to test for interaction terms), it is worth noticing that the effect size of the difference between groups was largest for music (r = 0.45), intermediate for words, houses, and tools (r = 0.38, 0.30, 0.28), and smallest for faces (r = 0.14).

Asymmetry maps

In agreement with LIs, the occipitotemporal cortex of both controls and musicians showed activations lateralized to the left for words, and to the right for music, faces, houses and tools. Consistently with the overall leftward shift of LIs in musicians, asymmetry maps showed a cluster mostly in the ITG, more left-lateralized in musicians than controls across all visual categories (Fig. 6, third column). In the
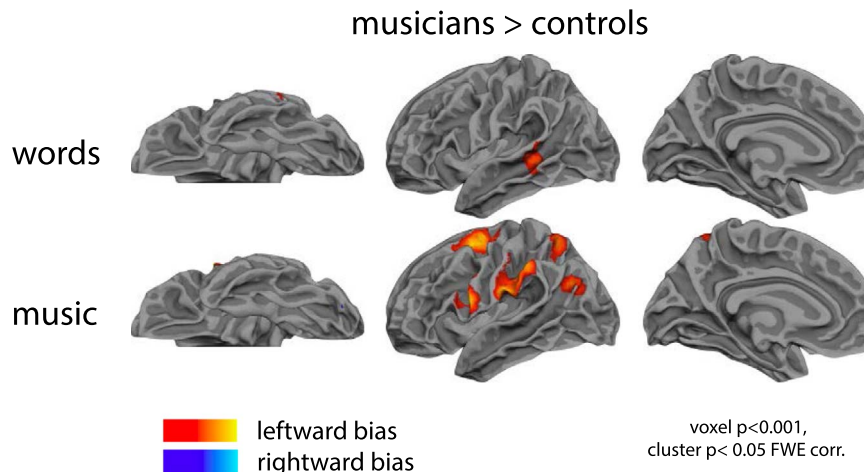
Fig. 4. : Asymmetry maps for differences between musicians and controls in category-specific activations (each category minus the others). Hot colors represent increased leftward asymmetry. Musicians had more left-lateralized category-specific activations for words and music. There was no significant difference for other categories.
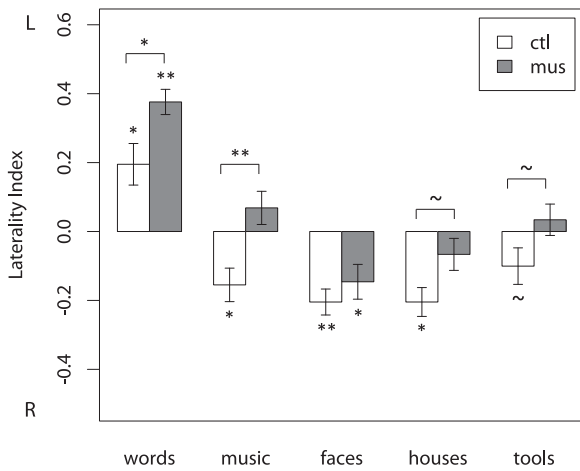
Fig. 5. : Laterality Indices of activations vs. rest in the ventral stream ROI (mean ± s.e.m.) for controls (ctl, white bars) and musicians (mus, gray bars). Positive (resp. negative) indices reflect a left-hemispheric (resp. right-hemispheric) advantage. Overall, activations in musicians were more left-lateralized than in controls. This difference was significant or marginal for all categories but faces. **: $p < 0.01$; *: $p < 0.05$; ~: $p < 0.06$.

conjunction analysis, this cluster peaked at MNI −43 −69 −19, with a more anterior subpeak at MNI −47 −60 −13. Interestingly, activation profiles (Supplementary Fig. 1) showed that the leftward shift resulted from both stronger activations in the left hemisphere and weaker activations in the right hemisphere for musicians as compared to controls.

In addition to this cluster of universal leftward shift, musicians also showed a rightward shift for faces, houses and music, located to the posterior fusiform (peak of conjunction: MNI −24 −74 −18) and

extending anteriorly in the fusiform gyrus for faces and houses (peak of conjunction: MNI −32 −46 −24).

As in the analyses of category-selective contrasts, there was a leftward shift of activations in musicians for words and music in perisylvian areas, plus smaller spots of leftward shift common to all categories (Supplementary Fig. 2).

The analyses of activations relative to rest may be summarized as follows. First, as compared to controls, musicians showed a general leftward shift of LIs for all visual categories, an effect that was not visible using category-selective contrasts. This leftward shift tended to be larger for musical notation. Voxel-based analyses allowed us to localize this shift to the posterior ITG for all categories. Second, there was a rightward shift of lateralization in musicians in the fusiform region. This rightward bias was observed for music, faces, houses, but not for words.

Correlations between the leftward and rightward asymmetries

The hypothesis that different categories would compete for hemispheric resources should result in negative correlations across subjects between asymmetries for different categories. We computed correlations between LIs for words, music and faces, with both category-selective activations and activations vs. rest. No significant negative correlation was observed, either in separate groups or pooling all participants.

Finally, we looked for negative correlations between the two overall lateralization shifts in musicians, to the left in the ITG and to the right in the fusiform gyrus. We extracted the individual values of asymmetry contrasts for all types of stimuli, at the two peaks of the leftward shift, and at the peak of the rightward shift (Fig. 6). We found again no significant correlation, either in separate groups or pooling all participants.
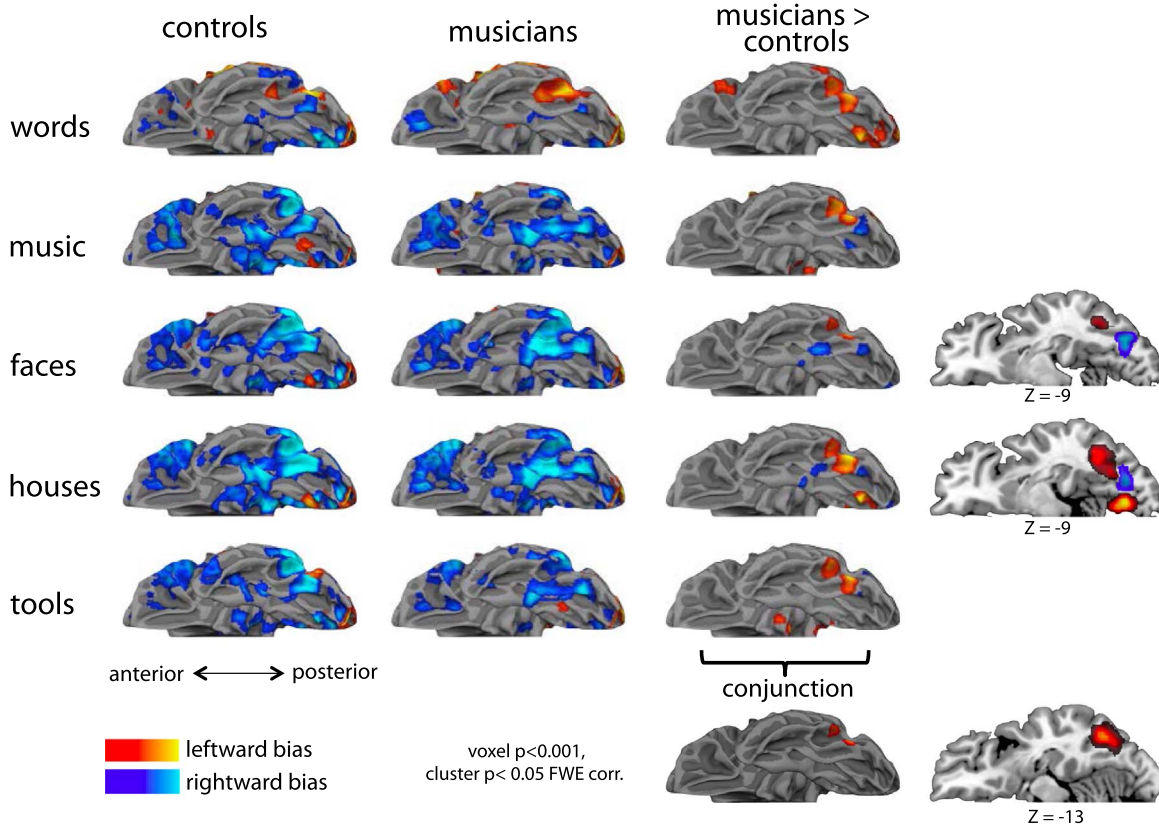
Fig. 6. Asymmetry maps of activations vs. rest. Ventral surfaces are displayed for each category (rows) vs. rest, for controls (first column), musicians (second column) and musicians > controls (third column and additional slices). Hot and cool colors represent leftward and rightward asymmetry, respectively. Musicians showed a reproducible leftward shift of activations relative to controls centered on the ITG (third column). In addition, they showed a shift of activations towards the right for music, faces and houses in the fusiform gyrus.

Discussion

We investigated whether musical expertise induces changes in the lateralization of activations in the ventral visual cortex, for music scores and faces, but also words, tools, and houses. We predicted that musical literacy would mainly induce a leftward shift in laterality for music notation, and a rightward shift for faces. Lateralization indices computed in a ventral ROI, combined with voxel-based analyses, generally support both those predictions, however with some further complexity, including a leftward shift common to all categories of visual stimuli, revealing a general impact of music training on visual object processing.

Although unlikely, it is in principle possible that the laterality differences that we observe between groups result from differences present before any musical training, in other words that people who wind up becoming skilled musicians start off with different brains. The issue can be settled conclusively only with longitudinal and cross-sectional designs. Such studies do exist for other aspects of musical skills, and show that indeed training has a measurable impact on brain structure and function (see for instance: Bengtsson et al., 2005; Gaser and Schlaug, 2003; Moreno et al., 2011, 2009; Stewart et al., 2003; or for reviews: Kraus and Chandrasekaran, 2010; Herholz and Zatorre, 2012; Peretz and Zatorre, 2005; Stewart, 2008). Moreover, the parallel between the effects we report and those observed for the acquisition of literacy also supports a causal link between training and changes in laterality. Thus, differences in the degree and in the laterality of activations have been observed between adults with various levels of reading proficiency (Dehaene et al., 2010, 2015; Pegado et al., 2014; Pinel et al., 2015), between children with different reading skills (e.g. Caffarra et al., 2017; Li et al., 2013), as well as between reading skills and behavioral hemispheric dominance (Dundas et al., 2013).

Lateralization of visual music processing

Music processing implies numerous cognitive abilities, touching auditory perception, semantics, memory, emotions, motor control, to name a few (Peretz and Zatorre, 2005). It is therefore not surprising that extensive brain networks with bilateral distribution should be involved. What concerns us here is how high-level musical expertise may impose laterality biases on those networks. As mentioned in the introduction, there is converging evidence that unlike non-musicians who exhibit a rightward advantage for music and pitch processing (Habibi et al., 2013; Matsui et al., 2013), professional musical expertise increases left hemisphere contribution to music processing. This has been demonstrated using a variety of imaging methods, for auditory perception tasks (Boh et al., 2011; Habermeyer et al., 2009; Habibi et al., 2013; Hirshkowitz et al., 1978; Matsui et al., 2013; Ohnishi et al., 2001; Ono et al., 2011), but also for musical motor tasks (Bangert et al., 2006; Pa and Hickok, 2008) and for music reading (Mongelli et al., 2017), and Fig. 4. Our first prediction was that this leftward lateralization of the music network should encourage a lateralization to the left of ventral visual areas involved in music reading.

This prediction was fully supported by the analysis of music-specific activations: in musicians, both the ROI and voxel-based approaches showed a clear advantage of the left hemisphere for the processing of musical stimuli in the ventral stream (Figs. 2 and 3 second column). In the case of activations vs. rest, music LIs relative to rest in musicians pointed non-significantly towards the left (Fig. 5), while the asymmetry map showed a massive cluster of rightward asymmetry (Fig. 6 second column), common to most categories in musicians and controls. This discrepancy between the ROI and voxel-based approaches actually results from differences in how the two methods assess asymmetry. On the one hand, asymmetry maps are sensitive only to differences between precisely homologous left- and right-hemispheric voxels, and only to asymmetries that pass both a voxelwise threshold and a threshold for cluster extent. Also, maps do not depend on absolute task-related activation level, but only on left/right differences. On the other hand, the LI method has no consideration for the topology and homology of activations within ROIs, and does not discard voxels for insufficient cluster extent. Moreover, it gives a larger weight to voxels with stronger task-related activations. Applying those observations to the current discrepancy, one may infer that the leftward bias of LI for music minus rest in musicians should reflect an overall leftward asymmetry in voxels outside the right-lateralized cluster shown in the asymmetry maps, particularly in voxels with strong task-related activations. This account was supported by a post-hoc analysis in which we thresholded the individual T-maps of the contrast of music minus rest (75% and 85% of robust range), and counted the voxels passing the threshold in the left and in the right ROI. This showed a slightly larger mean number of activated voxels in the left than in the right hemisphere (at 75% threshold: Left 48 voxels, Right 44 voxels; at 85% threshold: Left 32 voxels, Right 25 voxels), and a slightly higher mean T-value on the left than on the right (at 75% threshold: Left 11.05, Right 10.68; at 85% threshold: Left 11.92, Right 11.66). In sum, even considering activations minus rest, the highest activations to music were more left-lateralized than what asymmetry maps would suggest.

The left-hemispheric lateralization of activations to music reading is in agreement with Stewart et al. (2003), who found an increase in activation in the left fusiform region after training subjects to read music and play the keyboard, while no training effect was observed in the right ventral stream. Using EEG during music reading, Proverbio et al. (2013) found that during the 240–340 ms period, but not during the earlier N170, occipitotemporal activations were strongly left-lateralized in musicians but not in controls. One behavioral correlate of this functional asymmetry may be the right-hemifield advantage for music reading observed in proficient musicians (Hsiao and Wong, 2012).

More important than absolute lateralization, laterality indices (both vs. other types of stimuli and vs. rest) showed a leftward shift of activations in musicians relative to controls (see Fig. 2 and Fig. 4). When looking for voxels featuring such a leftward shift, we found a cluster mostly located to the ITG on the asymmetry map computed relative to rest (Fig. 6, third column). Because this shift was shared by all categories of stimuli, it cancelled out when comparing music to other stimuli (Fig. 3, third column). These differences between groups in the lateralization for music processing confirm our first prediction of a leftward shift for music in musicians. This shift of ventral activations parallels a leftward shift of brain-scale music networks. This is in agreement with the hypothesis that the asymmetry of visual regions is modulated by the asymmetry of distant networks to which they provide an input.

Leftward shift for words and other categories of stimuli

The leftward shift of activation which we observed in musicians was largest for music, but also affected the other types of stimuli, including words (Figs. 5 and 6). In the case of words, this shift in ventral activations was parallel to a leftward shift in the distant STS (Fig. 4). Because there was no category-specific shift in distant areas for faces, houses and tools, the difference in laterality for words in the ITG is unlikely to be caused by the change in the STS. It seems on the contrary that musical reading expertise changed intrinsic properties (in this case the lateralization) of parts of the ventral visual stream, yielding changes affecting any kind of images. Mongelli et al. (2017) found another instance of such interaction between categories, showing that, in the left occipitotemporal cortex of musicians, the extension of music-selective activations was accompanied by a slight displacement of word-related activations.

This general leftward functional shift may be related to anatomical correlates of musical expertise. There is indeed an increase in grey matter density in the ITG with musical practice (Gaser and Schlaug,

2003), and a significant leftward asymmetry at a location overlapping with the present leftward shift (Luders et al., 2004). Conversely, non-musicians show a rightward anatomical asymmetry in cortical thickness at this location (Luders et al., 2006).

This impact of a specific perceptual ability on general visual processing shows similarities to the changes induced by literacy acquisition. Indeed, in a recent cross-sectional MEG study of 4-to-8 year-olds, Caffarra and colleagues showed that while poor readers had right-lateralized visual activations to objects compared to scrambled objects, skilled readers showed an advantage of left posterior electrodes. They also showed a positive correlation of their amplitude for object viewing in the 200–500 ms window with reading skills, while no such correlation was observed in the right occipito-temporal cortex (Caffarra et al., 2017). In addition, as compared to illiterates, the early visual cortex of literate subjects shows enhanced activation, not only to words but also to faces or pictures, and even to checkerboards provided that those are displayed along the horizontal meridian (Dehaene et al., 2010; Pegado et al., 2014). There is evidence that such neural changes are correlated with general visual abilities. Thus, literates have an advantage in integrating line segments into overall shapes (Szwed et al., 2012) or in enjoying a more effective analytical perception of complex objects such as faces and houses (Ventura et al., 2013). Ossowski and Behrmann (2015) also showed that the right-hemifield advantages for reading and for processing high spatial frequencies emerge in a correlated manner as children learn to read, suggesting that literacy may have a general impact on the processing of spatial frequencies.

Similarly, one would expect, based on the domain-general changes we observe in the visual cortex of musicians, that professional musicians should display some behavioral advantage in non-musical visual perception tasks. Consistently, musicians perform three-dimensional rotation of mental objects with more ease than non-musicians (Sluming et al., 2007), in proportion to their music reading performance (Lee, 2012). Moreover, in addition to general better performance in visual attention tests (Rodrigues et al., 2013), musicians also show better processing of right-hemifield stimuli. First, they do not exhibit the usual deviation of about 2% to the left of the actual center when asked to bisect a line (pseudo-neglect), but show a smaller opposite bias towards the right (Hausmann et al., 2002). Second, they are also more accurate at classifying right-sided visual stimuli than non-musicians (Brochard et al., 2004; Patston et al., 2007a), and show a shorter interhemispheric transfer time of visual information than non-musicians in the left-right direction, as indexed by the N1 evoked potential (Patston et al., 2007b). As higher-level visual cortex retains a preference for contralateral stimuli far beyond V1 (Kravitz et al., 2010; Shmuelof and Zohary, 2005), it is plausible that the improved processing of right-sided stimuli in musicians should result from changes in the contralateral left visual cortex. A similar account has been proposed for the left visual field advantage for face perception, and the right visual field advantage for reading, which have been linked respectively to the opposite lateralization of the FFA (Yovel et al., 2008) and the VWFA (Barca et al., 2011; Cohen et al., 2002). In sum, the leftward shift of activations which we observed in the ITG of musicians for all types of stimuli may be one correlate of the rightward bias observed with various behavioral techniques, and possibly of other subtle changes in general visual abilities.

Lateralization of face processing

Drawing a parallel with the association between left lateralization for words and right lateralization for faces in the ventral stream, we predicted that the additional expertise for music reading should shift face-related activations even more to the right in professional musicians. This prediction was supported by the significant rightward shift of face-selective activations as measured with laterality indices (Fig. 2). However, there was no shift when considering activations relative to

rest (Fig. 5). Again, a more accurate understanding comes from the inspection of the asymmetry maps of activations vs. rest (Fig. 6). Those maps show that there was a rightward shift of activations for faces in the fusiform gyrus of musicians, and that the category-general leftward shift observed in the ITG was smaller for faces than for other categories. This pattern thus accounts for the lack of rightward shift as measured by LIs, as the leftward and rightward trends average out in the ROI approach. Asymmetry maps show that there was indeed such a rightward shift, albeit restricted to the fusiform cortex. Importantly, this fusiform shift overlapped with the face-selective FFA (MNI 42 −43 −21; Mongelli et al., 2017). Note that this rightward shift in the fusiform gyrus also concerned to a lesser extent music and houses.

In the case of literacy, it was proposed that the rightward shift of face-related activations was due to some form of competition for cortical space or neural resources between words and faces in the left ventral occipitotemporal cortex (Behrmann and Plaut, 2015; Dehaene et al., 2015). However, this hypothesis should not yet be fully taken for granted. Under the hypothesis of a competition, a negative correlation across subjects would be expected between lateralization of activations for words and for faces. Yet, such correlation was found neither by Pinel et al. (2015), nor by Davies-Thompson et al. (2016), nor in the present study. Furthermore, in children, the region which will later become the VWFA is not initially sensitive to faces, which argues against a direct competition between the two types of stimuli (Saygin et al., 2016). Nonetheless the integration of neural activity by fMRI over several seconds may conceal correlations in certain time-windows and justify some discrepancies between results obtained with EEG (Dundas et al., 2014, 2015) and fMRI (Davies-Thompson et al., 2016; Pinel et al., 2015). In addition, the laterality of the FFA, or its activation level in the right hemisphere, have clearly and reproducibly been linked to behavioral measures of reading fluency (Dehaene et al., 2010, 2015; Dundas et al., 2013; Li et al., 2013; Pinel et al., 2015). In the current study, there was too little variance in musicians' music reading skills to assess such brain-behavior relationships.

Conclusion

Professional-level music reading entails the fast encoding of highly complex visual displays, which requires the development of novel perceptual abilities. In the context of music reading, such abilities include a reduction of perceptual crowding (Wong and Gauthier, 2012), the encoding of frequent rhythmic, melodic, or chord patterns, and the development of automatic holistic perception (Wong and Gauthier, 2010). It should not be surprising that such changes in perceptual abilities extend beyond music reading, and indeed we reviewed before evidence for improved performance with right-sided stimuli, mental rotation, and attentional processing. In the present study, we focused on the impact that such expertise has on the functional lateralization in the ventral visual cortex. Our initial predictions concerned the lateralization of music-related and face-related activations. Those predictions were both supported, but it turned out that laterality shifts actually affected the processing of all types of visual stimuli. Those shifts may be roughly summarized as two general trends with a distinct topography. First, musicians showed a leftward shift of activations in posterior ITG, for music but also all other categories of stimuli. As this area was partly music-selective and partly category-general (Supplementary Fig. 1), its change in laterality was probably driven by a sustained practice of music reading, a change also visible when non-musical stimuli are fed to the visual system. Second, we observed a rightward shift in the fusiform cortex, concerning mostly faces but also music and houses. At least two open issues should be addressed in future research. Almost nothing is known about the visual abilities that may correlate with those neural changes. Musicians differing in music reading skills should be tested to investigate possible effects of music training onto exemplar discrimination, analytical vs holistic visual processing, and hemifield advantages for multiple visual

categories such as words, musical scores, objects and faces. Moreover, cohorts of children learning music at an early age could be followed longitudinally to clarify the causal relationships between music training and functional brain lateralization. A close monitoring of the development of their musical skills, together with a battery of behavioral measures for reading, speech and vision, would unravel dynamic changes of specialization in the ventral stream.

Acknowledgements

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.neuroimage.2017.04.027.

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