

Motor Learning induces plasticity in the resting brain - Drumming Up a Connection

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Abstract

Neuroimaging methods have recently been used to investigate plasticity-induced changes in brain structure. However, little is known about the dynamic interactions between different brain regions after extensive coordinated motor learning such as drumming. In this paper we have compared the resting state functional connectivity (rs-FC) in 15 novice healthy participants before and after a course of drumming (30-minute drumming sessions, 3 days a week for 8 weeks) and 16 age matched novice comparison participants. To identify brain regions showing significant FC differences before and after drumming, without a priori regions of interest, a multivariate pattern analysis was performed. Drum training was associated with an increased FC between the posterior part of bilateral superior temporal gyri (pSTG) and the rest of the brain (i.e. all other voxels). These regions were then used to perform seed-to-voxel analysis. The pSTG presented an increased FC with the premotor and motor regions, the right parietal lobe and a decreased FC with the cerebellum. Perspectives and the potential for rehabilitation treatments with exercise-based intervention to overcome impairments due to brain diseases are also discussed.

Keywords: fMRI, learning, music, neuroplasticity, resting-state

INTRODUCTION

Neuroplasticity (NP) is defined as the ability of the nervous system to respond to intrinsic or extrinsic stimuli by reorganizing its structure, function and connections. Neuroplasticity underlies not only normal development and maturation but also skill learning and memory, as well as the consequences of sensory deprivation or environmental enrichment (Kolb and Muhammad 2014). Even if NP was initially thought to be limited to critical periods in development, it is now largely accepted to occur throughout the lifespan. In fact, animal studies have identified an enhancement of adult neurogenesis, synaptogenesis, angiogenesis and the release of neurotrophins as a consequence of learning and/or physical exercise (Hötting and Röder 2013). Moreover, several famous neuroimaging investigations demonstrate adaptative neuroplastic modifications in the structure (Maguire et al. 2000; Draganski et al. 2004; Driemeyer et al. 2008) and function (Lewis et al. 2009) of the human brain in response to environmental demands in healthy adults (Wan and Schlaug 2010). Interestingly, few of these neuroimaging studies have investigated neuroplastic modifications following physical activity. These existing studies have mainly focused on cognitive facilitation by cardiovascular exercise in older adults, failing to investigate young participants or different types of physical activity (Voelcker-Rehage and Niemann 2013).

Over the past decades musical training has gained increasing interest as a paradigm to study human experience-related NP in the same general model framework (Herholz and Zatorre 2012). Playing a musical instrument is a highly complex task and requires multimodal skills such as bimanual motor activity dependent on multi-sensory feedback, fine motor skills coupled with metric precision, musical memorization (Wan and Schlaug 2010), and improvisation (Pinho et al. 2014; Beaty 2015). These skills involve complex interactions, between sensory and motor systems and high-order cognitive processes, which have to be coordinated at a high degree of synchrony and accuracy (Zatorre et al. 2007).

There is increasing evidence from several different neuroimaging modalities that NP is associated with musical training. By using structural neuroimaging, Gaser and Schlaug reported gray matter volume differences in motor, auditory, and visual-spatial brain regions when comparing professional musicians (keyboard players) with matched groups of amateur musicians and non-musicians (Gaser and Schlaug 2003). Cerebral activity patterns associated with musical perception in musicians have also been studied by using functional MRI (fMRI). A significant difference in the degree of activation between musicians and non-musicians was noted in the temporal regions and for musicians the degree of activation was correlated with the age at which the person had begun musical training (Ohnishi et al. 2001). Functional MRI was also used to explore the brain activations of novices trained to play sequences on a piano keyboard (Lahav et al. 2007; Chen et al. 2012; Herholz et al. 2015) or to listen and imitate different auditory rhythms (Chen et al. 2007). These studies showed complex interactions between auditory and motor brain regions that were associated with musical training.

Interestingly, drumming, which is a coordinative exercise combining musicality, body coordination, cardiovascular exercise, *bilateral* arm, leg movements, and sensory-motor integration processes (De La Rue et al. 2013), has not been studied extensively to date. Only expert drummers have been studied thus far. Whilst Tsai and colleagues have shown that the posterior temporal lobes are essential for audio-motor processing (Tsai et al. 2012), Petrini et al. showed that expert drummers present a reduced activation bilaterally during an audiovisual task in the cerebellum and the left parahippocampal gyrus, respectively involved in action-sound representation and audiovisual integration (Petrini et al. 2011).

Recently, resting-state functional connectivity (rs-FC) analyses have been widely used to investigate neuroplastic modifications. Rs-FC corresponds to the temporally correlated, low-frequency spontaneous fluctuations of blood oxygen level-dependent (BOLD) signals across brain regions that occur when a participant is not performing an explicit task (Fox and Raichle 2007). Temporal correlations do not appear to be random, as patterns of connectivity have been reliably identified across studies and participant. Moreover, it is now widely accepted that the strength of correlations

within and between networks has behavioural relevance (Guerra-Carrillo et al. 2014). Interestingly, it has been proposed that rs-fMRI is an effective measure of plasticity and that rest activity patterns reflect the history of repeated synchronized activation between brain regions. Thus, the study of rs-FC is particularly adapted to highlight neuroplastic modifications (Buckner and Vincent 2007; Guerra-Carrillo et al. 2014).

In this paper, we have compared the rs-FC in 15 novice healthy participants, by using a fully data-driven approach, before and after a course of drumming with another 16 novice participants who were again evaluated longitudinally but with no intervention. This longitudinal design was used to disentangle cause and effect by investigating the same participants before and after the course of drumming. We hypothesized that participants would exhibit a higher level of functional connectivity (FC) in the sensory and motor systems after drum training during the resting state, which could not be attributed to the MRI session effects (anxiety, novelty of the MRI environment).

MATERIAL AND METHODS

Participants

Thirty-one young healthy volunteers (16-19 years) with no prior drumming experience and with no psychiatric or neurological disorders participated in the study after providing written informed consent. The King's College London College Research Ethics Committee approved the experimental protocol. Participants were randomly divided into two groups: drum group and control group.

Procedure

Assessment

All participants were attended in to the Institute of Psychiatry Psychology and Neuroscience (IoPPN) at King's College London for two scanning sessions. At the first scanning session (t1) the Edinburgh Handedness Inventory Short Form (EHI) for daily activities (e.g. writing, throwing...)(Veale 2014) was used to assess each participant's hand dominance. Responses were coded to generate a Laterality Quotient (scores ranging from -100 to 100), which was then used to classify individuals into left handers (-100 to -61), mixed handers (-60 to 60) and right handers (61 to 100). Moreover, to assess the baseline drumming ability and musical experience, a self-report measure was created. Participants reported their level of skill and length of involvement in drumming, playing of another musical instrument and involvement in dance or singing. Responses for all domains were coded on an ordinal scale (0, no experience; 1, some experience, no formal instruction; 2, limited formal instruction but not recent; 3, formal instruction, less than 4 years but not current; 4, formal instruction, exams achieved, greater than 5 years involvement and current).

Drumming

Following the first drumming assessment and scanning session the drum group took part in three 30-minute low intensity group drumming sessions per week for 8 weeks. Each session was delivered by a professional drum tutor and comprised 4 integrated parts: (i) a warm up, focused on beating the drum with a relaxed and consistent motion of the drum sticks; (ii) snare drum 'rudimental' exercises, played on a single drum surface, adopting a 'flow sticking' approach to sequences of left and right hands (Queen 2007); (iii) coordinated 'groove' patterns, incorporating the interplay of bass drum (right foot) and the hi-hat pedal (left foot) with rock/pop back beat ostinato patterns played on the hi-hat or ride cymbal and snare drum, including eighth note (quaver), quarter note (crotchet), sixteenth note (semiquaver), syncopated quarter note and shuffle ostinato patterns (Chaffee 1980); and (iv) performance of learned 'grooves' and 'fill-ins' to accompany well-known popular music songs. The complexity of drumming tuition was increased on a weekly basis in line with participants' demonstration of improved drumming coordination and technique. The control participants were asked to not take part in any musical activities. After the 8 weeks (t2) participants came back to the IoPPN for a second drumming assessment and scanning session.

All of the drumming was performed on electronic drum sets for both drumming training (HD3, Roland, Nakagawa, Japan) and assessment (TD9, Roland, Nakagawa Japan) with a standard right handed five piece configuration comprising a snare drum, three tom-toms, hi-hat, ride cymbal, crash cymbal, bass drum and hi-hat pedal (played with the feet). Drumming was assessed following a short coaching period on the participants' ability to play a simple 4 quarter note pattern to the song 'Green Onions' (Booker T and the MGs, Stax / Atlantic, 1962) and a simple 8 eighth note pattern, consisting of regular eighth note hi-hats with alternating kick and snare on the main beats of the bar, to the song 'Billy Jean' (Michael Jackson, EPIC, 1982). Versions without tempo fluctuations were used, created using the software 'Live' (V9.1, Ableton, Berlin). This software analysed the beat points of the original recording and adapted them temporally to ensure that the version of the song heard by the

participants was at a constant tempo, with a consistent and precise inter beat interval so errors could be accurately recorded. The songs were played out of a single speaker on one channel, whilst the underlying beat locations were indicated by recording a click track on a second channel. A standard onset detection algorithm (Bello et al. 2005) was used to determine the audio buffer frame in which the transient of each beat in the click track occurred. A precise onset detection method was then used to find the onset location by iteratively dividing the audio buffer into window segments and determining the window in which the energy change was maximal at successively smaller window sizes. Thereby, a precise sample was specified for each beat location, accurately placed on the transient of each audible click (Robertson 2014). Timing data was exported from the drum set using the musical digital interface (MIDI) signal. A comparison with a piezo microphone placed on the snare indicated that the recorded MIDI events were a maximum of four milliseconds from the detected onset using audio-based methods, and generally much closer. Drumming ability was assessed objectively as the percentage of bars of both patterns that were completed during two 2-minute periods of data capture (1-3 minutes of each song). To record a completed bar all elements had to be present in each pattern and within half a beat (250 ms for 4 quarter note pattern and 125 ms for an 8 eighth note pattern) of the perfect timing. We also evaluated the error in events that should have been synchronous (flamming) as flam error per bar in milliseconds. For each note of the bar we evaluated the time between the two events. When three limbs were involved, we evaluated the difference between the first and last event. This was only evaluated for completed bars as it would be impossible to make a meaningful measurement where the pattern was breaking down or parts were missing. No practice of either song used in the assessment was included in the 8 weeks drumming training. Whilst a drum flam can be a sought-after stylistic feature of a pattern, flams were not part of the stylistically correct performance for the two chosen patterns.

MRI acquisition and preprocessing

All participants were scanned in a 3T MR scanner (Discovery MR750, General Electric, Milwaukee, WI, USA). All participants underwent an anatomical T1-weighted MRI using a gradient-echo sequence with the following scan parameters: 196 sagittal slices, TR = 7.3 ms, TE = 3 ms, TI = 400 ms, FA = 11°, FOV = 270 mm², matrix size = 256 x 256, voxel size = 1 × 1 × 1 mm³, slice thickness = 1.2 mm. The rs-fMRI was collected using an echo-planar imaging sequence with the following scan parameters: 180 volumes, interleaved ascending slice order, TR = 2000 ms, TE = 30 ms, FA = 75°, FOV = 211 mm², matrix size = 64 x 64, voxel size = 3 × 3 × 3 mm³, gap = 0.3 mm. Four dummy scans were obtained before each fMRI data acquisition to allow for the equilibration of the MRI signal. During acquisition, the participants remained with eyes-open attending a cross-hair on the screen in a wakeful resting state. Headphones and earplugs were used to attenuate the acoustic noise of the scanner.

The anatomical and functional data were preprocessed and analyzed using Statistical Parametric Mapping (SPM12) and the CONN toolbox Version 14p (<http://www.nitrc.org/projects/conn>) (Whitfield-Gabrieli and Nieto-Castanon 2012). Functional data were preprocessed using a slice scan time correction, realignment (motion correction), registration to structural images and spatial normalization to Montreal Neurological Institute (MNI) standardized space, smoothing with a Gaussian filter of 5.0 mm spatial full width at half maximum value (FWHM). A conventional band-pass filter over a low-frequency window of interest (0.008-0.09) was also applied to the resting-state time series. After these preprocessing steps, a CompCor strategy (Behzadi et al. 2007) was implemented, extracting signal to noise from the white matter (WM) and cerebrospinal fluid (CSF) by principal component analysis without affecting intrinsic FC (Chai et al. 2012). These components (WM and CSF) and motion parameters were included in the model and considered as covariates of no-interest.

Voxel-to-voxel analysis

To identify brain regions showing significant FC differences before and after drumming without having to restrict the analyses to one or several *a priori* regions of interest (ROI), whole-brain connectivity analysis was performed. In the present study we employed the *connectome-MVPA* approach (multivariate pattern analysis of whole-brain connectome) implemented in the CONN toolbox (Whitfield-Gabrieli and Nieto-Castanon, 2012). In this approach, a low-dimensional multivariate representation characterizing the connectivity pattern between one voxel and the rest of the brain was created for each voxel separately. This representation was defined by performing a Principal Component Analysis (PCA) characterizing the FC between this voxel and the rest of the brain. The resulting component scores were then stored as functional maps and entered into standard second-level analyses for between-condition tests (i.e. before and after drum training). Finally, an F-test was performed, comparing (for each voxel) the component scores across the two conditions. Therefore, the second-level statistical analysis provided a multivariate pattern of correlated voxel clusters associated with drumming. In other words, regions that are significant in the resulting voxel-level analyses indicate condition-related differences in connectivity between those areas and the rest of the brain. More technical details and an example of use of the connectome-MVPA method can be found in (Whitfield-Gabrieli et al. 2015) and in (Beaty et al. 2015).

Seed-to-voxel analyses

To explore the FC between clusters found in the voxel-to-voxel analysis and the rest of the brain between the conditions, a post hoc seed-to-voxel analysis was performed. Therefore, 10 mm spherical regions of interest (ROI) based on peak activation clusters from the whole-brain connectivity analysis were extracted and used as seeds to perform seed-to-voxel analysis. Correlations maps were then calculated for each participant, per condition, by extracting the mean signal time course from the seeds and computing Pearson's correlations coefficients with the time course of all other voxels of the brain. Those correlation coefficients were converted to normally distributed z-scores using the Fisher

transformation to allow for second-level general linear model (GLM) analyses. Second-level within group (one sample t-tests) and between group (ANOVA) analyses were performed on the average Z-maps from the new seeds source ROIs. Finally, a paired t-test was performed to examine the change of resting state connectivity before versus after drum training for all participants.

For confirmatory analysis, seed-to-voxel analyses were repeated using anatomically defined ROIs, free from concerns about circular analysis. For this analysis, the pSTG was chosen as it corresponds to the main region found in the voxel-to-voxel analysis (**See Table 1 and Figure 2**) and because it is selectively responsible for action-related sounds (Zatorre et al. 2007; Tsai et al. 2012). Two 10 mm spherical ROIs were created based on the Harvard-Oxford cortical atlas implemented in the CONN toolbox (Whitfield-Gabrieli and Nieto-Castanon, 2012). The MNI coordinates of left and right pSTG were respectively (-62, -29, 3) and (61, -24,1).

As gender and handedness may be a factor which modulates musical training (Koelsch et al. 2003; Klöppel et al. 2007) additional analyses including gender and handedness as covariates were conducted. The same 10 mm spherical ROIs were used as seeds in the control group in order to delineate brain changes which are specific to the drum training. To precisely identify the brain areas involved, the Harvard-Oxford Cortical and Subcortical Atlas (Desikan et al. 2006; Makris et al. 2006), the AAL Atlas (Tzourio-Mazoyer et al. 2002) and the Juelich Histological Atlas (Eickhoff et al. 2007) were used. All results were thresholded at a voxel-wise $p < 0.001$ and at the cluster extent $p < 0.01$ FWE corrected.

Correlations with drum progression

To evaluate the association between FC and drum progression, correlations (Pearson's coefficients) were performed between the drum progression scores in each participant and the connectivity values (z-scores) of regions showing significant differences after drum training from the seed-to-voxel analysis. Two scores were used. The first score corresponded to the mean number of

bars successfully completed ($\Delta\%$ bars completed) before versus after the drum training (t_2-t_1 difference) from 'Green onions' and 'Billy Jean'. The "combined progression score" corresponded to the proportion of bars successfully completed before versus after the drum training (t_2-t_1 difference) as the percentage of bars completed ($\Delta\%$ bars completed) from both songs.

Statistical analyses

Statistical analyses of demographic data and drum performance were performed using SPSS (SPSS version 18, Chicago, Illinois, USA). Independent sample t-tests or Mann-Whitney rank sum test, and paired t-tests were used to determine baseline differences, and the effects of drum training between and within groups. To test whether there was a significant interaction of group over time, we performed a repeated measures ANOVA model by specifying "time" as a within-subjects contrast (t_1-t_2 , i.e. before and after the drum training) followed by a between subject's contrast (drummers vs. controls). Significance was set at $p < 0.05$.

RESULTS

Participants and drum progression

Based on a self-report measure, the drum group ($n = 15$, 7 men, 8 women, 2 mixed-handed, age 16.8 ± 0.7 years) and the control group ($n = 16$, 8 men, 8 women, all right-handed, age 17.8 ± 1.4 years) presented no prior drumming experience (all scores ≤ 2). Moreover, there were no statistical differences between the two groups in terms of self-reported other musical instrument ($p = 0.53$ dance and singing experience ($p = 0.31$)).

At baseline, the mean number of bars successfully completed for 'Green Onions' and 'Billie Jean' was not significantly different between the two groups (respectively $p = 0.42$ and $p = 0.12$) (see **Figure 1**). After 8 weeks, the mean number of bars successfully completed was significantly increased in both groups and for the two songs (see **Figure 1**). The mean combined progression score was significantly higher ($p = 0.003$) for the drum group (mean = 0.45 ± 0.29) in comparison with the control group (mean = 0.17 ± 0.19). A before/after video is available for illustration (see <https://vimeo.com/141911618>).

For 'Green Onions', repeated measures ANOVA revealed no significant effect of group ($F = 3.9$, $p = 0.07$), a significant effect of time ($F = 19.9$, $p = 0.001$) and no group x time interaction ($F = 3.3$, $p = 0.091$). For 'Billie Jean', repeated measures ANOVA revealed a significant effect of group ($F = 26.1$, $p < 0.001$), a significant effect of time ($F = 36.1$, $p < 0.001$) and significant group x time interaction ($F = 21.9$, $p < 0.001$). There was no significant difference in flam error per bar between t_1 and t_2 in both groups ($p = 0.24$).

Voxel-to-voxel analysis

The *connectome-MVPA* analysis revealed two symmetric clusters associated with drum training (**$p < 0.005$, FWE correction**). These clusters consisted of the posterior division of the left and right superior temporal gyri (STG) and middle temporal gyri (MTG) and are described as pSTG throughout the manuscript (see **Table 1 and Figure 2**).

Seed-to-voxel analyses

Group-level seed-to-voxel analyses revealed increased FC after drum training when compared to before between left pSTG and left superior parietal lobule (SPL), left inferior temporal gyrus, right angular gyrus, right supramarginal gyrus, left and right lateral occipital cortex, right inferior temporal gyrus and left inferior frontal gyrus and a decreased FC between the right STG and MTG (posterior division) and left and right cerebellum crus I and II (see **Figure 3**). Peak spatial coordinates in the MNI space and the corrected p-value ($p < 0.01$, FWE correction) are reported in **Table 2**.

Group-level seed-to-voxel analyses revealed increased FC after drumming when compared to before between right pSTG and right supramarginal gyrus right angular gyrus, right SPL and right pre- and postcentral gyrus and a decreased FC with the left STG and MTG (posterior division), left temporal pole, bilateral cerebellum crus I and II, left paracingulate gyrus and right MTG (see **Figure 4**). Peak coordinates in the MNI space and the corrected p-value ($p < 0.01$, FWE correction) are reported in **Table 3**.

The supplementary inclusion of gender and handedness as covariates did not change the results as the same clusters were found. No significant FC differences were observed in the control group.

Improvement in performance and correlations with functional connectivity

Participants with higher improvement in performance had higher right seed-right parietal lobe connectivity scores. Indeed, there was a significant correlation between the improvement in the mean number of bars successfully completed for 'Billie Jean', the combined progression score and the right parietal lobe FC (including the right supramarginal gyrus, the right angular gyrus and the right SPL) from the right seed. The correlation coefficients were, $r = 0.60$ ($p = 0.02$) and $r = 0.57$ ($p = 0.03$), respectively (see **Supplementary Figure**). The improvement in performance did not correlate significantly with the FC of the other clusters.

Discussion

The main goal of this study was to determine whether we could visualise significant differences in the functional networks engaged in drum training in healthy participants by using rs-FC. Drum training was characterised behaviourally in significantly improved performance as assessed by the mean number of bars successfully completed for 'Green Onions' and 'Billie Jean'. Interestingly, after 8 weeks, the mean number of bars successfully completed was significantly increased in both groups and for the two songs. This increased drum performance in the age-matched control group can be explained by a learning or familiarisation effect since the two songs were no longer novel to the participants in both groups. However, the drum group has improved drum performance over and above this simple familiarisation effect. Indeed, the progression score was significantly higher for the drum group in comparison with the control group. Moreover, a significant effect of time (i.e. before and after 8 weeks) has been showed in both groups and for the two songs, and a significant group (i.e. drummers vs. controls) x time interaction was showed for 'Billie Jean'. We were unable to utilise more sophisticated measures of drumming performance (such as timing deviations) because we could only evaluate the timing scores from the data that made up the completed bars, since in this population (of novices) there were periods of no playing and patterns that needed to be stopped as they were playing incorrectly. Whilst timing deviation would be a representative statistic for more experienced drummers, this relies on the subject's ability to play the pattern correctly in order to be meaningful. Drum training was also associated with: (i) an increased FC between the posterior part of bilateral pSTG and the rest of the brain (i.e. all other voxels), (ii) an increased FC between pSTG and the premotor and motor regions, (iii) an increased FC between pSTG and the right parietal lobe which was correlated with drum performance and (iv) a decreased FC between regions of the cerebrum and the cerebellum. These results could not be attributed to the MRI session effects (anxiety, novelty of the MRI environment) or to the normal development (Power et al. 2010; Rubia 2013) as no significant FC differences were observed in the age-matched control group.

The whole-brain FC underlying drum training was explored and revealed two symmetric brain regions located in the pSTG (see **Figure 2**). This result is consistent with previous experiments about training to play a melody on piano keyboard (Chen et al. 2012), hammering or clapping (Lewis et al. 2005; Galati et al. 2008) and expert drummers (Tsai et al. 2012), which showed that the bilateral pSTG were selectively responsible for action-related sounds. Indeed, the pSTG is a crucial hub of the dorsal auditory streams which is engaged in sensorimotor integration and spatial processing ('how' and 'where') (Rauschecker and Tian 2000; Scott et al. 2009) and therefore plays an essential role in auditory–motor transformations ('do-pathway'), which is essential for music processing (Warren et al. 2005; Zatorre et al. 2007).

Interestingly, while using the pSTG as a seed to perform a seed-to-voxel analysis, an increased FC was found between the right pSTG and the left precentral and postcentral gyri including the ventral premotor cortex (vPMC) and the primary motor cortex. The premotor cortex can compute a variety of sensory–motor transformations that are relevant for music and is involved in the motor prediction and production of complex sequences (Zatorre et al. 2007). Specifically, the left vPMC, which might work in tandem with the pSTG (Hickok and Poeppel 2007; Tsai et al. 2012), could be associated with the serial sequence prediction and coupling between hearing music and the execution of a motor programme by the motor cortex, that enable the realisation of sensory-cued actions (Zatorre et al. 2007).

The left and right pSTG seed regions showed an increased FC respectively with the left and right SPL, a coupling essential in sensory-motor transformation (Hickok and Poeppel 2004; Zatorre et al. 2007). The SPL, which is anatomically connected to the posterior temporal lobe (Kamali et al. 2014), is critical for many sensory and cognitive processes, including sensorimotor (Wolpert et al. 1998) and somatosensory integration, motor learning, spatial perception, mental rotation, visuospatial attention, and memory (Wang et al. 2015). Moreover, it has been involved in the perception of bimanual interaction with an external object (Naito et al. 2008) and the storage of movements and kinematics

(Seitz et al. 1997). This appears to be very consistent with the present experiment involving drum training. In the music training framework, the SPL has also been suggested to coordinate the complex spatial and timing components of musical performance (Langheim et al. 2002). After drum training, both pSTG were also more functionally connected with the right inferior parietal lobule (IPL), which comprises of the angular and supramarginal gyri, and the intraparietal sulcus (IPS). Interestingly, the SPL and the IPL cluster, which includes the IPS, are part of the dorsal attention network (Petersen and Posner 2012). The dorsal attention network is involved in the maintenance of spatial priority maps for covert spatial attention, saccade planning, and visual working memory (Vossel et al. 2014). Moreover, our results are consistent with the right hemisphere dominance that has been described for visuospatial attention (de Schotten et al. 2011). Interestingly, these posterior parietal regions also support mental transformations of acoustic or visual information into motor representations (Warren et al. 2005; Zatorre et al. 2007; Herholz et al. 2015). The increased functional coupling between the bilateral pSTG and the right dorsal attention network might be associated with the improvement of the integration of sensory and motor functions, as the FC of the right parietal lobe cluster was significantly correlated with the improvement in drum performance.

The increased FC between the left pSTG and the inferior frontal gyrus (IFG) corresponds to the ventral auditory streams arising from the primary auditory cortex, and projecting anteriorly from the primary auditory cortex to the IFG along the STG (Scott et al. 2009). This ventral pathway, also known as the what-pathway, is involved in auditory object identification (Leaver and Rauschecker 2010). It is specialized for invariant auditory object properties, which are time-independent, and less related to motor systems (Zatorre et al. 2007). The left seed was more functionally connected with the left inferior temporal gyrus and the lateral occipital cortex. These are part of the ventral visual pathway involved in human object perception and recognition and in the encoding of spatial relationships between subparts of scenes (Grill-Spector and Weiner 2014). This increased FC reflects the audio-visual integration, which has been shown to be crucial in multimodal training (Paraskevopoulos et al. 2012).

Interestingly, both seeds also showed a decreased FC with the bilateral cerebellum (crus I and II). A recent meta-analytic connectivity study identified these two cerebellar subregions as part of a cerebellar cluster significantly associated with motor learning, working memory, recitation and repetition as well as music comprehension and production (Riedel et al. 2015). All integral components involved in learning to play the drums. According to the Marr-Albus-Ito theory on motor learning, cerebellar Purkinje cells (PC) learn to recognize contexts during rehearsal of an action, creating an anticipatory neural state (Marr 1969; Ito 1970; Albus 1971). Climbing fibres innervating the PC further encode possible errors, consequently suppressing the PC synapses involved in such erroneous performance with the help of long-term depression. Once the action has been learned, the occurrence of the context alone is enough to fire the PC to cause the next elemental movement. This increase in efficiency in turn decreases cerebellar activity in the region used, which enables a resource allocation to other areas (Petrini et al. 2011). When such movement involves excitatory output to the cerebral cortex, PC form inhibitory synapses with the deep cerebellar nuclei. As a result, an increase in cerebellar activity would induce a decrease in activity in cortical target regions and vice versa (Vahdat et al. 2011). As a result, the cerebellum is able to integrate and coordinate motor and sensory signals, react quicker and with less error, creating a smooth motor performance. With this increase of efficiency, a decrease of cerebellar activation in regions required for motor learning, music comprehension and production can be expected after drum training.

Both pSTG also showed a decreased FC with the contralateral STG and the right pSTG showed a decreased FC with the ipsilateral anterior part of the MTG. These decreased FC can reflect complex interferences between the ipsilateral and contralateral auditory pathways (Pantev et al. 1986) that can be associated to the synaptic inhibition involved in sound localisation (Grothe 2003). In fact, auditory pathways are formed by excitatory and inhibitory neural connections and networks. It is now well known that music induced lateral inhibition in the human auditory cortex (Pantev et al. 2012). Moreover, reductions in temporal gyrus activity were reported previously for auditory perceptual pitch

training (Jäncke et al. 2001) and discrimination training for micromelodies (Zatorre et al. 2012). The right pSTG was also less functionally connected with more frontal regions, such as the paracingulate gyrus, which can reflect interactions in top-down strategies. The frontal regions may be involved in the control of action plans and in the selection and/ or inhibition of action chunks. This is particularly important for musical performance, as chunking is defined as the re-organization or re-grouping of movement sequences into smaller sub-sequences during performance, to facilitate the smooth performance of complex movements and to improve motor memory (Zatorre et al. 2007). Those kinds of patterns involving networks with increased and decreased activations or FC have already been described for motor training (Allison et al. 2000; Voelcker-Rehage and Niemann 2013) and in the music literature (Lahav et al. 2007; Petrini et al. 2011; Chen et al. 2012; Pinho et al. 2014). They are furthermore thought to be associated with greater automaticity in cognitive processes (Voelcker-Rehage and Niemann 2013; Beaty 2015).

Finally, the fact that the adult brain is capable of NP modifications, as demonstrated here, highlights the potential of rehabilitation treatments designed to induce plastic changes to overcome impairments due to brain diseases (Wan and Schlaug 2010), which may include stroke, traumatic brain injury and a range of neuropsychiatric disorders (Cramer et al. 2011). Intriguingly, most regions highlighted by our analyses (IPL, SPL, MTG and STG) are part of the human mirror neurons system (MNS), which is activated when an individual performs an action and when a similar or identical action is passively observed (Molenberghs et al. 2012). (Molnar-Szakacs and Overy 2006)[71]From a clinical perspective, our results could be particularly interesting to consider a drum-based intervention in disorders involving a MNS dysfunction such as in autism spectrum disorders (ASD) (Molnar-Szakacs and Heaton 2012). Drumming with a social partner could then be particularly relevant for individuals with ASD. Previous studies investigating interpersonal body movement synchronization and social processes found that drumming could improve social interaction (Hove and Risen 2009; Kirschner and Tomasello 2009; Yun et al. 2012).

By using additional neuroimaging methods, future studies should also investigate further the functional interplay between cortical and cerebellar regions. Here, DTI tractography and/or structural MRI analyses could explore whether the changes in FC are accompanied by structural changes, which would help illuminate the role of the cerebellum in multimodal action learning. Furthermore, the complex interplay between the left-right hemispheres, as showed in our FC results, should be specifically investigated. Indeed, it is now well known that musical ability is associated with left-right differences in brain structure and function (Schlaug et al. 1995). However, drummers are unique in that they combine both independent and multi-limb coordination when playing, which is necessary for the physical multitasking of drumming and which can lead to complex inter-hemispheric interactions. Adding an active control group participating in non-musical motor activities would also help distinguish motor action and higher functions involved in music training. Such an active control condition could consist of learning a new physically demanding multi-limb motor sport (such as for example playing basketball). Finally, adolescence is characterised by changes in brain structure and function, particularly in regions of the cortex, notably the frontal, parietal and temporal regions, that are involved in higher-level cognitive processes (e.g. memory), for which capacity may be increased in adolescence. It has thus been suggested that adolescence might represent a second ‘window of opportunity’ in brain development (Fuhrmann et al. 2015). Hence, future experimental studies are needed to compare effect of environment manipulation, such as drum training, in child, adolescent, and older adult groups.

In conclusion, this is the first FC study to compare novice healthy participants before and after an extensive coordinated motor learning such as drumming. An agnostic data-driven approach, i.e. resting-state MVPA, was used to examine the FC of all voxels in the brain, independent of a priori anatomical hypotheses. This method allowed us to highlight the central role of the posterior part of the STG in this task. Moreover, by using the MVPA results as seeds to compute a seed-to-voxel analysis, we showed complex patterns of increased and decreased FC associated with drum training that were

partly correlated with the improvement in drum performance. Indeed, as musical training has been shown to modulate unimodal as well as multimodal cortical processing, the seed-to-voxel analyses provide important information on the interaction between the cortical areas involved within the whole network supporting the instrumental performance (Pantev and Herholz 2011). Finally, one can argue that our drum training regimen is a relevant task to highlight the neuroplastic mechanisms involved in motor learning in a naïve population and that drum-based intervention could be relevant to overcome impairments due to brain diseases.

Conflict of interest

The authors declare no conflict of interest.

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TABLES CAPTIONS

Table 1. Whole-brain *connectome*-MVPA analysis (voxel-to-voxel analysis). MNI coordinates (x, y, z) represent peaks within a cluster. Cluster size corresponds to spatial extent (i.e. number of voxels). Correction for multiple comparisons was performed using family-wise error correction at the cluster level. L/R = left/ right side of the brain.

Cluster size	Side (L/R)	Brain areas	MNI coordinates			F max	Z max	P _{corr} value
			x	y	z			
160	L	Superior Temporal Gyrus (posterior division)	-64	-28	12	15.02	4.78	<0.001
		Middle Temporal Gyrus (posterior division)	-58	-26	-8	9.00	3.72	
49	R	Superior Temporal Gyrus (posterior division)	64	-18	02	11.71	4.25	<0.005
		Middle Temporal Gyrus (posterior division)	70	-28	0	8.80	3.67	

Table 2. Functional connectivity of the left pSTG. MNI coordinates (x, y, z) represent peaks within a cluster. Cluster size corresponds to spatial extent (i.e. number of voxels). Correction for multiple comparisons was performed using family-wise error correction at the cluster level. L/R = left/ right side of the brain.

	Cluster size	Brain areas	Side (L/R)	MNI coordinates			T max	P _{corr} value
				x	y	z		
Post > Pre								
Cluster 1	741	Superior Parietal Lobule	L	-36	-50	50	7.85	<0.0001
		Lateral Occipital Cortex	L	-24	-60	34	7.54	
Cluster 2	526	Inferior Temporal Gyrus	L	-50	-46	-18	6.36	<0.0001
Cluster 3	424	Angular Gyrus	R	40	-54	52	6.34	<0.0001
		Supramarginal Gyrus	R	42	-36	44	6.24	
		Lateral Occipital Cortex	R	32	-64	42	5.93	
Cluster 4	103	Inferior Temporal Gyrus	R	56	-46	-28	8.45	<0.01
Cluster 5	103	Inferior frontal gyrus	L	-30	48	-2	6.43	<0.01
Post < Pre								
Cluster 1	276	Superior Temporal Gyrus	R	54	-30	4	-6.74	<0.001
		Middle Temporal Gyrus	R	68	-42	0	-6.54	
Cluster 2	152	Cerebellum Crus I and II	L	-18	-76	-36	-6.50	<0.001
Cluster 3	159	Cerebellum Crus I and II	R	22	-72	-28	-5.77	<0.001

Table 3. Functional connectivity of the right pSTG. MNI coordinates (x, y, z) represent peaks within a cluster. Cluster size corresponds to spatial extent (i.e. number of voxels). Correction for multiple comparisons was performed using family-wise error correction at the cluster level. L/R = left/ right side of the brain.

	Cluster size	Brain areas	Side (L/R)	MNI coordinates			T max	P _{corr} value
				x	y	z		
Post > Pre								
Cluster 1	388	Supramarginal Gyrus	R	38	-48	38	6.19	<0.0001
		Angular Gyrus	R	42	-54	50	6.09	
		Superior Parietal Lobule	R	32	-54	44	5.73	
Cluster 2	309	Precentral Gyrus	L	-48	-10	32	5.67	<0.0001
		Postcentral Gyrus	L	-44	-20	32	5.56	
Post < Pre								
Cluster 1	1010	Middle Temporal Gyrus	L	-52	-24	-12	-7.64	<0.001
		Temporal Pole	L	-50	20	-20	-7.53	
		Superior Temporal Gyrus	L	-58	-32	-2	-7.19	
Cluster 2	137	Cerebellum Crus I and II	L	-20	-76	-34	-8.88	<0.001
Cluster 3	134	Cerebellum Crus I and II	R	26	-80	-34	-8.28	0.001
Cluster 4	122	Paracingulate Gyrus	L	2	50	14	-6.36	<0.01
Cluster 5	116	Middle Temporal Gyrus	R	48	4	-28	-7.20	<0.01

FIGURES

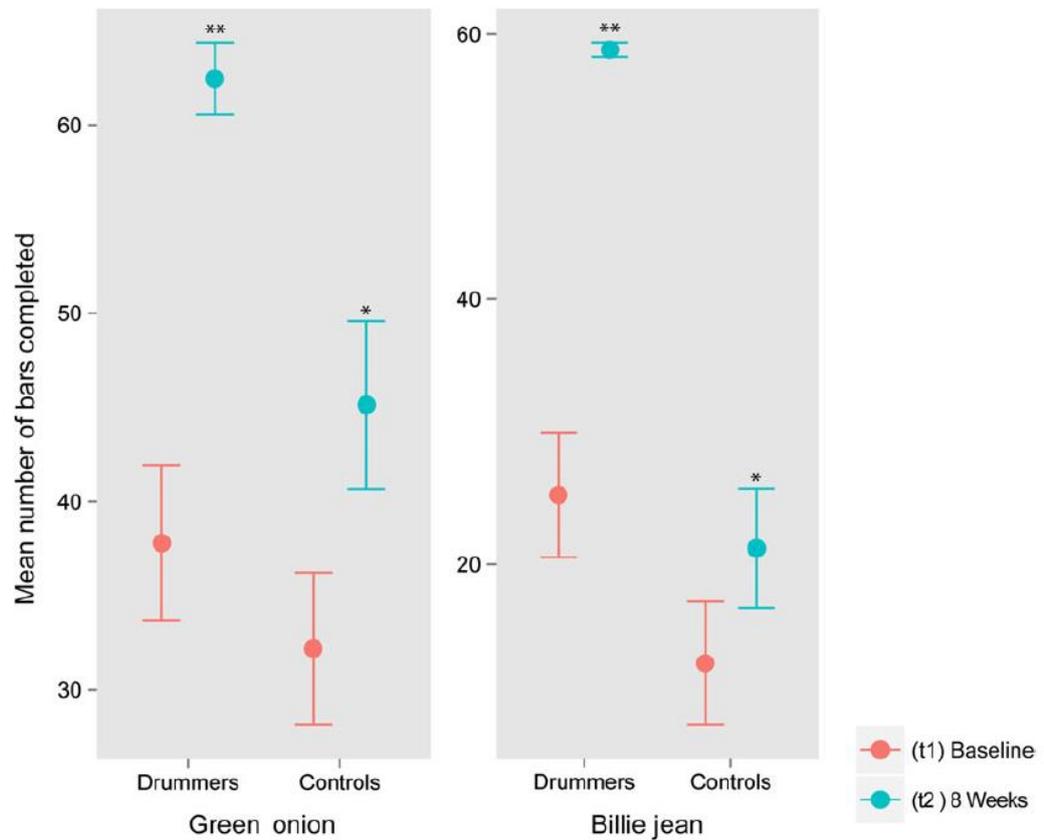


Figure 1. Mean number of bars successfully completed for 'Green Onions' and 'Billie Jean' before and after the drum training. At baseline, the mean number of bars successfully completed was not significantly different between the two groups for the both songs (respectively $p = 0.42$ and $p = 0.12$). After 8 weeks, the mean number of bars successfully completed was significantly increased in both groups and for the two songs. Error bars denote the standard deviation. * significant at $p < 0.05$; ** significant at $p < 0.001$

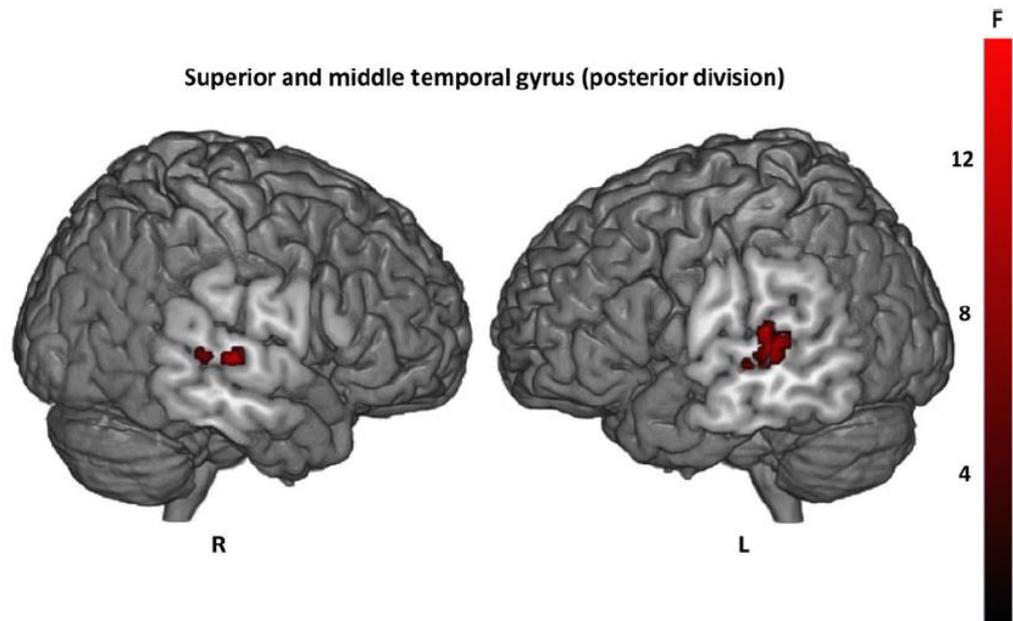


Figure 2. Results from the voxel-to-voxel analysis showing areas of highest connectivity in the whole brain by comparing before vs after drum training. These clusters consisted of the posterior division of the left and right superior temporal gyri (STG) and middle temporal gyri (MTG) and are described as pSTG. This map is based on F-contrasts thresholded at $p < 0.01$, FWE corrected. Clusters were rendered on the “ch256” brain template using MRICroGL (<http://www.mccauslandcenter.sc.edu/mricrogl/>). L/R = left/ right side of the brain.

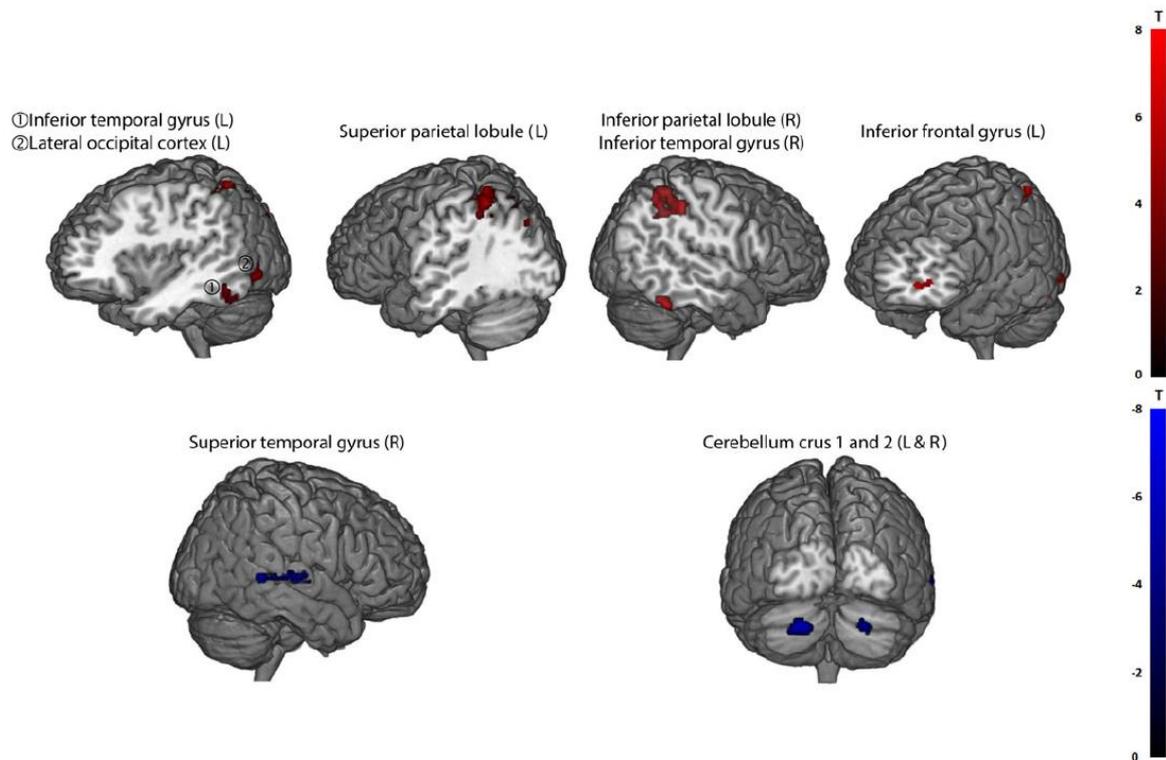


Figure 3. Results from seed-to-voxel functional connectivity (FC) of the left pSTG seed (results of voxel-to-voxel analysis). Higher FC was detected after drum training within left superior parietal lobule, left inferior temporal gyrus, right inferior parietal lobule (angular gyrus and supramarginal gyrus), left and right lateral occipital cortex and left inferior frontal gyrus (upper panel, $p < 0.01$, FWE corrected). A decreased FC was measured after drum training within right superior and middle temporal gyrus (posterior division) and left and right cerebellum crus (lower panel, $p < 0.01$, FWE corrected). Clusters were rendered on the “ch256” brain template using MRICroGL (<http://www.mccauslandcenter.sc.edu/mricrogl/>). L/R = left/ right side of the brain.

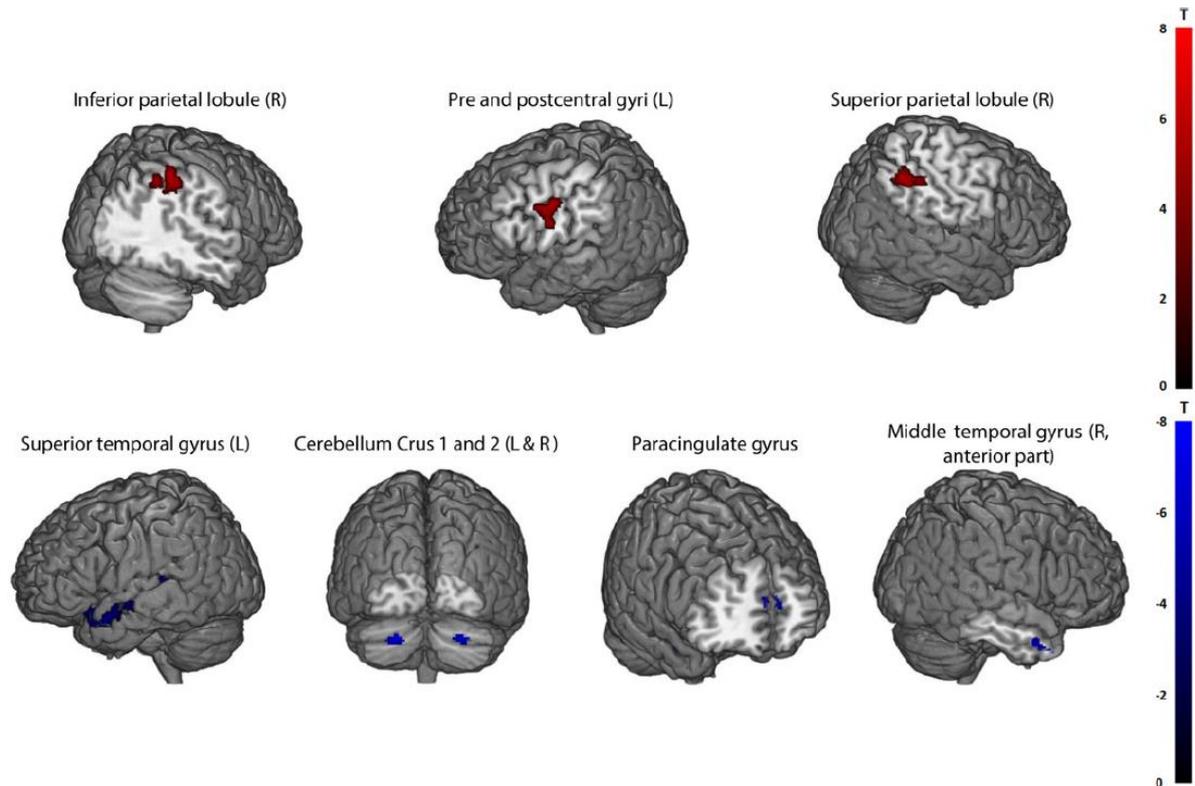


Figure 4. Results from seed-to-voxel functional connectivity (FC) of the right pSTG seed (results of voxel-to-voxel analysis). Higher FC was detected after drum training within right inferior parietal lobule (angular gyrus and superior parietal lobule) and right pre and postcentral gyri (upper panel, $p < 0.01$, FWE corrected). A decreased FC was measured after drum training within left superior and middle temporal gyrus, left temporal pole, left and right cerebellum crus, paracingulate gyrus and the anterior part of the right MTG. Clusters were rendered on the “ch256” brain template using MRICroGL (<http://www.mccauslandcenter.sc.edu/mricrogl/>). L/R = left/ right side of the brain.

Supplementary figure. Significant correlation between the right seed-right parietal lobe and the drum progression scores.

References

- Albus JS. 1971. A theory of cerebellar function. *Math Biosci.* 10:25–61.
- Allison JD, Meador KJ, Loring DW, Figueroa RE, Wright JC. 2000. Functional MRI cerebral activation and deactivation during finger movement. *Neurology.* 54:135–142.
- Beaty RE. 2015. The neuroscience of musical improvisation. *Neurosci Biobehav Rev.* 51:108–117.
- Beaty RE, Benedek M, Kaufman SB, Silvia PJ. 2015. Default and Executive Network Coupling Supports Creative Idea Production. *Sci Rep.* 5:10964.
- Behzadi Y, Restom K, Liu J, Liu TT. 2007. A Component Based Noise Correction Method (CompCor) for BOLD and Perfusion Based fMRI. *NeuroImage.* 37:90–101.
- Bello JP, Daudet L, Abdallah S, Duxbury C, Davies M, Sandler MB. 2005. A tutorial on onset detection in music signals. *Speech Audio Process IEEE Trans On.* 13:1035–1047.
- Buckner RL, Vincent JL. 2007. Unrest at rest: default activity and spontaneous network correlations. *NeuroImage.* 37:1091–1096.
- Chaffee G. 1980. *Time Functioning Patterns.* GC Music. ed. USA: Warner Bros Publications.
- Chai XJ, Castañón AN, Öngür D, Whitfield-Gabrieli S. 2012. Anticorrelations in resting state networks without global signal regression. *NeuroImage.* 59:1420–1428.
- Chen JL, Penhune VB, Zatorre RJ. 2007. Moving on Time: Brain Network for Auditory-Motor Synchronization is Modulated by Rhythm Complexity and Musical Training. *J Cogn Neurosci.* 20:226–239.
- Chen JL, Rae C, Watkins KE. 2012. Learning to play a melody: An fMRI study examining the formation of auditory-motor associations. *NeuroImage.* 59:1200–1208.
- Cramer SC, Sur M, Dobkin BH, O'Brien C, Sanger TD, Trojanowski JQ, Rumsey JM, Hicks R, Cameron J, Chen D, Chen WG, Cohen LG, deCharms C, Duffy CJ, Eden GF, Fetz EE, Filart R, Freund M, Grant SJ, Haber S, Kalivas PW, Kolb B, Kramer AF, Lynch M, Mayberg HS, McQuillen PS, Nitkin R, Pascual-Leone A, Reuter-Lorenz P, Schiff N, Sharma A, Shekim L, Stryker M, Sullivan EV, Vinogradov S. 2011. Harnessing neuroplasticity for clinical applications. *Brain.* 134:1591–1609.
- De La Rue SE, Draper SB, Potter CR, Smith MS. 2013. Energy expenditure in rock/pop drumming. *Int J Sports Med.* 34:868–872.
- de Schotten MT, Dell'Acqua F, Forkel SJ, Simmons A, Vergani F, Murphy DGM, Catani M. 2011. A lateralized brain network for visuospatial attention. *Nat Neurosci.* 14:1245–1246.
- Desikan RS, Ségonne F, Fischl B, Quinn BT, Dickerson BC, Blacker D, Buckner RL, Dale AM, Maguire RP, Hyman BT, Albert MS, Killiany RJ. 2006. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *NeuroImage.* 31:968–980.
- Draganski B, Gaser C, Busch V, Schuierer G, Bogdahn U, May A. 2004. Neuroplasticity: changes in grey matter induced by training. *Nature.* 427:311–312.
- Driemeyer J, Boyke J, Gaser C, Büchel C, May A. 2008. Changes in Gray Matter Induced by Learning—Revisited. *PLoS ONE.* 3:e2669.
- Eickhoff SB, Paus T, Caspers S, Grosbras M-H, Evans AC, Zilles K, Amunts K. 2007. Assignment of functional activations to probabilistic cytoarchitectonic areas revisited. *NeuroImage.* 36:511–521.
- Fox MD, Raichle ME. 2007. Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nat Rev Neurosci.* 8:700–711.
- Fuhrmann D, Knoll LJ, Blakemore S-J. 2015. Adolescence as a Sensitive Period of Brain Development. *Trends Cogn Sci.* 19:558–566.
- Galati G, Committeri G, Spitoni G, Aprile T, Di Russo F, Pitzalis S, Pizzamiglio L. 2008. A selective representation of the meaning of actions in the auditory mirror system. *NeuroImage.* 40:1274–1286.

- Gaser C, Schlaug G. 2003. Brain Structures Differ between Musicians and Non-Musicians. *J Neurosci.* 23:9240–9245.
- Grill-Spector K, Weiner KS. 2014. The functional architecture of the ventral temporal cortex and its role in categorization. *Nat Rev Neurosci.* 15:536–548.
- Grothe B. 2003. New roles for synaptic inhibition in sound localization. *Nat Rev Neurosci.* 4:540–550.
- Guerra-Carrillo B, Mackey AP, Bunge SA. 2014. Resting-state fMRI: a window into human brain plasticity. *The Neuroscientist* 4. 20:522–533.
- Herholz SC, Coffey EBJ, Pantev C, Zatorre RJ. 2015. Dissociation of Neural Networks for Predisposition and for Training-Related Plasticity in Auditory-Motor Learning. *Cereb Cortex.* in press.
- Herholz SC, Zatorre RJ. 2012. Musical Training as a Framework for Brain Plasticity: Behavior, Function, and Structure. *Neuron.* 76:486–502.
- Hickok G, Poeppel D. 2004. Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language. *Cognition, Towards a New Functional Anatomy of Language.* 92:67–99.
- Hickok G, Poeppel D. 2007. The cortical organization of speech processing. *Nat Rev Neurosci.* 8:393–402.
- Hötting K, Röder B. 2013. Beneficial effects of physical exercise on neuroplasticity and cognition. *Neurosci Biobehav Rev.* 37:2243–2257.
- Hove MJ, Risen JL. 2009. It's All in the Timing: Interpersonal Synchrony Increases Affiliation. *Soc Cogn.* 27:949–960.
- Ito M. 1970. Neurophysiological aspects of the cerebellar motor control system. *Int J Neurol.* 7:162–176.
- Jäncke L, Gaab N, Wüstenberg T, Scheich H, Heinze HJ. 2001. Short-term functional plasticity in the human auditory cortex: an fMRI study. *Brain Res Cogn Brain Res.* 12:479–485.
- Kamali A, Sair HI, Radmanesh A, Hasan KM. 2014. Decoding the superior parietal lobule connections of the superior longitudinal fasciculus/arcuate fasciculus in the human brain. *Neuroscience.* 277:577–583.
- Kirschner S, Tomasello M. 2009. Joint drumming: social context facilitates synchronization in preschool children. *J Exp Child Psychol.* 102:299–314.
- Klöppel S, van Eimeren T, Glauche V, Vongersichten A, Münchau A, Frackowiak RSJ, Büchel C, Weiller C, Siebner HR. 2007. The effect of handedness on cortical motor activation during simple bilateral movements. *NeuroImage.* 34:274–280.
- Koelsch S, Maess B, Grossmann T, Friederici AD. 2003. Electric brain responses reveal gender differences in music processing. *Neuroreport.* 14:709–713.
- Kolb B, Muhammad A. 2014. Harnessing the power of neuroplasticity for intervention. *Front Hum Neurosci.* 8:377.
- Lahav A, Saltzman E, Schlaug G. 2007. Action representation of sound: audiomotor recognition network while listening to newly acquired actions. *J Neurosci.* 27:308–314.
- Langheim FJP, Callicott JH, Mattay VS, Duyn JH, Weinberger DR. 2002. Cortical systems associated with covert music rehearsal. *NeuroImage.* 16:901–908.
- Leaver AM, Rauschecker JP. 2010. Cortical representation of natural complex sounds: effects of acoustic features and auditory object category. *J Neurosci.* 30:7604–7612.
- Lewis CM, Baldassarre A, Committeri G, Romani GL, Corbetta M. 2009. Learning sculpts the spontaneous activity of the resting human brain. *Proc Natl Acad Sci.* 106:17558–17563.
- Lewis JW, Brefczynski JA, Phinney RE, Janik JJ, DeYoe EA. 2005. Distinct cortical pathways for processing tool versus animal sounds. *J Neurosci.* 25:5148–5158.
- Maguire EA, Gadian DG, Johnsrude IS, Good CD, Ashburner J, Frackowiak RS, Frith CD. 2000. Navigation-related structural change in the hippocampi of taxi drivers. *Proc Natl Acad Sci U S A.* 97:4398–4403.
- Makris N, Goldstein JM, Kennedy D, Hodge SM, Caviness VS, Faraone SV, Tsuang MT, Seidman LJ. 2006. Decreased volume of left and total anterior insular lobule in schizophrenia. *Schizophr Res.* 83:155–171.

- Marr D. 1969. A theory of cerebellar cortex. *J Physiol.* 202:437–470.
- Molenberghs P, Cunnington R, Mattingley JB. 2012. Brain regions with mirror properties: A meta-analysis of 125 human fMRI studies. *Neurosci Biobehav Rev.* 36:341–349.
- Molnar-Szakacs I, Heaton P. 2012. Music: a unique window into the world of autism. *Ann N Y Acad Sci.* 1252:318–324.
- Molnar-Szakacs I, Overy K. 2006. Music and mirror neurons: from motion to 'e'motion. *Soc Cogn Affect Neurosci.* 1:235–241.
- Naito E, Scheperjans F, Eickhoff SB, Amunts K, Roland PE, Zilles K, Ehrsson HH. 2008. Human superior parietal lobule is involved in somatic perception of bimanual interaction with an external object. *J Neurophysiol.* 99:695–703.
- Ohnishi T, Matsuda H, Asada T, Aruga M, Hirakata M, Nishikawa M, Katoh A, Imabayashi E. 2001. Functional Anatomy of Musical Perception in Musicians. *Cereb Cortex.* 11:754–760.
- Pantev C, Herholz SC. 2011. Plasticity of the human auditory cortex related to musical training. *Neurosci Biobehav Rev, Wired for Sound.* 35:2140–2154.
- Pantev C, Lütkenhöner B, Hoke M, Lehnertz K. 1986. Comparison between simultaneously recorded auditory-evoked magnetic fields and potentials elicited by ipsilateral, contralateral and binaural tone burst stimulation. *Audiol Off Organ Int Soc Audiol.* 25:54–61.
- Pantev C, Okamoto H, Teismann H. 2012. Music-induced cortical plasticity and lateral inhibition in the human auditory cortex as foundations for tonal tinnitus treatment. *Front Syst Neurosci.* 27.
- Paraskevopoulos E, Kuchenbuch A, Herholz SC, Pantev C. 2012. Evidence for Training-Induced Plasticity in Multisensory Brain Structures: An MEG Study. *PLoS ONE.* 7:e36534.
- Petersen SE, Posner MI. 2012. The Attention System of the Human Brain: 20 Years After. *Annu Rev Neurosci.* 35:73–89.
- Petrini K, Pollick FE, Dahl S, McAleer P, McKay L, Rocchesso D, Waadeland CH, Love S, Avanzini F, Puce A. 2011. Action expertise reduces brain activity for audiovisual matching actions: An fMRI study with expert drummers. *NeuroImage.* 56:1480–1492.
- Pinho AL, de Manzano Ö, Fransson P, Eriksson H, Ullén F. 2014. Connecting to create: expertise in musical improvisation is associated with increased functional connectivity between premotor and prefrontal areas. *J Neurosci.* 34:6156–6163.
- Power JD, Fair DA, Schlaggar BL, Petersen SE. 2010. The development of human functional brain networks. *Neuron.* 67:735–748.
- Queen J. 2007. *The Next Level : Rudimental Snare Drum Techniques.* United States: Hudson Music.
- Rauschecker JP, Tian B. 2000. Mechanisms and streams for processing of “what” and “where” in auditory cortex. *Proc Natl Acad Sci.* 97:11800–11806.
- Riedel MC, Ray KL, Dick AS, Sutherland MT, Hernandez Z, Fox PM, Eickhoff SB, Fox PT, Laird AR. 2015. Meta-analytic connectivity and behavioral parcellation of the human cerebellum. *NeuroImage.* 117:327–342.
- Robertson A. 2014. Bassline Pitch Prediction for Real-Time Performance Systems. *Int Comput Music Conf Proc.* 2014.
- Rubia K. 2013. Functional brain imaging across development. *Eur Child Adolesc Psychiatry.* 22:719–731.
- Schlaug G, Jäncke L, Huang Y, Steinmetz H. 1995. In vivo evidence of structural brain asymmetry in musicians. *Science.* 267:699–701.
- Scott SK, McGettigan C, Eisner F. 2009. A little more conversation, a little less action — candidate roles for the motor cortex in speech perception. *Nat Rev Neurosci.* 10:295–302.
- Seitz RJ, Canavan AG, Yáguez L, Herzog H, Tellmann L, Knorr U, Huang Y, Hömberg V. 1997. Representations of graphomotor trajectories in the human parietal cortex: evidence for controlled processing and automatic performance. *Eur J Neurosci.* 9:378–389.
- Tsai C-G, Fan L-Y, Lee S-H, Chen J-H, Chou T-L. 2012. Specialization of the posterior temporal lobes for audio-motor processing – evidence from a functional magnetic resonance imaging study of skilled drummers. *Eur J Neurosci.* 35:634–643.

- Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B, Joliot M. 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *NeuroImage*. 15:273–289.
- Vahdat S, Darainy M, Milner TE, Ostry DJ. 2011. Functionally Specific Changes in Resting-State Sensorimotor Networks after Motor Learning. *J Neurosci*. 31:16907–16915.
- Veale JF. 2014. Edinburgh Handedness Inventory - Short Form: a revised version based on confirmatory factor analysis. *Laterality*. 19:164–177.
- Voelcker-Rehage C, Niemann C. 2013. Structural and functional brain changes related to different types of physical activity across the life span. *Neurosci Biobehav Rev*. 37:2268–2295.
- Vossel S, Geng JJ, Fink GR. 2014. Dorsal and Ventral Attention Systems. *The Neuroscientist*. 20:150–159.
- Wan CY, Schlaug G. 2010. Music Making as a Tool for Promoting Brain Plasticity across the Life Span. *Neurosci Rev J Bringing Neurobiol Neurol Psychiatry*. 16:566–577.
- Wang J, Fan L, Wang Y, Xu W, Jiang T, Fox PT, Eickhoff SB, Yu C, Jiang T. 2015. Determination of the posterior boundary of Wernicke’s area based on multimodal connectivity profiles. *Hum Brain Mapp*.
- Warren JE, Wise RJS, Warren JD. 2005. Sounds do-able: auditory–motor transformations and the posterior temporal plane. *Trends Neurosci*. 28:636–643.
- Whitfield-Gabrieli S, Ghosh SS, Nieto-Castanon A, Saygin Z, Doehrmann O, Chai XJ, Reynolds GO, Hofmann SG, Pollack MH, Gabrieli JDE. 2015. Brain connectomics predict response to treatment in social anxiety disorder. *Mol Psychiatry*. in press.
- Whitfield-Gabrieli S, Nieto-Castanon A. 2012. Conn: A Functional Connectivity Toolbox for Correlated and Anticorrelated Brain Networks. *Brain Connect*. 2:125–141.
- Wolpert DM, Goodbody SJ, Husain M. 1998. Maintaining internal representations: the role of the human superior parietal lobe. *Nat Neurosci*. 1:529–533.
- Yun K, Watanabe K, Shimojo S. 2012. Interpersonal body and neural synchronization as a marker of implicit social interaction. *Sci Rep*. 2:959.
- Zatorre RJ, Chen JL, Penhune VB. 2007. When the brain plays music: auditory-motor interactions in music perception and production. *Nat Rev Neurosci*. 8:547–558.
- Zatorre RJ, Delhommeau K, Zarate JM. 2012. Modulation of auditory cortex response to pitch variation following training with microtonal melodies. *Front Psychol*. 3:544.