

Musical mirror-symmetrical movement tasks: comparison of rhythm versus melody-playing

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Bimanual mirror-symmetrical movement (MSM) is relatively easy to control movement. Different MSM tasks may have different activations and interhemispheric interactions. The purpose of this study is to compare anatomo-physiological features such as hemispheric activations and dominance of two different MSMs, namely melody-playing and rhythm. We examined functional MRI (fMRI) recordings in a group of fifteen right-handed pianists performing two separate tasks: bimanual rhythm and bimanual melody-playing on two different keyboards with standard key order for right hand and reversed for left hand, which allows homolog fingers' movements. Activations and laterality indices on fMRI were examined. The results show that significant cerebellar activations (especially in anterior cerebellum) in both groups. Significant primary sensorimotor cortical activations are observed in the melody-playing group. While there are also bilaterally symmetric activations, and laterality indices suggest overall lateralization towards the left hemisphere in both groups. Activations in the left fronto-parietal cortex, left putamen and left thalamus in conjunction with right cerebellar activations suggest that the left cortico-thalamo-cerebellar loop may be a dominant loop. Dynamic causal modeling (DCM) indicates the presence of causal

influences from the left to the right cerebral cortex. In conclusion, melody-playing with bimanual MSM is a complex in-phase task and may help activate the bilateral cortical areas, and left hemisphere is dominant according to laterality indices and DCM results. On the other hand, bimanual rhythm is a simpler in-phase task and may help activate subcortical areas, which might be independent of the voluntary cortical task. *NeuroReport* 31: 523–529 Copyright © 2020 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction

In-phase movement (mirror-symmetrical movement, MSM) is a bimanual movement that is relatively easy to control tasks in many organisms. In MSMs, relaxed contralateral hand muscles are simply facilitated during voluntary contraction of the ipsilateral homolog muscle [1]. As such, in-phase movement can lead to decreased inter-cortical inhibition and increased excitatory effects [2]. Several in-phase tasks including bimanual voluntary tapping, mirror writing, mirror drawing, or navigation were examined in the literature [3–7]. These studies examined the effects of bimanual coordination on the stability of motor tasks and their neural mechanisms (Text 1, Supplemental Digital Content 1, <http://links.lww.com/WNR/A582>). Taken together, prior literature indicates that bimanual in-phase MSMs elicit reduced responses compared to anti-phase and unimanual movements in a

set of regions including left primary motor cortex (M1), right dorsal premotor cortex and supplementary motor area (SMA) and that interhemispheric talk at the level of M1 plays a role in movement stabilization.

Although bimanual MSMs are simple, stable motor movements, musical in-phase tasks remain understudied to the best of our knowledge. Therefore, the main motivation of the current study was to comparatively examine anatomo-physiological features –including interhemispheric crosstalk – of two musical bimanual MSMs in pianists, namely melody-playing and rhythm. Prior studies suggest a more efficient neural organization for hand motor control in pianists due to long-term motor practice [8] (see for a discussion Text 2, Supplemental Digital Content 1, <http://links.lww.com/WNR/A582>) [9–11]. Therefore, we recruited pianists here to increase sensitivity to potential differences in anatomo-physiological features between the MSM tasks.

Here, we consider a bimanual rhythm task that involves simple homolog finger movements. We also introduce

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bimanual piano playing, where homolog fingers play the same notes that significantly differs from prior methods [12–14] (see Text 2, Supplemental Digital Content 1, <http://links.lww.com/WNR/A582>) [15,16]. This in-phase melody-playing task involves bimanual movement where a regular keyboard for the right hand and a reversed keyboard for the left-hand is used (Supplemental Digital Content 2, <http://links.lww.com/WNR/A583>). Bimanual movement is transformed from anti-phase to in-phase movement similar to a ‘phase transition’ [17]. This allows the homolog fingers to play the same notes.

We performed fMRI on a group of fifteen right-handed pianists, where the group implemented both the bimanual rhythm task and the melody-playing task. Activations and laterality indices on fMRI were examined. Dynamic causal modeling (DCM) was performed where three different hypotheses were tested: modulation from only left-to-right, only right-to-left or in both directions. Based on experimental results, we discuss how the different in-phase tasks may contribute to bilateral activations in the scope of neurophysiology literature.

Methods

Subjects

This study included 15 (8 female/7 male) volunteering right-handed pianists with an average of 7 years (interquartile range: 5–7) of music experience (see for details Text 3, Supplemental Digital Content 1, <http://links.lww.com/WNR/A582>) [18,19]. Approval forms and written informed consent were obtained from all participants. Experimental procedures were approved by the local ethics committee. The study was performed in accordance with the Declaration of Helsinki.

Experimental design

The subjects were asked to tap the rhythm and perform melody-playing with two keyboards. In our design, the notes on the keyboard used for left hand were symmetrical to the keyboard used for right hand, which allows

subjects to play the same notes with the same fingers in the melody-playing as an in-phase MSM (Fig. 1). Having had no prior experience with the setup, the subjects could nevertheless play two keyboards with ease. Later, the subjects were immediately directed to fMRI examinations.

Behavioral procedures

The active phase consisted of two procedures:

- (1) A simple known melody at a tempo of 55 beats per minute was used. Melody-playing with the flexion of the proximal interphalangeal joint of all fingers for sequential finger movements with imaginary keyboards was performed. Hands were placed near their knees.
- (2) Rhythm tapping with the flexion of the proximal interphalangeal joint of all fingers simultaneously for all fingers (Text 3, Supplemental Digital Content 1, <http://links.lww.com/WNR/A582> for further details).

Functional MRI procedures

Brain images were acquired on a 1.5 Tesla MRI device equipped with an eight-channel head coil (Magnetom Symphony, Siemens, Erlangen, Germany) in the supine position where the head was restrained via a standard head bandage. Whole-brain functional MRI data were collected with blood oxygen level-dependent (BOLD) contrast. Functional images were collected with a T2*-weighted single-shot gradient echo-planar imaging sequence. The acquisition parameters for functional imaging were a flip angle of 90°, a time repetition/time echo (TR/TE) of 4010/50 ms, a number of excitations of 1, a field-of-view (FOV) of 211 mm, a resolution of 3.3×3.3×3 mm³, and an interslice space of 0.75 mm. A readout bandwidth of 1475 Hz/pixel was used. For each subject, fMRI data were acquired in a single series with 60-time points, with a total scan time of 4 min 5 s. Each series were composed of 3 active phase blocks with 10 images in each block, and 3 resting phase blocks with 10

Fig. 1



Recording procedure: Two keyboards (the left one modified reversely).

images in each block. Anatomical images were collected with T1-weighted spin-echo pulse sequences. The acquisition parameters for anatomical imaging were a flip angle of 70° , a TR/TE of 500/12 ms, a FOV of 211 mm, a resolution of $1.1 \times 1.47 \times 3 \text{ mm}^3$, and an interslice space of 0.75 mm. Thirty-six slices were acquired. A readout bandwidth of 130 Hz/pixel was used. Each acquisition lasted 2 min 28 s. Functional images were registered with T1-weighted anatomical images and functional mapping of brain anatomy was performed. See Text 3, Supplemental Digital Content 1, <http://links.lww.com/WNR/A582> for data preprocessing procedures.

Statistical analysis for functional MRI

General linear models

Voxel-by-voxel statistical analysis was conducted on each subject using the general linear model to correlate the time course of measured BOLD signals with the reference function generated by a box-car function convolved with the hemodynamic response function. For all 15 subjects, 60 functional volumes were used. Task-related activations were evaluated using four different general linear models. The first model evaluated activations related to melody-playing via a contrast vector [0 1] between melody-playing and resting. The second model evaluated activations related to rhythm via a contrast vector of [0 1] between rhythm and resting. The third model used a contrast vector of [1 -1] to distinguish the activated brain regions between melody-playing and rhythm. The fourth model used a contrast vector of [1 -1] to distinguish the activated brain regions between rhythm and melody-playing. For all general linear models, design matrices were constructed using the above-mentioned contrast vectors and the scan timing parameters. In all four models, cluster-forming thresholding was applied ($P < 0.001$). Each model was separately fit across the whole brain. Both individual-subject and group-level analyses were performed. For group-level assessment, a fixed-effects analysis was performed for improved sensitivity. Voxel time courses and design matrices were aggregated by concatenating the respective time courses across subjects. Voxel-by-voxel statistical analysis was then conducted using the multi-subject time courses and the multi-subject design matrix as in the individual-subject case.

Laterality index

Laterality indices numerical data were imported into SPSS 15 (version 15.0: SPSS Inc, Chicago, Illinois, USA) for descriptive analysis and graphical visualization. Significance of differences between the melody-playing and rhythm tasks in predefined regions of interests were assessed with Mann-Whitney *U* tests (see Text 3, Supplemental Digital Content 1, <http://links.lww.com/WNR/A582>) [20].

Dynamic causal modeling

DCM was applied to assess connectivity between left and right hemispheres in melody-playing and rhythm

(see Text 3, Supplemental Digital Content 1, <http://links.lww.com/WNR/A582>) [21,22]. Knowing both left and right hemispheres are activated, both tasks were specified as a direct effect on both hemispheres. Three different models, each of which corresponds to three different hypotheses, were tested:

- (1) Task acts as modulatory input from left to right.
- (2) Task acts as modulatory input from right to left.
- (3) Task acts as modulatory input from both left to right and right to left.

For all three models, analyses were conducted by extracting and fitting time-series from left hemisphere and right hemisphere. Modulatory inputs were assumed to be bilinear. Number of states per each region was assumed to be one. Stochastic effects and center inputs were not considered. DCM was applied independently to all 15 subjects. Results were then averaged across subjects using Bayesian parameter averaging. Finally, to test the validity of these models Bayesian model comparison was applied. A threshold probability of 0.9 was used to determine whether direct or modulatory effects were present. To control for multiple comparisons, cluster-forming thresholding was applied ($P < 0.001$) at the voxel level.

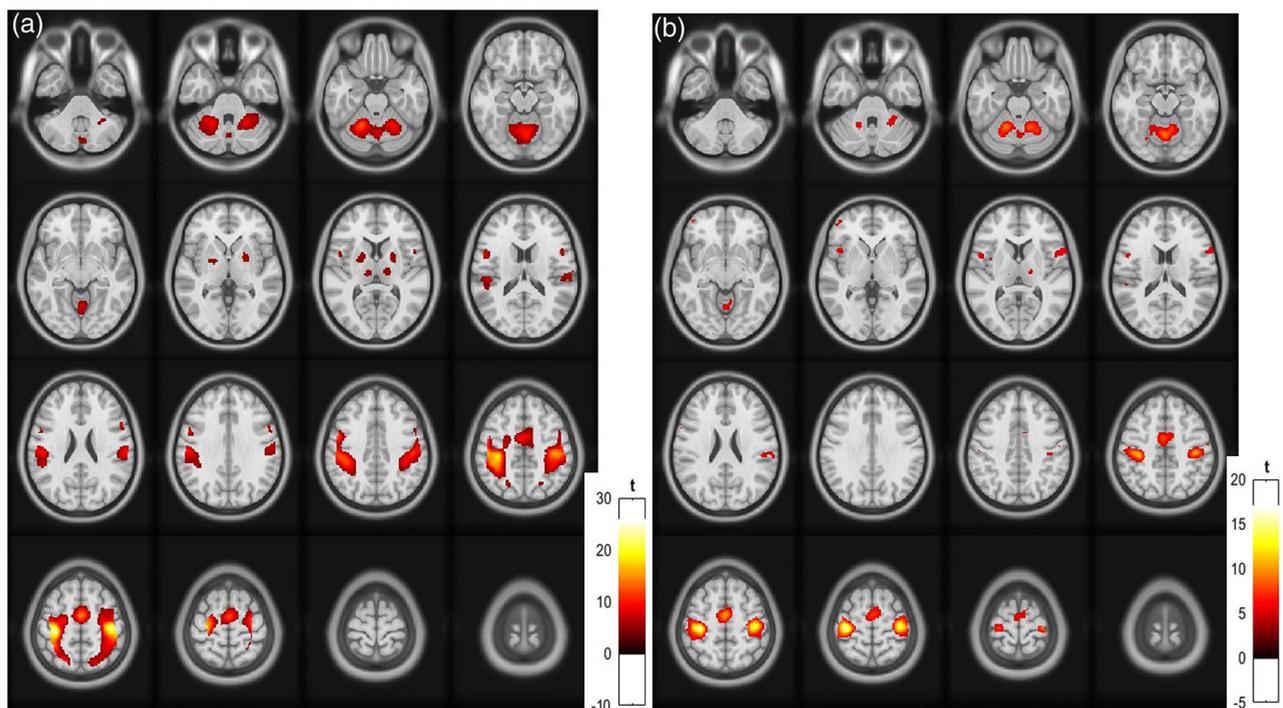
Results

Functional MRI findings

Activations were evaluated for melody-playing vs. rest and rhythm vs. rest contrasts for individual subjects and for the group-level separately ($P < 0.001$). In the individual-subject analysis, for both melody-playing and rhythm tasks, bilateral activations in the primary sensorimotor cortices, the SMA, the anterior lobe of the cerebellum, left thalamus and left putamen were observed for all 15 subjects. For the rhythm task, activations in anterior lobe of the cerebellum, across superior vermis and paravermian areas were observed in 12 subjects. Moreover, distinctively for the melody-playing task as opposed to the rhythm task, PPC activation was observed for 9 subjects.

In the group-level analysis, in both melody-playing and rhythm tasks, significant activations were observed across cortical areas and the cerebellum. In both tasks, there were bilateral activations in the primary sensorimotor cortices, the SMA, the anterior lobe of the cerebellum, left thalamus and left putamen. In the melody-playing task, symmetric activations were present in the posterior parietal cortices (PPC) (Fig. 2a). Global maximal activation was in the right fronto-parietal cortices (Table 1). In the rhythm task, significant activations were observed in the anterior lobe of the cerebellum, across superior vermis and paravermian areas, partially spreading to the cortices (Fig. 2b). However, PPC activation, which was observed during the melody-playing task, was not observed. For the rhythm task, global maximal activation was in the anterior lobe of the cerebellum (Table 1).

Fig. 2



The contrasts in cerebral activations comparing melody vs. rest (a) and comparing rhythm vs. rest (b) were demonstrated. Activations occurring were demonstrated on 16 equispaced slices across the volume. (a) Significant activations were observed across cortical areas and the cerebellum. Bilateral activations in the primary sensorimotor cortices, the SMA, the anterior lobe of the cerebellum, PPC left thalamus and left putamen were observed ($P < 0.001$). (b) Activations were observed across cortical areas and the cerebellum. Bilateral activations in the primary sensorimotor cortices, the SMA, left thalamus and left putamen were observed. There were activations in the anterior lobe of the cerebellum, across superior vermis and paravermian areas, partially spreading to the cortices ($P < 0.001$). See color bar for the strength of activations. PPC, posterior parietal cortices; SMA, supplementary motor area.

Table 1 MNI coordinates of local maxima for cerebral areas showing task-related activation in melody playing and rhythm groups. For melody-playing, fronto-parietal area spanned across precentral, postcentral regions, and supplementary motor area. Cerebellum anterior lobe includes vermis area for both tasks

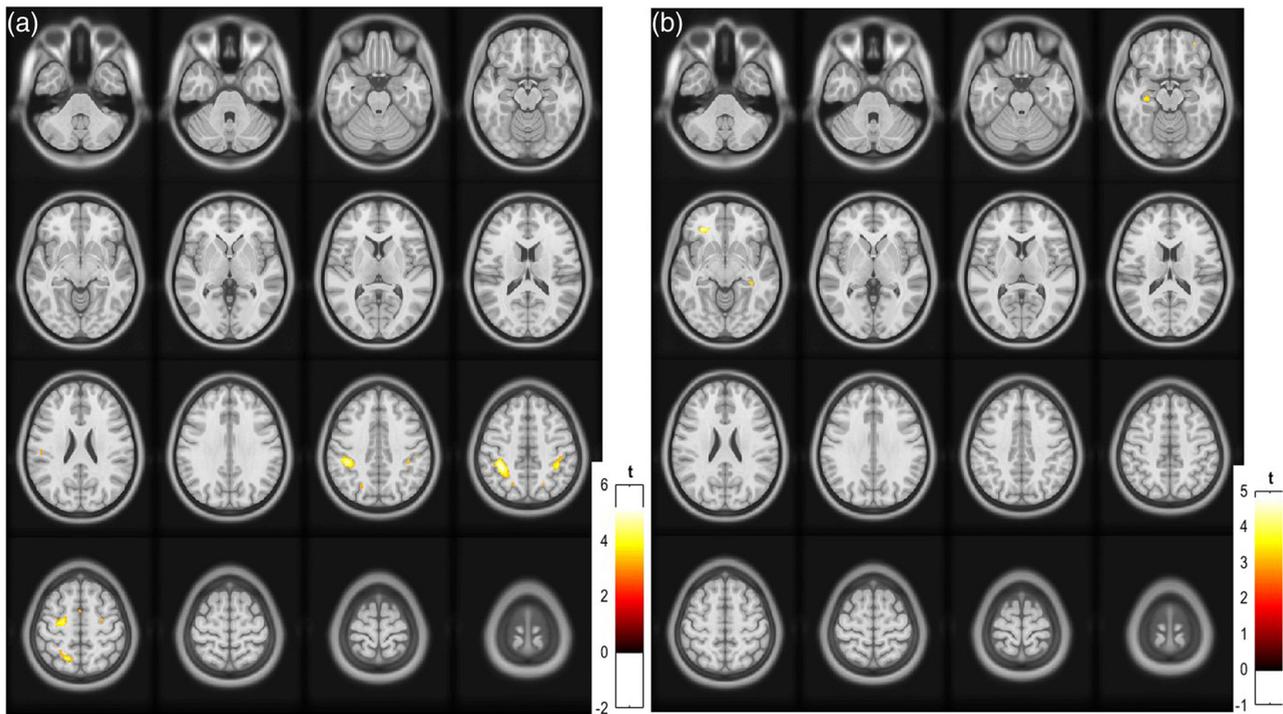
Melody-playing					Rhythm				
Region	<i>x, y, z</i>	<i>T</i>	<i>Z</i>	<i>P</i> -cor	Region	<i>x, y, z</i>	<i>t</i>	<i>Z</i>	<i>P</i> -cor
Right fronto-parietal	38, -26, 62	17.2	6.5	0.000	Cerebellum anterior lobe	2, -62, -10	13.8	6.0	0.000
Left fronto-parietal	-34, -26, 60	13.5	6.0	0.000	Right cerebellum	12, -54, -20	10.2	5.4	0.004
Cerebellum anterior lobe	4, -60, -18	11.8	5.7	0.001	Left cerebellum	-8, -58, -20	8.6	5.0	0.026
Left cerebellum	-16, -54, -24	10.8	5.5	0.003	Right SMA	4, -10, 54	7.3	7.3	0.099
Right cerebellum	14, -54, -24	8.9	5.1	0.022	Left SMA	-5, -4, 44	7.3	4.6	0.108
Left putamen	-22, 4, 8	8.2	4.9	0.047	Left fronto-parietal	-36, -32, 54	6.8	4.5	0.177
Left thalamus	-12, -18, 10	5.9	4.1	0.481	Right fronto-parietal	36, -28, 56	7.2	4.6	0.121
Left brainstem	-6, -36, -44	5.5	3.9	0.682	Left thalamus	-16, -16, 8	7.1	4.6	0.127
Left cerebellum posterior	-12, -54, -40	5.4	3.9	0.729	Left temporal	-42, 2, 8	5.3	3.9	0.693

MNI, Montreal Neurological Institute; *P*-cor, *P*-corrected; SMA, supplementary motor area.

To quantitatively assess the observed differences between melody-playing and rhythm tasks, activations were evaluated for melody-playing vs. rhythm and rhythm vs. melody-playing contrasts. In the melody-playing vs. rhythm contrast, significant activations were detected in PPC (Fig. 3a). No significant activations were detected in the rhythm vs. melody-playing contrast (Fig. 3b).

Laterality indices were calculated to assess hemispherical dominance during the melody-playing and rhythm tasks. Weak lateralization was observed in most of the brain regions with laterality indices in the range of laterality indices ≤ 0.2 , considered as bias. Only in the frontal lobe and basal ganglia laterality indices (respectively, laterality indices: 0.23 ± 0.14 ; laterality indices: 0.38 ± 0.24 ; $P < 0.05$) were slightly lateralized to left hemisphere in

Fig. 3



The contrasts in cerebral activations comparing melody-playing vs. rhythm (a) and comparing rhythm vs. melody-playing (b) were demonstrated. Activations occurring were demonstrated on 16 equispaced slices across the volume. (a) Significant activations were observed in PPC ($P < 0.001$). (b) No significant activations were observed ($P < 0.001$). See color bar for the strength of activations. PPC, posterior parietal cortices.

the melody-playing task, while parietal lobe, midline, and cerebellum were symmetric (respectively, laterality indices: 0.09 ± 0.17 , laterality indices: 0.13 ± 0.18 , laterality indices: 0.07 ± 0.12 ; $P > 0.05$). For rhythm, frontal lobe, parietal lobe, midline basal ganglia, and cerebellum have symmetric activity (respectively, 0.05 ± 0.21 , 0.03 ± 0.09 , 0.07 ± 0.17 , 0.14 ± 0.18 , -0.17 ± 0.20 , $P > 0.05$). To observe differences in hemispheric dominance between melody-playing and rhythm tasks laterality index differences were calculated. There were no significant differences in parietal, temporal, midline (e.g. SMA) cerebellar and basal ganglia laterality indices between melody-playing and rhythm tasks ($P > 0.05$). Only frontal laterality indices during rhythm was significantly lower (more symmetric) than the melody-playing task ($z: -2.24$; $P = 0.025$).

DCM was performed to assess whether causal interactions existed between the left and right hemispheres during melody-playing and rhythm tasks. Action of melody-playing as a direct effect on both hemispheres was verified. The strength of hemodynamic responses with direct effects to left hemisphere (L1) and to right hemisphere (R1) was found to be 0.144 and 0.821 Hz, respectively. The probability of a direct effect on L1 and R1 being present were both found to be 1. Melody-playing was observed to be acting as a modulatory input from left to right hemisphere. No modulatory effect was observed

in the right-to-left direction. The strength of hemodynamic responses with modulatory effects to left hemisphere (L1) and to right hemisphere (R1) were -0.079 and 2.586 Hz, respectively. These results suggested that a strong modulatory effect was present from the left hemisphere to the right hemisphere. The probability of a modulatory effect from left-to-right was found to be 1 whereas the probability of a right-to-left modulatory effect remained below threshold at a probability of 0.736. No causal interactions were observed during the rhythm task (see Fig. 1, Supplemental Digital Content 1, <http://links.lww.com/WNR/A582>).

Discussion

Given that bimanual MSMs are relatively easy to control movements and the neural organization of pianists is more efficient as opposed to nonpianists (see for a broader discussion Text 4, Supplemental Digital Content 1, <http://links.lww.com/WNR/A582>), investigating different musical tasks such as melody-playing and rhythm could reveal findings regarding the neural underpinnings of these tasks which could have potential use in various neurophysiology applications. Driven by this motivation, this study aims to draw attention to the fact that different in-phase movements may have different bimanual interaction mechanisms, which may be of importance

for neurophysiology literature and motor rehabilitation approaches. Here, we examined two different MSM tasks, comparing their anatomo-physiological features including hemispheric activations and dominance. In our study; primary sensorimotor cortices, SMA, anterior lobe of the cerebellum, putamen and thalamus were activated during both melody-playing and rhythm tasks. In particular, SMA was bilaterally activated during the sequential movement of either hand with no difference in the activation between the right and left hemispheres [23]. This finding is consistent with a previous study by Toyokura *et al.* [24], which suggests a larger role for the SMA proper in executive processing during bimanual, mirror performance of a complex movement. Meanwhile, left putamen and thalamic activations in both groups were left lateralized. Previous studies suggest that putamen plays a role in movement initiation, motor programming, general attention or intention [25]. This role can be attributed to the serial connectivity of the basal ganglionic structure and the funneling of efferent projections to the ventrolateral thalamus and to the motor cortex [26].

In contrast, bilateral posterior parietal cortical activations were only detected during melody-playing. PPC activation is related to the performance of sequences [27]. Sequential finger movements as in melody-playing, where the sequence has to be performed from memory, are more complex than simple repetitive movements as in the rhythm task. Thus, the PPC activation observed here could be attributed to task complexity. This explanation is also in line with previous reports that underline the importance of increasing task complexity [28,29]. Another difference that the melody-playing task shows relate to hemispheric dominance. Here DCM analyses in melody-playing reveal that this task acts as a modulatory input on the left-to-right connection. Both DCM analysis and laterality indices have pointed out that the melody-playing task may be controlled by the dominant hemisphere. These results are consistent with a recent study that suggests that coordinated bilateral hand movements may be controlled from the dominant left hemisphere [30].

In the literature, bilateral cerebellar activation is not only attributed to sensory (e.g. auditory) or cognitive processing, but also to motor processing during music performance [31]. Motor topography is considered to be present in the anterior lobe of the contralateral cerebellum, closer to the vermis, and to partly extend into the hemispheres [32]. Specifically, it has been reported that the cerebellum, projecting to the counter-dorsal prefrontal cortex, modulates the high cognitive function during the executive process of contralateral cerebrocerebellar loop movement and modulates the acuity timing of previously learned behavior [33]. In alignment with these previous reports, here, simple repetitive movement (rhythm) and sequential complex movement (melody-playing) evoked

activations in the vermian and paravermian areas of the anterior lobe of the cerebellum, and to a lesser degree in cerebral hemispheres.

Electroencephalography and transcranial magnetic stimulation studies report that as opposed to anti-phase, in-phase bimanual training increases M1 excitability [2]. The underlying neurophysiological mechanisms remain unclear [2,34–37] (Text 5, Supplemental Digital Content 1, <http://links.lww.com/WNR/A582>) [38–44]. Corpus callosum is frequently used during movements of attention and bimanual learning, and callosal transmission affects the degree of bilateral synchrony [23,45]. In our study, because of large cortical activations in melody-playing, intercortical interaction via corpus callosum seems to be more apparent in melody-playing than rhythm. However, interaction via corpus callosum might be mostly based on inhibitory characteristics imposed by in-phase movements. When it is freed from the corpus callosum-related intercortical inhibition, especially in-phase bimanual movement may be made easier as in callosotomy and patients with split-brain [28]. On the other hand, patients with split-brain show difficulty in performing anti-phase bimanual movements in contrast to in-phase movement [42]. We argue that the melody-playing with MSM may contribute to bilateral cortical activation by using a different interaction way from anti-phase movement. Future studies are required for the verification of this argument (see Text 5, Supplemental Digital Content 1, <http://links.lww.com/WNR/A582>).

Here, we examined anatomo-physiological features of two MSM tasks in healthy subjects. An implicit motivation was that the proposed tasks could only be considered as potential candidates for rehabilitation if they produce significant activations in regions commonly associated with the respective motor deficits. Our findings indicate that the melody-playing task might be more relevant for deficits such as cortical infarcts associated with the primary motor cortex. Furthermore, the homologous information provided in bimanual melody-playing from the opposite hemisphere, and the subcortical control in rhythm might be beneficial in motor rehabilitation. Future studies are needed to evaluate the utility of MSM tasks in patient populations.

Conclusion

In this study, we examined the anatomo-physiological features of two musical tasks based on in-phase motor behavior: namely melody-playing and rhythm. In both melody-playing and rhythm tasks, bilateral activations were observed in sensorimotor and SMAs, cerebellum, putamen, and thalamus. Yet, symmetric activations of posterior parietal areas were only observed in the melody-playing task. While most activations were bilateral, thalamo-cortical circuit activations were left dominant. Activation in anterior lobe of the cerebellum, especially

the superior vermis and paravermis, suggests that these areas serve a critical role in subcortical control of bimanual in-phase movements. In the melody-playing task, which likely leads to a different interhemispheric interaction via MSM, bilateral symmetrical activations were detected and classical right-hand information could be transferred to the left one in the first trial. Laterality index and DCM results indicate the presence of causal influences from the left to the right cerebral cortex.

Acknowledgments

Conflicts of interest

There are no conflicts of interest.

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