

Intercerebellar Coupling Contributes to Bimanual Coordination

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Abstract

■ Compared to unimanual task execution, simultaneous bimanual tapping tasks are associated with a significantly reduced intertap variability. It has been suggested that this *bimanual advantage* is based on the integration of timing signals which otherwise control each hand independently. Although its functional and anatomic foundations are poorly understood, functional coupling between cerebellar hemispheres might be behind this process. Because the execution of fast alternating fingertaps increases intertap variability, it is hypothesized that intercerebellar coupling is reduced in such tasks. To shed light on the functional significance of intercerebellar coupling, 14 right-handed subjects performed unimanual right, bimanual simultaneous, and bimanual alternating synchronization tasks with respect to a regular auditory pacing signal. In all conditions, within-hand intertap interval was 500 msec. Continuous neuromagnetic activity, using a 122-channel whole-

head neuromagnetometer and surface electromyograms of the first dorsal interosseus muscle of both hands, were recorded. For data analysis, we used the analysis tool *Dynamic Imaging of Coherent Sources*, which provides a tomographic map of cerebromuscular and cerebrocerebral coherence. Analysis revealed a bilateral cerebello-thalamo-cortical network oscillating at alpha (8–12 Hz) and beta (13–24 Hz) frequencies associated with bimanual synchronization. In line with our hypothesis, coupling between cerebellar hemispheres was restricted to simultaneous task execution. This result implies that intercerebellar coupling is key for the execution of simultaneous bimanual movements. Although the criticality of a specific magneto-encephalography pattern for behavioral changes should be interpreted with caution, data suggest that intercerebellar coupling possibly represents the functional foundation of the bimanual advantage. ■

INTRODUCTION

The execution of simple finger movements synchronized to an explicit timing signal is characterized by a certain intertap variability that is reduced during simultaneous bimanual task execution (reviewed by Ivry, Spencer, Zelaznik, & Diedrichsen, 2002). It has been argued that this “bimanual advantage” is due to the integration of otherwise independent timing signals prior to movement execution (Ivry & Hazeltine, 1999; Helmuth & Ivry, 1996). Timing signals are assumed to determine the point in time when a specific response should be initiated. Traditionally, the cerebellum has been related to such explicit timekeeping functions (for an overview, see Ivry et al., 2002). Specifically, lateral portions of cerebellar hemispheres seem to be strongly involved in mechanisms which are critical for accurate timing with respect to explicit signals (Ivry, Keele, & Diener, 1988). Lesions within the cerebellum cause significantly increased variability of the ipsilesional hand (Spencer, Zelaznik, Diedrichsen, & Ivry, 2003; Franz, Ivry, & Helmuth, 1996; Ivry et al., 1988), an effect remedied by

simultaneous bimanual task execution (Franz et al., 1996). These results suggest that timing signals of both hands are integrated during simultaneous bimanual movements, resulting in reduced timing variability of the impaired hand. Although there are various subcortical candidates for this assumed integration process (Ivry & Hazeltine, 1999), data from our recent magneto-encephalography (MEG) study revealed evidence supporting the assumption that functional connectivity between cerebellar hemispheres might be critical for the “bimanual advantage” (Pollok, Sudmeyer, Gross, & Schnitzler, 2005). Such functional connectivity represents a mechanism for neural communication in spatially distributed brain networks. It can be investigated by coherence analysis (for an overview, see Fries, 2005; Schnitzler & Gross, 2005).

In our previous study, subjects performed a simultaneous bimanual synchronization task, which was associated with functional coupling between cerebellar hemispheres. However, this coupling was not evident when subjects performed the same task unimanually (Pollok, Gross, Müller, Aschersleben, & Schnitzler, 2005), which would suggest that intercerebellar coupling is solely related to simultaneous bimanual task

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execution. A direct comparison of intercerebellar coupling strength during unimanual and bimanual synchronization, however, is still needed.

It is well known that fast (i.e., 200–400 msec) alternating finger taps of both hands result in increased intertap variability, compared to unimanual task performance (Keller & Repp, 2004; Wing, Church, & Gentner, 1989). Assuming that integration of timing signals is represented by intercerebellar coupling, increased variability—indicating decoupling of timing signals—should be associated with the absence or at least reduction of functional coupling between cerebellar hemispheres.

To further clarify our previous hypothesis that functional connectivity between left and right cerebellar hemispheres might be associated with the bimanual advantage, the present study aims at investigating whether increased variability evoked by bimanual alternating tapping is associated with decreased intercerebellar coherence strength.

METHODS

Subjects and Paradigm

Fourteen healthy right-handed volunteers, seven of whom were men and seven women, participated in this study. Mean age was 29.9 ± 1.7 years (mean \pm SEM) and overall age ranged between 22 and 45 years. Subjects gave their written informed consent prior to the MEG measurement. They were naive with regard to the purpose of the experiment. The study was approved by the local ethics committee and was in accordance with the Declaration of Helsinki.

We used a finger tapping task, which required subjects to synchronize their finger taps to an external auditory pacing signal. To this end, subjects performed brisk alternating finger flexions and extensions of the index finger. Subjects performed four experimental tasks consecutively for 4 min, respectively: (i) tapping with the right hand only (*right*), (ii) tapping with both hands simultaneously (*simultaneous*), (iii) alternating tapping of the left and right hand (*alternate*), and, finally, (iv) a rest condition in which the pacing signal was presented while no motor task was required (*rest*). The order of experimental runs was counterbalanced across subjects. Finger-taps were synchronized with a regular auditory pacing signal (400 Hz, 10 msec duration). Within-hand intertap interval was 500 msec in all movement conditions. Consequently, during rest, unimanual, and simultaneous tapping, the pacing signal was presented with an interstimulus interval (ISI) of 500 msec, whereas during the alternate condition, the ISI of the pacing signal was 250 msec. During this latter condition, subjects were instructed to synchronize taps of the left and right index fingers alternately with each tone resulting in one tap per tone. The pacing signal was delivered by a synthesizer (HP 33120A) and was presented binaurally

through plastic tubes. Handedness was assessed using the Edinburgh inventory (Oldfield, 1971).

Data Collection

Subjects were comfortably seated in a magnetically shielded room while performing their tasks. Both arms rested on wooden panels fixed laterally to the chair. To make sure that the instruction was understood correctly, subjects performed a short training period of about 10 taps in each condition just before the MEG measurement. The onset of finger-taps was determined by a photoelectric barrier mounted on a pad for each hand. Neuromagnetic activity was measured with a helmet-shaped 122-channel whole-head neuromagnetometer (Neuromag). Simultaneously, we recorded muscle activity using surface electromyograms (EMGs) placed on the first dorsal interosseus (FDI) muscle of both hands, respectively. MEG and EMG signals were recorded with a bandpass filter of 0.03–330 Hz, digitized with 1000 Hz, and stored digitally for off-line analysis. Eye blinks were controlled by vertical electrooculogram (EOG).

We determined the exact position of each subject's head with respect to the sensor-array by measuring the magnetic signals of four coils placed on the scalp. High-resolution T1-weighted magnetic resonance images (MRI) were obtained from each subject. Three anatomical landmarks (nasion, left and right preauricular points) were localized in each individual and used for the alignment of the MRI and MEG coordinate system. Because it has been shown that rectification of the EMG signal enhances the firing rate information of muscle activity (Myers et al., 2003), EMG signals were rectified off-line. Additionally, before rectification, EMG was high-pass filtered at 20 Hz to remove movement artifacts due to cables and electrodes.

Data Analysis

For the identification of brain areas associated with task execution, we used the analysis tool *Dynamic Imaging of Coherent Sources* (DICS; Gross et al., 2001), which provides tomographic maps of cerebromuscular and cerebrocerebral coherence. By using a spatial filter algorithm and a realistic head model, DICS allows for the detection of oscillatory activity within the entire brain (Gross, Timmermann, Kujala, Salmelin, & Schnitzler, 2003). Coherence is a normalized measure quantifying dependencies in the frequency domain. Values can range between 0, indicating independence of two signals, and 1, indicating a perfectly linear relationship. After applying a Hanning window, fast Fourier transform (FFT) was applied to all EMG and MEG signals using the Matlab FFT function (www.mathworks.com). Values were calculated with a resolution of 1.3 Hz. FFT was calculated on 256 samples. Windows overlapped with half the FFT size (i.e., 128 sam-

ples). In each condition, approximately 600 FFT segments were averaged. Subsequently, cross-spectral density was computed to all signal combinations and averaged across the whole measurement period. Finally, a spatial filter was applied to voxels of the entire brain in order to create tomographic maps of coherent activity. Voxel size was $6 \times 6 \times 6$ mm. In a first step, we identified the brain area with the strongest coherence to muscle activity. We identified this source as reference region for the detection of further brain areas subserving task execution. Cerebro-muscular coherence was calculated at movement frequency (i.e., 2 Hz). Coupling between brain areas was calculated at alpha (8–12 Hz) and at beta (13–24 Hz) frequencies, respectively. Frequencies were chosen because a vast variety of previous studies have evidenced that oscillatory activity as well as coupling between brain sites at both frequencies is closely related to motor control (for an overview, see Schnitzler & Gross, 2005). Indeed, Figure 3A nicely demonstrates that, in the present data, brain sources showed discernible peaks principally at these frequencies. For coherence analysis in each individual, the voxel showing coherence toward the reference region was identified. Hereby, a tomographic map of coherent activity was created in each volunteer. Because this procedure does not allow an estimation of significant coherence, each identified brain area (i.e., the voxel representing a specific brain area) was determined and introduced into a separate analysis which estimates coherence between all detected brain sites in each individual. By calculating a significance level for each combination, significant coherence was identified. For cerebro-muscular coherence, a confidence level was calculated according to Halliday et al. (1995). For coupling between brain sites, confidence limits were computed from surrogate data by randomly shuffling the original time courses, destroying all actual coherence. Only sources exceeding a 95% confidence level were taken into account for further analysis. To identify a consistent coupling pattern across subjects, we calculated coherence between all possible source combinations. Consistency was defined as significant coherence in at least eight subjects in at least one bimanual condition. As we presumed the alternating tapping task to be more complex than the unimanual and simultaneous bimanual execution, we took data from this condition for source localization. The detected brain sites were introduced into all other conditions. This procedure was chosen because, with respect to both bimanual tasks, we did not expect localization differences at least within a cerebello-thalamo-cortical network subserving motor control. However, we expected the more complex task to be associated with a more extensive network. This hypothesis is strongly supported by imaging studies (e.g., Debaere, Wenderoth, Sunaert, Van Hecke, & Swinnen, 2004).

We identified the position of each source in three-dimensional space. Mean localization maps of identified sources were calculated after normalization of anatomic

and functional data using SPM99 (Wellcome Department of Cognitive Neurology, Institute of Neurology, University College London, UK; www.fil.ion.ucl.ac.uk/spm). Spectral power of all detected brain areas was calculated as a measure of local neural activity. To reduce inter-individual variance, power was estimated by logarithmic transformation (Halliday et al., 1995).

Finally, to estimate coupling direction, we calculated the directionality index (DI) according to Rosenblum and Pikovsky (2001). DI provides information whether the phase dynamics of one oscillator is influenced by the phase dynamics of another one. Values range from -1 to 1 , with -1 and 1 corresponding to unidirectional coupling away and toward the reference region, respectively. Zero indicates symmetric bidirectional coupling between two areas. Unambiguous coupling direction was defined as the same sign (positive or negative) in more than half the subjects showing significant coherence, and—in addition—individual and mean DI values significantly different from zero. Values were calculated at alpha frequency, as coherence between brain sites occurred predominantly within this range.

Alpha adjustments for all repeated test procedures were achieved with the sequentially rejective Bonferroni test (Holm, 1979).

We were mainly interested in whether the previously demonstrated coupling between bilateral cerebellar hemispheres is predominantly related to simultaneous bimanual coordination. With this in mind, coherence strength between both cerebellar hemispheres during simultaneous tapping was compared to all other conditions. Further analysis of coherence between brain sites and local power was restricted to the comparison between simultaneous and alternating tapping.

RESULTS

Behavioral Data

The handedness test revealed a mean laterality quotient of 98.1 ± 1.0 (mean \pm SEM; range 88.0–100.0), suggesting that all subjects were strictly right-handed.

Mean negative asynchrony was -53.8 ± 6.4 msec (unimanual right hand), -44.0 ± 4.5 msec (simultaneous right hand), -48.4 ± 5.2 msec (simultaneous left hand), -51.2 ± 8.1 msec (alternate right hand), and -55.2 ± 5.9 msec (alternate left hand). No significant differences between hands or conditions were evident (Figure 1A). To estimate behavioral variability, two measures were calculated: mean individual standard deviation and mean within-hand intertap variability. Whereas the former indicates the temporal variability of the taps with respect to the pacing signal, the latter delineates tapping variability with respect to the previous tap.

Mean individual standard deviation (SD) was 34.8 ± 3.5 msec (unimanual right), 29.1 ± 2.5 msec (simultaneous right), 31.2 msec (simultaneous left), 51.6 ± 5.5 msec

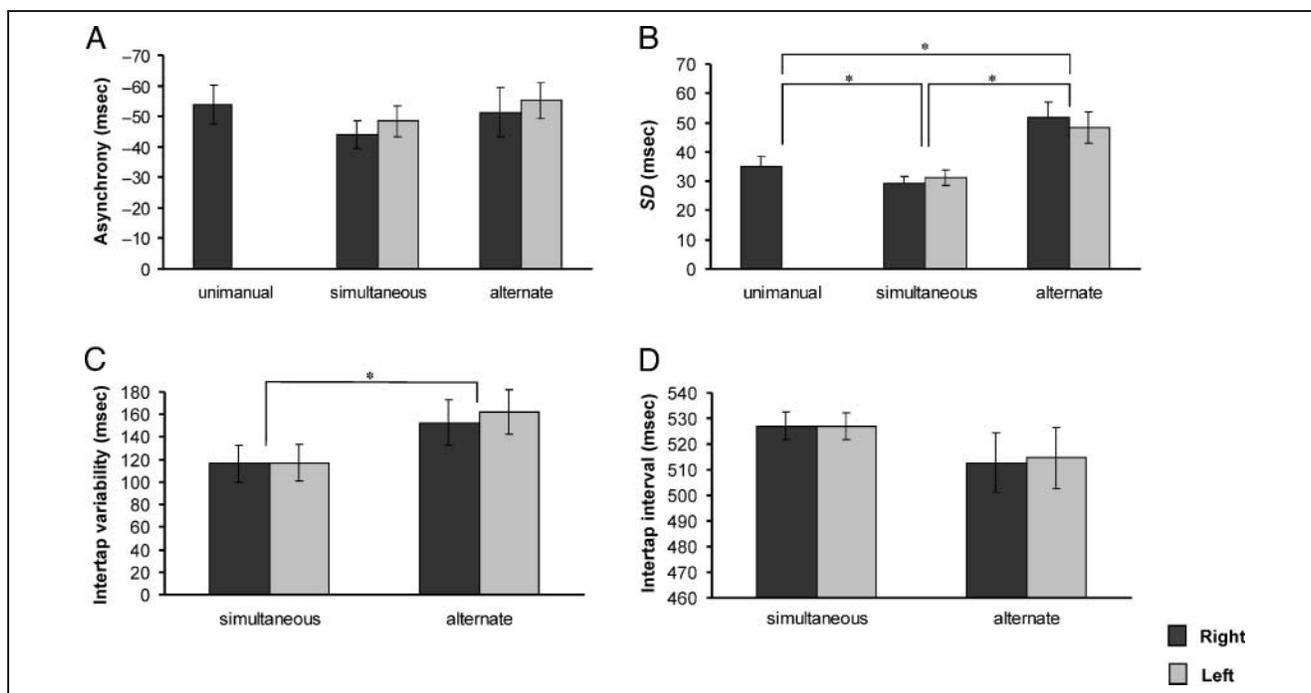


Figure 1. Summary of behavioral data. (A) Mean negative asynchrony during unimanual, simultaneous, and alternate tapping. No significant differences were evident between tapping conditions. (B) Mean standard deviation of negative asynchrony as a measure of intertap variability. Variability of each tap was estimated with respect to the pacing signal. Statistical analysis revealed that alternate tapping was more variable as compared to unimanual and simultaneous tapping. (C) Mean within-hand intertap variability (i.e., variability with respect to the previous tap) was significantly increased during alternating tapping, showing that the timing pattern was less stable during this condition. (D) Analysis of mean within-hand intertap interval demonstrated that subjects performed the required pattern sufficiently well in both bimanual conditions.

(alternate right), and 48.3 ± 5.4 msec (alternate left). Statistical analysis using repeated one-way analyses of variance, with factors condition (unimanual vs. simultaneous vs. alternating) and hand (left vs. right), revealed a main effect of condition [$F(2,26) = 14.1, p = .002$]. Post hoc paired comparisons demonstrated that *SD* during simultaneous tapping was significantly reduced ($p < .01$), whereas it was significantly increased during alternating tapping ($p < .01$) as compared to all other movement conditions (Figure 1B). Accordingly, analysis of mean within-hand intertap variability demonstrated that during alternate tapping the required pattern was more variable [$F(1,13) = 10.1, p = .007$; Figure 1C]. Mean values were: 116.3 ± 16.1 msec (simultaneous right), 117.0 ± 16.0 msec (simultaneous left), 152.6 ± 20.3 msec (alternate right), and 161.9 ± 19.9 msec (alternate left). To estimate whether subjects performed the movement tasks correctly, mean within-hand intertap interval, mean between-hand intertap interval, and mean error rate were calculated. Error rate was defined as number of taps which were not performed in an alternate but simultaneous manner during the alternating task. Analysis revealed mean within-hand intertap interval of 527.0 ± 5.4 msec (simultaneous right), 526.9 ± 5.3 msec (simultaneous left), 512.8 ± 5.4 msec (alternate right), and 514.6 ± 11.5 msec (alternate left). No significant differences between conditions or hands were evident (Fig-

ure 1D). Mean between-hand intertap interval during alternate tapping was 252.9 ± 3.6 msec. Mean error rate during this condition was $7.8 \pm 1.1\%$ (right hand) and $8.4 \pm 0.8\%$ (left hand). Both latter results indicate that subjects performed the alternate pattern sufficiently well. Because no difference between left and right hand occurred ($p > .3$) in any of the bimanual conditions, no evidence for one hand leading the other one was found.

Coherence between Brain Sites

Source Localization and Power

In all subjects, the source showing the strongest coherence to the FDI muscle was localized within the contralateral primary sensorimotor (S1/M1) hand area. Using S1/M1 of each hemisphere as reference region, we localized coherent activity within the bilateral premotor (PMC) and posterior parietal (PPC) cortex, the cerebellum, and the thalamus, within the supplementary motor area (SMA) and the anterior cingulum (ACC). With respect to the pacing signal, additional sources were localized within the temporal sulcus of each hemisphere corresponding to the auditory cortex. The ACC was localized in 12 of 14 subjects. The left auditory cortex was detected in 13 volunteers. All other sources were evident in all subjects. Figure 2 delineates mean source lo-

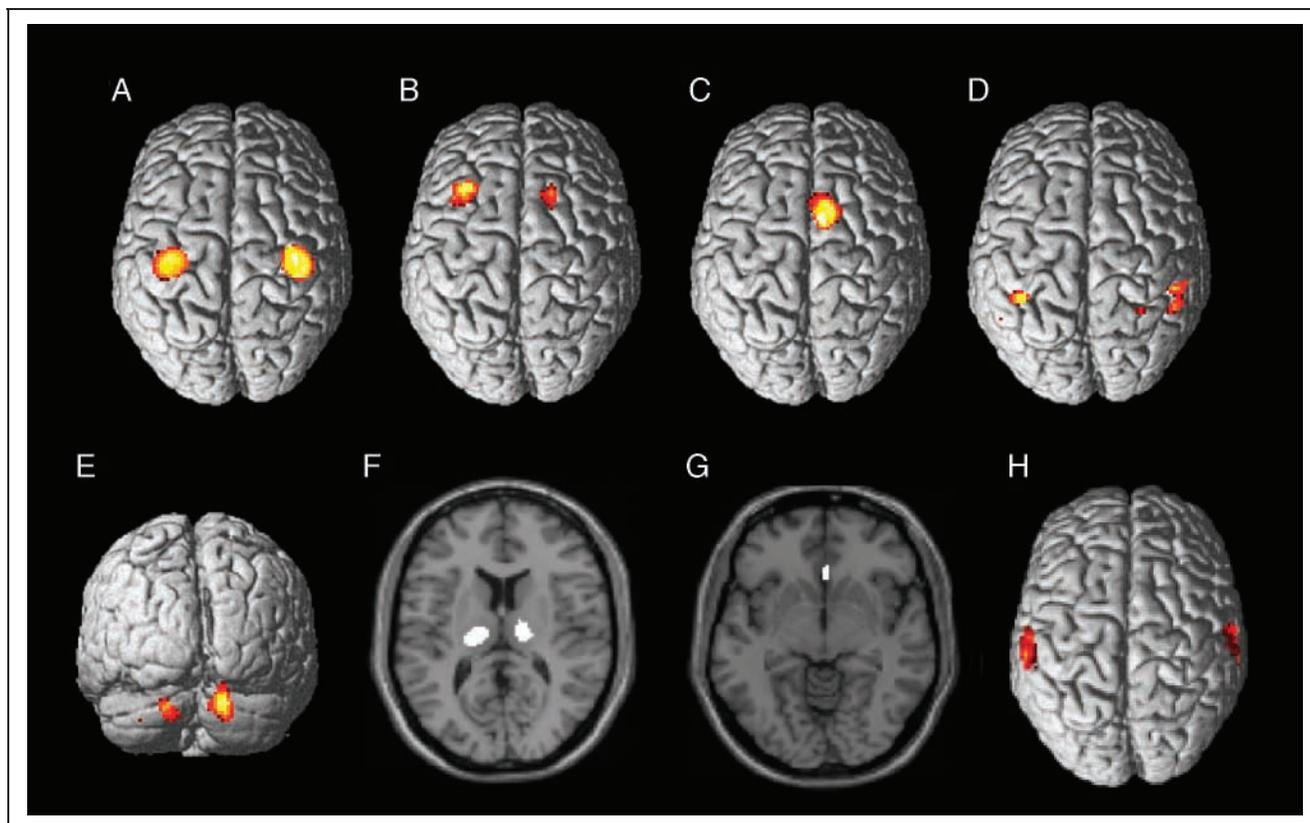


Figure 2. Mean source localization of coherent oscillatory activity at alpha and beta frequencies. Sources being consistently evident across subjects were localized within the bilateral (A) primary sensorimotor cortex (S1/M1), (B) the premotor cortex (PMC), (C) the supplementary motor cortex (SMA), (D) the superior posterior parietal cortex (PPC), (E) the cerebellum, (F) the thalamus, (G) the anterior cingulum, and (H) the auditory cortex. All sources were localized with respect to the alternate condition.

Table 1. Talairach Coordinates of Mean Source Localization for Each Brain Area Showing Consistently Coherence Values above the 95% Confidence Limit

Source	<i>x</i> Axis (mm)	<i>y</i> Axis (mm)	<i>z</i> Axis (mm)	BA
M1 left	-38	-22	62	4
M1 right	38	-22	62	4
PMC left	-32	22	48	8
PMC right	18	18	60	6
SMA	8	6	64	6
PPC left	-44	-44	56	40
PPC right	52	-48	50	40
Auditory cortex left	-58	-24	12	42
Auditory cortex right	60	-22	12	42
Anterior cingulum	4	30	-6	24
Thalamus left	-18	-18	12	
Thalamus right	16	-16	12	
Cerebellum left	-16	-82	-34	
Cerebellum right	16	-86	-30	

localizations as revealed by SPM99 and Table 1 summarizes the attendant Talairach coordinates.

Power spectral analysis using Wilcoxon test revealed significantly reduced power during alternating tapping within the left PMC and SMA at beta frequency, and within the left S1/M1 at alpha frequency as compared to simultaneous bimanual tapping ($p < .05$). Additionally, at alpha frequency, power of the left cerebellar hemisphere was significantly increased during alternating tapping as compared to simultaneous performance ($p = .03$). To rule out the possibility that the left cerebellar hemisphere might be inactive during alternate tapping, we compared left cerebellar activity with that of the right cerebellum in both bimanual conditions. However, analysis revealed no significant differences ($p > .1$). Along the same line, local power of the left cerebellum during rest was significantly increased as compared to both bimanual conditions, respectively ($p < .01$). Figure 3A illustrates local power of selected brain areas in one representative subject. Figure 3B summarizes mean power levels associated with both bimanual tapping conditions and during rest.

To ascertain whether power changes might be related with behavioral variability, Spearman rank order correlation was calculated. Only power changes of SMA at

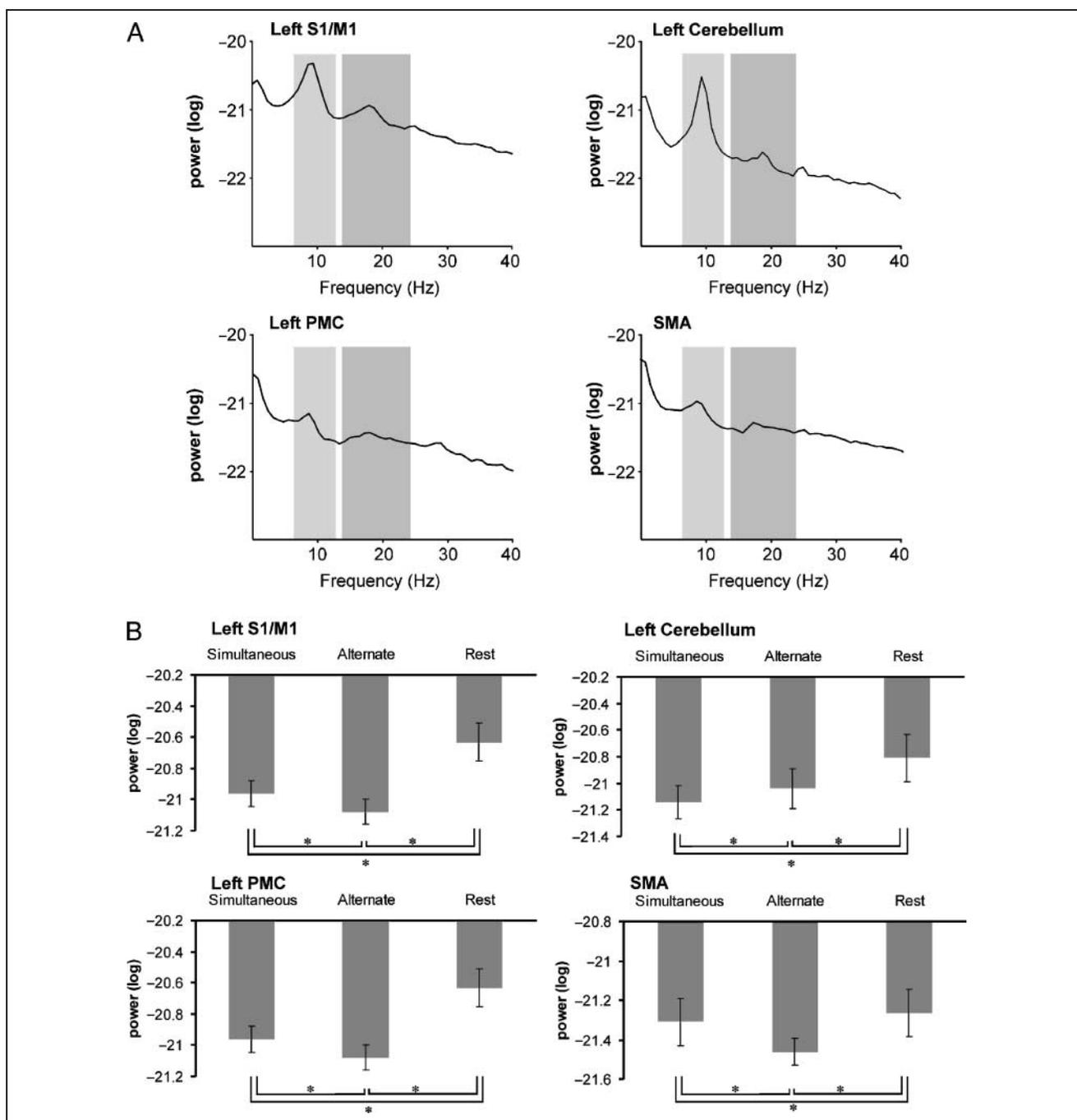


Figure 3. Local power as a measure of neural activity in detected brain sites. (A) Power of selected sources in one representative individual during alternate tapping. In all sources, discernible peaks at alpha (labeled light gray) and at beta frequency (gray) were evident. Moreover, in most sources, an additional peak at 25 Hz occurred, most likely representing the first subharmonic of the well-known 50-Hz artifact caused by electric current. (B) Mean power of brain areas showing significant differences between alternate and simultaneous bimanual conditions ($p > .05$). Error bars indicate standard error of mean (SEM). Power was estimated by logarithmic transformation in order to reduce interindividual variance. Mean logarithmic values are shown. Please note that increased power represents reduced neural activation in a given structure. Thus, in both bimanual conditions, neural activation was increased as compared to rest ($p < .01$).

20 Hz significantly correlated with behavioral variability ($\rho = .62$; $p = .05$).

Coupling Pattern

Figure 4 summarizes significant coherent couplings across all subjects associated with simultaneous and

alternating tapping at alpha frequency. Consistency was defined as significant coherence in at least eight subjects in one of the bimanual conditions. Alpha frequency was chosen for illustration because significant coupling was most prominent within this range. Table 2 summarizes mean cerebrocerebral coherence strength values.

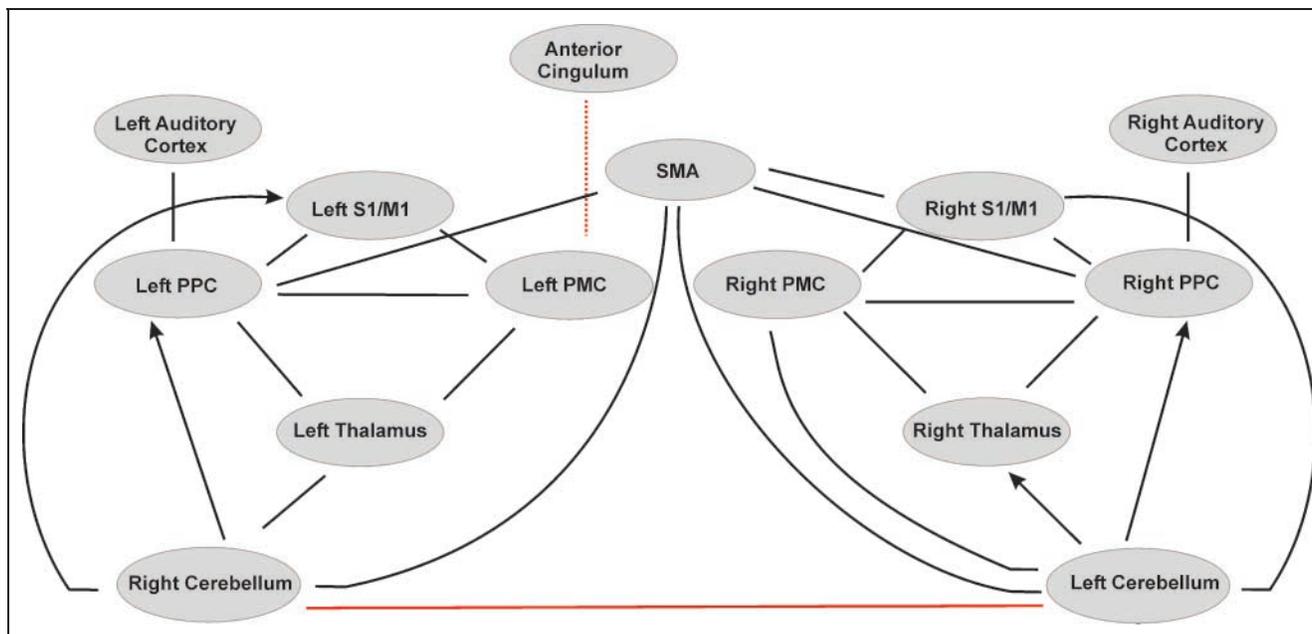


Figure 4. Coupling pattern consistently detected during alternating and simultaneous bimanual tapping. Please note that depicted connections occurred in at least eight subjects in at least one of both bimanual conditions. Arrows indicate main coupling direction, lines without arrowhead delineate bidirectional coupling (i.e., DI values not significantly different from zero). Additionally, the figure represents differences of functional connectivity between both bimanual conditions: Coherence between the left PMC and the ACC occurred more often during alternate tapping (red dotted line), whereas coherence between bilateral cerebellar hemispheres was significantly stronger and occurred more frequently during simultaneous tapping (red line). The figure indicates coupling at alpha frequency as differences between both bimanual conditions occurred at this frequency only.

Calculation of the DI revealed that bidirectional coupling was evident in majority of the couplings (i.e., values were not significantly different from zero). Couplings with unambiguous DI values are indicated in Figure 4. Values are listed in Table 3.

Statistical analysis using the Cochran Q test revealed that at alpha frequency coupling between both cerebellar hemispheres occurred significantly more often during simultaneous tapping as compared to all other conditions [$\chi^2(3) = 9.0, p = .03$]. Mean coherence strength was $13.1 \pm 4.4\%$ (*simultaneous*), $11.7 \pm 3.8\%$ (*alternate*), $10.9 \pm 4.2\%$ (*right*), and $9.8 \pm 3.8\%$ (*rest*). Consequently, coherence was significantly stronger during simultaneous tapping as compared to all other experimental conditions [Friedman test, $\chi^2(3) = 8.6, p = .04$]. At beta frequency neither number of significant couplings between left and right cerebellum nor coupling strengths differed significantly between conditions. Figure 5 summarizes relative number of significant coherences (A) and intercerebellar coupling strength at alpha frequency (B) during four experimental conditions.

From this analysis, however, we cannot rule out that the observed coupling between cerebellar hemispheres might be simply due to an entrainment of each hemisphere with external cues during simultaneous tapping (i.e., pacing signal and simultaneous movements of both hands). To ascertain that intercerebellar coherence is “real,” additional partial coherence analysis was performed (Ohara, Mima, Baba, & Ikeda, 2001; Mima,

Matsuoka, & Hallett, 2000). Partial coherence represents strength of functional interaction between two signals after eliminating a possible common input from a third signal. This analysis indicates how much of coupling between two signals (e.g., brain areas) can be explained by independent coupling of both signals with a third one (e.g., auditory stimulus or another brain site). Thus, this analysis allows an estimation of “true” coherence. Analysis demonstrates that partial coherence slightly increased as compared to original coherence values ($15.2 \pm 4.6\%$ after eliminating right-hand muscle signal; $14.3 \pm 4.5\%$ after eliminating left-hand muscle signal; $14.3 \pm 4.5\%$ after eliminating the pacing signal; $15.1 \pm 4.4\%$ after eliminating left S1/M1; $15.8 \pm 4.4\%$ after eliminating right S1/M1; $17.2 \pm 4.9\%$ after eliminating left auditory source; and $15.1 \pm 4.5\%$ after eliminating right auditory source). Statistical analysis revealed no significant differences between intercerebellar coherence and partial coherence values (Wilcoxon test: $p > .5$).

Furthermore, to rule out the possibility that decrease of intercerebellar coupling during alternating tapping is simply due to an increase of behavioral variability, we calculated Spearman rank order correlation between intercerebellar coupling strength and behavioral variability. However, analysis did not reveal a significant relation ($p > .1$). Finally, we calculated the correlation between local power within each cerebellar hemisphere at alpha frequency and intercerebellar coupling strength to investigate whether the decrease of intercerebellar coherence

Table 2. Mean Cerebrocerebral Coherence at Alpha Frequency Calculated for Alternate and Simultaneous Bimanual Tapping

	<i>Simultaneous</i>	<i>Alternate</i>
Cerebellum right–Thalamus left	6.5 ± 1.1	6.8 ± 1.1
Cerebellum left–Thalamus right	7.3 ± 1.9	6.6 ± 2.1
Cerebellum right–PPC left	1.3 ± 0.2	1.8 ± 0.5
Cerebellum left–PPC right	2.1 ± 0.7	1.7 ± 0.4
Cerebellum right–S1/M1 left	1.8 ± 0.4	1.5 ± 0.2
Cerebellum left–S1/M1 right	3.3 ± 1.7	2.6 ± 1.0
Cerebellum right–SMA	2.2 ± 0.4	1.9 ± 0.3
Cerebellum left–SMA	2.1 ± 0.7	1.7 ± 0.4
Cerebellum left–PMC right	1.6 ± 0.3	2.0 ± 0.4
Thalamus left–PPC left	6.6 ± 1.3	5.4 ± 1.2
Thalamus right–PPC right	3.4 ± 0.6	2.8 ± 0.4
Thalamus left–PMC left	7.7 ± 2.2	8.3 ± 2.1
Thalamus right–PMC right	8.3 ± 1.7	10.1 ± 1.7
PMC left–PPC left	8.2 ± 2.6	8.6 ± 1.9
PMC right–PPC right	3.3 ± 0.7	5.0 ± 1.3
PMC left–S1/M1 left	18.7 ± 4.7	19.1 ± 4.9
PMC right–S1/M1 right	11.2 ± 2.4	11.6 ± 2.8
PPC left–S1/M1 left	15.3 ± 3.3	16.7 ± 4.4
PPC right–S1/M1 right	14.0 ± 4.8	12.4 ± 4.2
PPC left–SMA	4.0 ± 1.0	4.5 ± 1.2
PPC right–SMA	5.5 ± 2.3	4.2 ± 1.8
ACC–PMC left	6.6 ± 1.6	6.2 ± 1.5

Listed are values in percent ($\pm SEM$).

might be caused by power changes of the left cerebellum. Calculation of Spearman rank order correlation did not reveal a significant relation between local cerebellar activity and intercerebellar coupling strength ($p > .3$).

Coupling between the ACC and the left PMC at alpha frequency occurred significantly more often during the

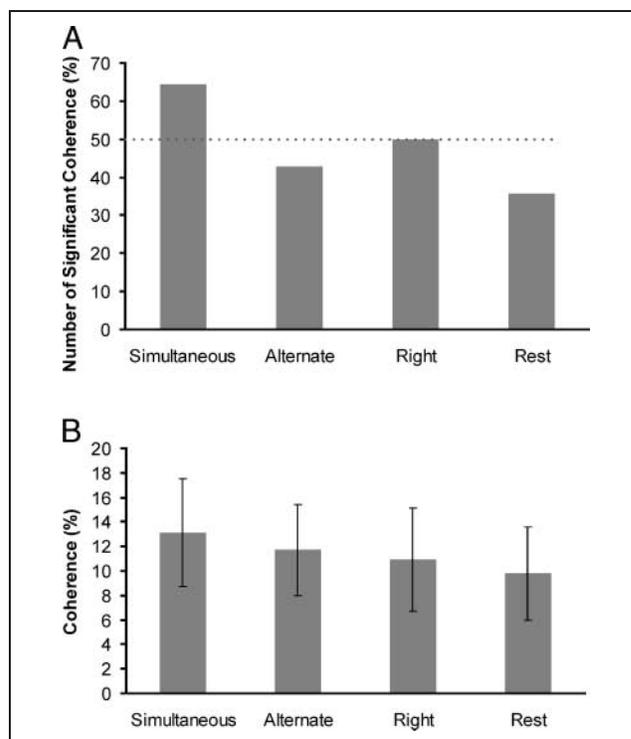


Figure 5. Relative number of significant coherence (A) and mean coherence strength (B) of intercerebellar coupling associated with four experimental conditions. The dotted line indicates the 50% level of chance. Coherence between bilateral cerebellar hemispheres occurred significantly more frequently and was significantly stronger during simultaneous performance as compared to all other conditions. Number of significant coherence as well as coherence strength did not differ significantly between alternate, right hand, and rest condition, respectively.

alternate condition [Cochran Q test: $\chi^2(3) = 14.4$, $p < .001$]. Once more, no differences between conditions were evident at beta frequency. Additionally, no further differences of number of significant couplings or coupling strength between both bimanual conditions at alpha or beta frequencies occurred.

DISCUSSION

The present study aimed at elucidating whether functional coupling between bilateral cerebellar hemispheres

Table 3. Mean DI Values ($\pm SEM$) Indicating Unambiguous Coupling Direction in at Least One Bimanual Condition

<i>Condition</i>	<i>Hemisphere</i>	<i>Cerebellum–Thalamus</i>	<i>Cerebellum–PPC</i>	<i>Cerebellum–S1/M1</i>
Simultaneous	Left	0.03 (± 0.07)	0.17 (± 0.07)*	0.15 (± 0.06)*
Alternate		0.01 (± 0.04)	0.03 (± 0.07)	0.05 (± 0.05)*
Simultaneous	Right	0.06 (± 0.09)	0.13 (± 0.06)*	–0.08 (± 0.06)
Alternate		0.21 (± 0.06)*	0.00 (± 0.07)	0.01 (± 0.07)

Asterisks indicate values being significantly different from zero. Please note that positive signs indicate main coupling from the first toward the second brain area.

is related to simultaneous bimanual movements. We hypothesized that this functional connectivity represents a neurophysiological correlate of a process integrating timing signals from both cerebellar hemispheres associated with reduced intertap variability. Data analysis revealed significantly stronger and more common coupling between both cerebellar hemispheres during simultaneous task execution as compared to unimanual and bimanual alternating tapping. Such differences occurred at alpha frequency. All in all, our results substantiate the hypothesis that intercerebellar coupling is strongly related to simultaneous bimanual tasks. Thus, data reveal a piece of evidence that intercerebellar coupling might reflect signal integration from both hemispheres, possibly resulting in the bimanual advantage. However, one should have in mind that a specific pattern of MEG activation cannot uniquely be related to behavioral changes. Thus, the present data should be interpreted cautiously.

Behavioral Data

Analysis showed that subjects performed the required patterns sufficiently well. As compared to all other experimental conditions, intertap variability was significantly reduced during simultaneous tapping, and increased during alternating performance. Reduced intertap variability during simultaneous bimanual tapping is a well-established phenomenon probably due to the integration of timing signals from both cerebellar hemispheres (for an overview, see Ivry et al., 2002). Accordingly, increased variability during bimanual alternating tapping also replicates previous findings (Keller & Repp, 2004; Wing et al., 1989). Although the lack of integration might explain increased variability during alternating as compared to simultaneous tapping, the question remains as to why variability is increased even when compared to unimanual task execution. Therefore, the observed changes during alternating tapping cannot be explained by a lack of timing signal integration alone, as this would result in variability comparable to that during unimanual tapping. This result might be due to the fact that alternating tapping requires a higher degree of motor control, which might have led to increased variability. Alternatively, higher attentional demands most likely have also contributed to this result. Numerous studies substantiate a strong relationship between attentional demands and bimanual pattern stability (for an overview, see Monno, Temprado, Zanone, & Laurent, 2002). These studies strongly reinforce that preferred bimanual coordination patterns are associated with less attentional demands and vice versa. Data of the present study reveal evidence for both, higher demands of the motor system—represented by stronger neural activation of the left PMC and S1/M1, and the SMA—as well as higher attentional demands, indicated by the involvement of the ACC, during alternating tapping.

Coherence between Brain Sites

Source Localization

Analysis revealed that the alternating bimanual task requires a bilateral cerebello-thalamo-cortical network, which is in line with our previous findings investigating the oscillatory network of simultaneous bimanual coordination (Pollok, Sudmeyer, et al., 2005). Unambiguous coupling direction was observed in a cerebello-thalamo-cortical network. Within this network, main coupling led from the cerebellum toward the contralateral thalamus, the PPC, and S1/M1, replicating our previous findings. In contrast to this study, present analysis of the DI revealed bidirectional coupling in the majority of connections. Although we do not have a conclusive explanation for this discrepancy, one might speculate that movement frequency might have influenced this result. In our previous study, the pacing signal was presented with an ISI of 800 msec, whereas it was 500 msec in the present study. However, we realize that this idea is highly speculative and needs to be tested in further studies.

Data reveal additional activation of the ACC, which was not evident during simultaneous tapping. The anterior cingulate gyrus and adjacent structures are assumed to constitute the core structure of an anterior attentional system (Posner & Petersen, 1990). In fact, several lines of evidence point to the significance of this structure for attentional control mechanisms (Horn, Syed, Lanfermann, Maurer, & Dierks, 2003; Waberski, Gobbele, Darvas, Schmitz, & Buchner, 2002; for an overview, see Carson & Kelso, 2004). Thus, activation of this structure is most likely due to higher attentional demands of the alternate task. Data of the present study suggest that attentional control—although generally assigned to the right hemisphere—seems to influence the left PMC, substantiating the superior role of the left hemisphere for motor control in right-handed subjects (e.g., Haaland, Elsinger, Mayer, Durgerian, & Rao, 2004; Grafton, Hazeltine, & Ivry, 2002; Viviani, Perani, Grassi, Bettinardi, & Fazio, 1998).

Power Analysis

It has been shown that spontaneous oscillations at alpha and beta frequencies within the sensorimotor system are dampened by limb movements and tactile stimulation. Thus, suppression of such oscillations is assumed to indicate an increase of neural activation (for an overview, see Hari & Salmelin, 1997). Analysis of local power indicated decreased power during alternate tapping within left PMC and SMA at 20 Hz, and within the left S1/M1 at 10 Hz, showing that these areas are more strongly activated during the more complex task. This interpretation tallies with imaging studies showing that neural activation within S1/M1 (Verstynen, Diedrichsen, Albert, Aparicio, & Ivry, 2005; Ullen, Forssberg, & Ehrsson, 2003; Toyokura, Muro, Komiya, & Obara, 1999; Jancke

et al., 1998; Viviani et al., 1998; Sadato, Campbell, Ibanez, Deiber, & Hallett, 1996; Shibasaki et al., 1993), the SMA (Meister et al., 2005; Lewis, Wing, Pope, Praamstra, & Miall, 2004; Ullen et al., 2003; Deiber, Honda, Ibanez, Sadato, & Hallett, 1999; Toyokura et al., 1999; Boecker et al., 1998; Shibasaki et al., 1993), and the PMC (Meister et al., 2005; Haaland et al., 2004; Lewis et al., 2004; Ullen et al., 2003; Sadato et al., 1996) increases with task complexity. Additionally, it has been shown that repetitive transcranial magnetic stimulation (rTMS) of the primary motor cortex disrupts complex sequential movements (Gerloff, Corwell, Chen, Hallett, & Cohen, 1998). Our data suggest an asymmetry of primary and premotor areas during alternating tapping with stronger activation of the left hemisphere. This observation is in line with the traditional view that, at least in right-handed subjects, the left hemisphere is specialized for skilled movements (for an overview, see Serrien, Ivry, & Swinnen, 2006). This hypothesis is based on functional as well as anatomical asymmetries of primary and secondary motor areas (reviewed in Serrien et al., 2006). More specifically, it has been shown that the execution of complex movements as compared to simple movements could be attributed to the left hemisphere (Haaland et al., 2004), a result nicely replicated by the present data. However, it should be stressed that the left hemispheric dominance for motor control has been queried. TMS (Meyer-Lindenberg, Ziemann, Hajak, Cohen, & Berman, 2002), as well as imaging studies (Stephan, Binkofski, Posse, Seitz, & Freund, 1999; Sadato, Yonekura, Waki, Yamada, & Ishii, 1997), revealed a superior role of right or bilateral (Aramaki, Honda, Okada, & Sadato, 2006; Ullen et al., 2003; Meyer-Lindenberg et al., 2002) PMC activation during antiphase (i.e., alternate) movements.

At the same time, at alpha frequency, left cerebellar power increased during alternate as compared to simultaneous task execution. Such power increase most likely indicates a decrease of neural activation. This result was surprising because previous studies demonstrated an increase of cerebellar activation during bimanual antiphase as compared to in-phase movements (Aramaki et al., 2006; Debaere et al., 2004; Tracy et al., 2001). However, paradigms used in these studies considerably differ from that used in the present one. Debaere et al. (2004) investigated wrist movements, a movement type most likely performed in a continuous manner. There is mounting evidence that continuous and discrete movements—such as finger tapping tasks—are based on different neural processes (Kennerley, Diedrichsen, Hazeltine, Semjen, & Ivry, 2002; Ivry & Hazeltine, 1999). Although Aramaki et al. (2006) used a finger tapping task, data might be confounded by an additional spatial task because left index and right middle fingers alternated periodically. Ullen et al. (2003), using a finger tapping paradigm comparable to that used in our study, showed the right cerebellar hemisphere to be more strongly involved in in-phase movements. These data

nicely demonstrate an asymmetry of cerebellar activation with stronger right cerebellar activation during simultaneous tapping. In the present data, weaker left cerebellar activation during alternate as compared to simultaneous tapping was evident. Taken together, both results imply a superior role of the right cerebellar hemisphere for the control of bimanual movements. This asymmetry—at first glance—contradicts the idea that the cerebellum is involved in timing for both bimanual conditions. However, comparing left and right cerebellar activation in each condition did not reveal a significant difference. Thus, both hemispheres are involved in the control of simultaneous as well as alternate movements.

One might question whether power changes within the cerebellum, and cortical structures represent the same mechanism. Because cerebellar power during rest was significantly increased as compared to movement, data suggest that power increase within the cerebellum also represents decrease of neural activation.

Functional Significance of Motor-related Structures for Bimanual Coordination

For bimanual coordination, a superior role of primary and premotor cortices has been evidenced (for reviews, see Cardoso de Oliveira, 2002; Gerloff & Andres, 2002; Swinnen, 2002). Specifically, it has been argued that stable in-phase (i.e., simultaneous) bimanual movements might be due to (i) a single motor command controlling both hands (i.e., generalized motor program [GMP]; Schmidt, 1975) or to (ii) cross-talk between brain signals controlling each hand (Marteniuk & MacKenzie, 1980). A likely candidate for the site of a GMP is the primary motor cortex (for review, see Cardoso de Oliveira, 2002). Although there is some evidence that S1/M1 of the left hemisphere might be more important for bimanual performance (Ullen et al., 2003; Jancke, Shah, & Peters, 2000; Urbano et al., 1998; Oda & Moritani, 1996), different lines of evidence suggest that both primary motor cortices act as one functional unit (for review, see Cardoso de Oliveira, 2002).

The cross-talk model assumes that bimanual coordination is mediated by interhemispheric interactions (reviewed by Cardoso de Oliveira, 2002). The primary motor and premotor cortices represent likely candidates for higher-level crosstalk (for review, see Gerloff & Andres, 2002). Studies on patients with acquired callosal damage substantiate the functional significance of interhemispheric information transfer, as such patients demonstrate striking disturbances of bimanual coordination—particularly during antiphase movements (Serrien, Nirkko, & Wiesendanger, 2001). Accordingly, Andres et al. (1999) demonstrated increased interhemispheric coupling during performance of a newly learned bimanual movement sequence by using electroencephalography (EEG). These results imply that interhemispheric coupling might represent transcallosal inhibition, which is assumed to play

a crucial role to reduce interference between both hemispheres (Daffertschofer, Peper, & Beek, 2005). Serrien and Brown (2002) investigated the effect of movement velocity during in-phase and antiphase movements on interhemispheric coupling between electrodes covering bilateral S1/M1. Interestingly, they found stronger interhemispheric coherence during antiphase movements when subjects performed the task with an ISI of 900 and 700 msec. However, when movement speed increased up to 500 msec, the reversed pattern occurred. At the same time, behavioral stability dramatically decreased during the short ISI. This result is in line with the hypothesis that coherence between bilateral S1/M1 represents inhibition to reduce interference specifically during antiphase movements, and thus, leads to behavioral stability. However, when movements exceed a certain velocity, interhemispheric coherence breaks down, possibly leading to the observed decrease of behavioral stability. Therefore, these results suggest that interhemispheric coupling is crucial for alternate movements. Present data did not reveal evidence for interhemispheric coupling between bilateral S1/M1. Assuming that such functional connectivity represents transcallosal inhibition, it was not expected for simultaneous but for alternate movements. Data support the first mentioned hypothesis but not the latter one. Although we do not have a conclusive answer, one might speculate that this result might be due to the pacing velocity, which tallies with that used by Serrien and Brown. In this study, the fastest movements were associated with a striking decrease of intercerebellar coupling.

Taken together, these data suggest that interhemispheric coupling between bilateral S1/M1 most likely represents transcallosal inhibition, which is effective for newly learned or alternating movements. However, they do not support a specific meaning of these brain areas for simultaneous movements, an interpretation which nicely fits with the present data.

Additionally, it has been argued that increased variability during antiphase movements might be due to signal interference mediated by ipsilateral corticospinal pathways (e.g., Kagerer, Summers, & Semjen, 2003; for an overview, see Carson, 2005). According to this concept, a part of neural signals controlling each hand are also descending ipsilaterally. As a consequence, each hand is assumed to be under the influence of the contralateral as well as the ipsilateral motor cortex. Because during alternate bimanual movements both signals are in conflict, temporal accuracy of both hands is more variable (Kagerer et al., 2003). Another possibility to account for the observation that in-phase movements are more stable than antiphase movements is the hypothesis that information from both hemispheres might be integrated within the SMA, resulting in reduced variability. This hypothesis is in line with an EEG study showing coherence between electrodes covering the bilateral S1/M1 and SMA during the execution of a bimanual task (Andres et al., 1999). Moreover, disruption of SMA acti-

vation by using rTMS results in reduced interhemispheric coherence—most likely between bilateral S1/M1—and in impaired temporal coordination of bimanual movements (Serrien, Strens, Oliviero, & Brown, 2002). Although stronger SMA activation during bimanual simultaneous movements as compared to unimanual movements has been shown (e.g., Jancke, Peters, Himmelbach, Nösselt, & Steinmetz, 2000; Stephan, Binkofski, Halsband, et al., 1999; Sadato et al., 1997), subsequent studies revealed growing evidence for the assumption that the SMA is not specific to bimanual movements but is associated with task complexity (Nair, Purcott, Fuchs, Steinberg, & Kelso, 2003; Steyvers et al., 2003; Ullen et al., 2003; Meyer-Lindenberg et al., 2002; Immisch, Waldvogel, van Gelderen, & Hallett, 2001; Stephan, Binkofski, Posse, et al., 1999; Toyokura et al., 1999; Sadato et al., 1997). Present data confirm this hypothesis as SMA activation increased during the more complex alternate task. Moreover, we found SMA activation to be correlated with behavioral variability. In the light of the cited studies, this result most likely indicates two effects of task complexity: (i) increase of behavioral variability and (ii) increase of SMA activation.

Evidence for the superior role of premotor areas for the execution of alternate movements comes from TMS studies (Meyer-Lindenberg et al., 2002) and patient studies (Dick, Benecke, Rothwell, Day, & Marsden, 1986; Freund & Hummelsheim, 1985; Laplane, Talairach, Meininger, Bancaud, & Orgogozo, 1977). Meyer-Lindenberg et al. (2002) demonstrated that a transient disturbance of the SMA and the PMC results in transitions from antiphase toward in-phase movements, supporting the specific significance of both structures for the control of complex movements. Along this line, SMA lesions are associated with deficient alternating movements (Dick et al., 1986; Freund & Hummelsheim, 1985; Laplane et al., 1977).

All in all, these data suggest that premotor areas are not exclusively related to bimanual tasks but govern complex movements. Consequently, they do not support an outstanding significance of premotor areas for behavioral stability during in-phase movements. Thus, power changes within primary and premotor regions observed in the present data most likely reflect higher degrees of task complexity during alternating tapping. Assuming that these brain areas might be critical for the *bimanual advantage*, one would expect stronger activation during simultaneous performance. Because the contrary occurred, the observed activation changes could not serve as an explanation for the bimanual advantage.

Coupling between Cerebellar Hemispheres

The foremost result evident from the present data is that coupling between both cerebellar hemispheres occurred significantly more often and significantly stronger during simultaneous tapping than during any other task. This result is consistent with our hypothesis that

coupling between cerebellar hemispheres might be crucial for simultaneous bimanual movements, possibly representing the neurophysiological correlate of the assumed integration of cerebellar timing signals (Ivry & Hazeltine, 1999; Franz et al., 1996; Helmuth & Ivry, 1996; Ivry et al., 1988). Assuming that both hands become temporally uncoupled during alternating tapping, at least weakening of coupling strength should occur, a hypothesis confirmed by the present data. Accordingly, it has been shown that in-phase coordination relies less on cortical but on cerebellar processes (Ullen et al., 2003), an interpretation which agrees with studies investigating callosotomy patients (Kennerley et al., 2002; Ivry & Hazeltine, 1999). However, one might question whether intercerebellar coupling is really a “true” phenomenon or whether it might be simply due to an entrainment of cerebellar hemispheres with a common peripheral event such as the pacing signal or muscle activity of both hands. Along this line, reduced intercerebellar coupling during alternate tapping might be a consequence rather than a cause of enhanced behavioral variability. Analysis of partial coherence demonstrated that the observed intercerebellar coupling cannot be accounted for such an entrainment because partial coherence values were slightly larger than the original coherence values. Although at first glance this result is striking, it is most likely due to the fact that eliminating one source is accompanied by removal of a certain degree of noise resulting in an increase of partial coherence. We observed this effect in a previous study (Pollok, Gross, Dirks, Timmermann, & Schnitzler, 2004), and simulations substantiate this hypothesis. To rule out the possibility that decrease of intercerebellar coupling strength during alternating tapping is due to an increase of behavioral variability, we additionally calculated the correlation between behavioral variability and intercerebellar coherence strength. Because no significant correlation was evident, we can rule out this possible explanation as well.

Another possibility to account for the observed differences between intercerebellar coupling during alternate and simultaneous tapping is based on the observation that activation of the left cerebellum was reduced during alternate as compared to simultaneous tapping. One might speculate that such a reduction results in reduced functional coupling, as there is no need for a less or even inactive area to be functionally connected to other brain areas. However, two results contradict this hypothesis: (i) Neural activation of the left cerebellum during rest was significantly reduced as compared to alternate performance and no significant differences between the left and right cerebellum were evident during alternate tapping. Thus, we can rule out that the left cerebellum was inactive during this condition. (ii) We found no significant correlation between cerebellar activity and intercerebellar coupling strength. Therefore, observed changes of intercerebellar coherence strength does not

seem to be influenced by power changes of cerebellar hemispheres.

Although analysis of coupling strength is in line with the hypothesis that intercerebellar coupling might be associated with the assumed integration of cerebellar signals, the present source localization of cerebellar activity is at odds with the observation that, specifically, lateral cerebellar portions are critical for timing processes (Ivry et al., 1988). As demonstrated in Figure 2 and Table 1, cerebellar sites detected in the present data are localized rather medially. However, one has to exercise caution when interpreting this result. One of the disadvantages of MEG data is the reduced localization accuracy (e.g., as compared to fMRI data). In particular, localization in deep brain structures such as the cerebellum is less accurate because MEG is less sensitive to neural activity in the center of the head and remote from the sensors (Gross et al., 2003). Having this in mind, source localization—specifically in deep brain structures—should not be overestimated. Thus, from the present data, we can conclude that both cerebellar hemispheres are involved in bimanual tapping tasks, but the exact localization of coherent activity within the cerebellum (i.e., lateral vs. medial structures) is unclear. Along the same line, it should be stressed that localization of oscillatory activity within the thalamus is affected in the same way, weakening the precision of localization in this brain structure as well (Gross et al., 2002). However, despite these known inaccuracies, it should be stressed that the feasibility of localizing oscillatory activity within the thalamus by means of MEG has been evidenced in several studies of our own (for an overview, see Schnitzler & Gross, 2005) and also of other working groups (Bish, Martin, Houck, Ilmoniemi, & Tesche, 2004; Mecklinger et al., 1998; Tesche, 1996a, 1996b).

Beside the cerebellum, the basal ganglia complex is also assumed to be crucial for the integration of timing signals (Ivry & Hazeltine, 1999). And indeed, it has been shown that patients with Parkinson’s disease (PD) show increased variability during the execution of bimanual tasks (Johnson et al., 1998). However, there is mounting evidence that this structure might be primarily involved in the selection (Jueptner & Weiller, 1998) or implementation (Penhune, Zatorre, & Evans, 1998) of movements. The cerebellum, on the other hand, seems to be crucial for monitoring and optimizing movements by using sensory—particularly proprioceptive—feedback information (Penhune et al., 1998; for an overview, see Jueptner & Weiller, 1998). Along this line, a recent study investigating patients with PD reveals some evidence against the assumption that the basal ganglia complex might contribute to explicit timing within the millisecond range, as PD patients showed no impaired timing abilities as compared to healthy controls (Spencer & Ivry, 2005). Although the latter result queries a specific meaning of the basal ganglia complex for timing processes, it does not necessarily rule out the opportunity

that, during bimanual simultaneous movements, timing signals from the cerebellum might be integrated on the level of the basal ganglia complex. However, present data do not confirm this possibility.

Functional Role of Somatosensory Information for the Bimanual Advantage

It has been argued that the bimanual advantage is due to the integration of timing signals prior to movement execution, and thus, due to processes on the efferent side (Ivry & Hazeltine, 1999). Alternatively, there is some evidence suggesting the importance of somatosensory information for this phenomenon. However, its functional influence remains controversial. On the one hand, contact-free tapping of one hand results in a reduction of the bimanual advantage in healthy subjects (Drewing, Hennings, & Ascherleben, 2002), corroborating the suggestion of a specific significance of somatosensory information for the effect observed. On the other hand, a somatosensory deafferented patient showed a bimanual advantage similar to healthy controls (Drewing, Stenneken, Cole, Prinz, & Aschersleben, 2004), which would undermine this hypothesis. In the present study, coupling between cerebellar hemispheres occurred mainly at alpha but not at beta frequency. Although the functional meaning of these frequencies is still under debate, one might speculate that coupling at alpha frequency represents the integration of sensory information, an idea corroborated by the findings of Drewing et al. (2002) in their investigation of healthy subjects.

Anatomical Foundations of Intercerebellar Coupling

Although Saito (1922) proposed the existence of a cerebellar commissural fiber system linking both cerebellar hemispheres, the anatomical basis for inter-cerebellar coupling is not yet understood. Berry et al. (1995) demonstrated that deep cerebellar nuclei in rats are interconnected through the anterior medullary velum. Additionally, anatomical studies in cats (Rosina & Provini, 1984) and rats (Mihailoff, 1983) demonstrated that ponto-cerebellar axons branch within the cerebellum, linking both cerebellar hemispheres. However, these data imply that inter-cerebellar coherence shown in the present study does not represent a direct interaction between both cerebellar hemispheres but should be mediated via a third source, probably localized within the pons. Although we did not find further oscillatory activity, we cannot rule out that this is simply due to insensitivity of the MEG device used in the present study to activity within this structure. Recent studies suggest an interesting alternative model to account for inter-cerebellar coupling specifically by means of coherence (Braitenberg, 2002; Braitenberg, Heck, & Sultan, 1997). Braitenberg and colleagues argue that sequences of disparate events might be represented within the cere-

bellum by successive excitation in a transversally oriented row of granular cells. By means of spatio-temporal summation in the parallel fiber system, information might be transferred along the whole length of the cerebellar cortex, even across the midline. Anatomical features of the cerebellum support this hypothesis because—in contrast to the telencephalon—the cerebellar cortical neuropil is continued without interruption between both hemispheres (Braitenberg et al., 1997). All in all, the exact anatomic foundations of the observed inter-cerebellar coupling are widely unknown. Although it might be due to direct interaction, possibly by successive excitation along transversally oriented cells as proposed by Braitenberg and coworkers, we cannot rule out that a third source, probably localized within the pons, mediates inter-cerebellar coupling.

In conclusion, data of the present study confirm the hypothesis that inter-cerebellar coupling is exclusively related to simultaneous bimanual performance. Results support the view that functional connectivity between bilateral cerebellar hemispheres might represent a neurophysiological correlate of the assumed integration of timing signals resulting in the bimanual advantage. However, one should bear in mind that, from the present data, it remains a moot issue, whether increased behavioral variability is cause or effect of reduced inter-cerebellar coupling.

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