Cerebellar Activation During Simple and Complex Bimanual Coordination

The Cerebellum
https://doi.org/10.1007/s12311-021-01261-8

REVIEW

Cerebellar Activation During Simple and Complex Bimanual Coordination: an Activation Likelihood Estimation (ALE) Meta-analysis

Kim van Dun[1] · Pia Brinkmann[2] · Siel Depestele[1] · Stefanie Verstraelen[1] · Raf Meesen[1,3]

Accepted: 15 March 2021

Abstract

Bimanual coordination is an important part of everyday life and recruits a large neural network, including the cerebellum. The specific role of the cerebellum in bimanual coordination has not yet been studied in depth, although several studies indicate a differential role of the anterior and posterior cerebellum depending on the complexity of the coordination. An activation likelihood estimation (ALE) meta-analysis was used combining the data of several functional MRI studies involving bimanual coordination tasks with varying complexities to unravel the involvement of the different areas of the cerebellum in simple and complex bimanual coordination. This study confirms the general bimanual network as found by Puttemans et al. (Puttemans et al. in J Neurosci 25:4270–4278, 2005) and highlights the differences between preferred in-phase (simultaneous movements of homologous muscle groups) and anti-phase movement conditions (alternating movements of homologous muscle groups), and more complex, non-preferred bimanual movements (e.g., out-of-phase movements). Our results show a differential role for the anterior and posterior vermis in bimanual coordination, with a role for the anterior vermis in anti-phase and complex bimanual coordination, and an exclusive role for the posterior vermis in complex bimanual movements. In addition, the way complexity was manipulated also seems to play a role in the involvement of the anterior and posterior vermis. We hypothesize that the anterior vermis is involved in sequential/spatial control, while the posterior vermis is involved in temporal control of (bimanual) coordination, though other factors such as (visual) feedback and continuity of the movement also seem to have an impact. More studies are needed to unravel the specific role of the cerebellar vermis in bimanual coordination.

Keywords Bimanual coordination · Complexity · Cerebellar vermis · Anterior cerebellum · Posterior cerebellum

Introduction

Tasks requiring coordinated movements of both hands are crucial for performing everyday tasks such as household activities, typing, driving, or playing an instrument. In comparison with unimanual (UM) movements, bimanual (BM) movements occur approximately twice as often in everyday functioning [1, 2]. Some of these BM movements are easy to perform since they consist of the same, mirrored, movements performed by both hands/arms simultaneously, e.g., rowing or opening a bag of nuts. Other movements consist of either alternating the same movements with both hands/arms, e.g., kayaking or crawl swimming, or executing the movements in parallel, e.g., moving an object with both hands from one side to the other. However, most BM movements require a more complex coordination of both hands, such as buttoning your shirt. In healthy young adults, successful BM coordination relies on a widespread neural network spanning cortical and subcortical areas [3, 4]. The general BM network identified by Puttemans et al. [3] includes the primary sensorimotor areas (S1/M1), the supplementary motor area (SMA), the ventral and dorsal premotor regions (PMv, PMd), the cingulate motor cortex, the areas in the lateral prefrontal cortex, the supramarginal gyrus, the inferior frontal and opercular areas, the cuneus, and the regions in the middle temporal cortex [3]. Subcortically, the basal

✉ Kim van Dun
kim.vandun@uhasselt.be

[1] Neuroplasticity and Movement Control Research Group, Rehabilitation Research Institute (REVAL), Hasselt University, Agoralaan A, 3590 Diepenbeek, Belgium

[2] Faculty of Psychology and Neuroscience, Department of Neuropsychology and Psychopharmacology, Maastricht University, Maastricht, The Netherlands

[3] Movement Control and Neuroplasticity Research Group, Department of Movement Sciences, Group Biomedical Sciences, KU Leuven, Leuven, Belgium

Published online: 30 September 2021

ganglia (putamen, globus pallidus), the thalamus, and the cerebellum (CB) are also involved [3, 5].

However, the amount of activation in different regions of the BM network is partly determined by the level of coordination complexity. Complexity can be manipulated by varying relative phase, temporal (relative interlimb frequency), and/or spatial (direction and amplitude) characteristics in BM tasks [6, 7]. Different constraints can be manipulated simultaneously, and the more constraints act in coalition, the more stable the coordination pattern will be [8]. Preferred and non-preferred movements have thus been identified depending on these coordination constraints [8]. In literature, relative phase has been classified in three conditions: BM in-phase (IP, relative phase $\Phi = 0°$) movements, BM anti-phase (AP, relative phase $\Phi = 180°$) movements, and BM out-of-phase movements (e.g., 90° phase offset or 45° phase offset). IP (i.e., mirrored-symmetrical) movements involve simultaneous contractions of homologous muscle groups, while AP (i.e., parallel-asymmetrical) movements involve contractions of homologous muscle groups in an alternating pattern. For example, moving both index fingers inwards and outwards with respect to the body midline with both palms down is considered IP movement, while moving both index fingers from the left to the right with both palms down is considered AP movement [9]. Both IP and AP movements are considered preferred movements [6, 7], but IP movements are easier to perform and are executed with higher accuracy than AP movements [9, 10]. It is known that if the frequency during AP movements is increased, participants automatically switch to IP movements, suggesting that IP movements are more stable [9, 10]. Thus, AP movements require a higher level of coordination. An even higher level of coordination is needed to perform 90° out-of-phase cyclical movements [5, 11]. Here, participants have to perform the task with one hand leading the other by a quarter of a cycle (i.e., relative phase $\Phi = 90°$). Next to phase manipulations, the level of complexity can also be increased by manipulating relative interlimb frequency. Simple rhythms (1:1 or 1:2), where both hands move at the same frequency (1:1) or one hand moves twice as fast as the other (1:2 or 2:1), are preferred over more complex polyrhythms (3:2 or 3:5) where the frequency of one hand is not an integer multiple of the frequency of the other hand [8]. Isofrequent movements (1:1), where both hands (homologous limbs) are moved in synchrony, are considered to be the most stable [8]. Similarly, complexity can be increased by manipulating spatial characteristics such as amplitude and direction. Moving both hands with different amplitudes or in different directions (e.g., moving one hand vertically and the other horizontally) are considered non-preferred movements [6, 7]. Taken together, when performing non-preferred movements, there is a general tendency to synchronize homologue limb movements both in space and time (i.e., tendency towards preferred patterns). Furthermore, whereas preferred movements belong to the intrinsic motor repertoire of human systems and thus do not require practice, accurate performance of non-preferred movements requires practice [6, 7].

Importantly, the BM coordination network also depends on performance speed and experience [8]. Debaere et al. [5] found that relative phase complexity and movement frequency (i.e., performance speed) interact in BM coordination tasks, showing increased activity patterns bilaterally in the PMd and in cerebellar regions (vermis of lobules VIII and VI, and hemispheres of lobule V). These areas of the CB have been primarily linked to sensorimotor processing [12] and are consistently observed in imaging studies using BM coordination paradigms [11, 13–16]. Debaere et al. [5] concluded that the CB was one of the critical regions for the control of BM coordination, as was already speculated by Tracy et al. [15], who linked the CB to the increased degree of coordination effort of AP movements as compared to UM movements. They found a specific involvement of the vermal regions of lobules VI and VIII, and of the right lateral part of lobule V in diadochokinesis, a clinical task to assess cerebellar function which involves alternating supination and pronation of the hands starting with one palm face up, and the other face down [15]. Schlerf et al. [17], however, showed that the posterior CB is not exclusively linked to BM coordination, but can also be activated in unilateral complex movements in contrast to unilateral simple movements. Especially the recruitment of the posterior lobe has therefore been attributed to the complexity of motor movements [18]. Experience is also a crucial factor to take into account when investigating complex BM coordination. For example, complex BM movements can be practiced extensively until automatization is reached, reducing the complexity of the BM coordination. Moreover, it has been shown that different brain regions are involved in the different stages of skill acquisition [3]. Usually, motor learning is divided into three stages: (1) the initial highly attention-demanding stage, (2) the intermediate stage characterized by a more established performance level and an increase in speed, and (3) the advanced automatized stage [3, 19]. Here, we focus on the role of the CB in BM coordination after an established performance level has been reached.

Lobule VII, part of the prefronto-cerebellar loop, might be recruited when executive functions are required to execute the requested movements correctly, especially in the initial motor learning stages [18]. This could be related to the crucial role of the dorsolateral prefrontal cortex in the initial stages of BM motor learning [6, 7, 20]. However, even in the later stages of motor learning, lobule VII can be recruited due to executive requirements [18].

The functional role of the CB has traditionally been studied in motor control [18, 21] and in motor learning [3, 22, 23]. However, little is still known about the specific role of

the CB in BM coordination. The aim of this study was to disentangle the role of the CB in BM coordination tasks with different levels of complexity primarily during the intermediate stage of motor learning. Four activation likelihood estimation (ALE) meta-analyses were performed. First, overall BM coordination across all complexity conditions was investigated. Next, a distinction was made between IP and AP (i.e., preferred movements that were isofrequent), and Complex (i.e., non-preferred movements due to relative phase, relative interlimb frequency, and/or different direction/amplitude) BM tasks. Our hypothesis was that the CB will be increasingly activated with increasing BM coordination complexity (IP < AP < Complex), and that especially the posterior part is involved in complex BM coordination, with a possible involvement of the executive lobule VII in the Complex condition.

Materials and Methods

Literature Review

Literature on functional imaging studies focusing on BM coordination were searched via PubMed and Web of Science (WoS) using search terms "functional MRI" OR "fMRI" OR "PET" OR "positron emission tomography", AND "bimanual coordination" (last search performed on 25 October 2019). The abstracts were screened, and articles that did not include functional imaging or BM coordination were removed, as well as non-original research (e.g., reviews, meta-analyses) or data of other population groups (e.g., monkeys, children, or patients). Articles that did not report coordinates, or reported contrasts that did not involve BM coordination, were eliminated, as well as connectivity studies and region of interest (ROI) analyses. All contrasts involving BM coordination were included (e.g., BM tasks versus rest, BM tasks versus UM tasks, and AP versus IP BM tasks). Contrasts that focused on different learning stages (e.g., Intermediate > Initial stage) were excluded. The included contrasts were subdivided in three conditions: in-phase (IP), anti-phase (AP), and Complex BM coordination. If a contrast involved more than one condition (e.g., IP and AP coordination versus rest), it was allocated to both conditions. The literature search and screening were performed by KvD and PB independently. The allocation to the different conditions was thoroughly discussed.

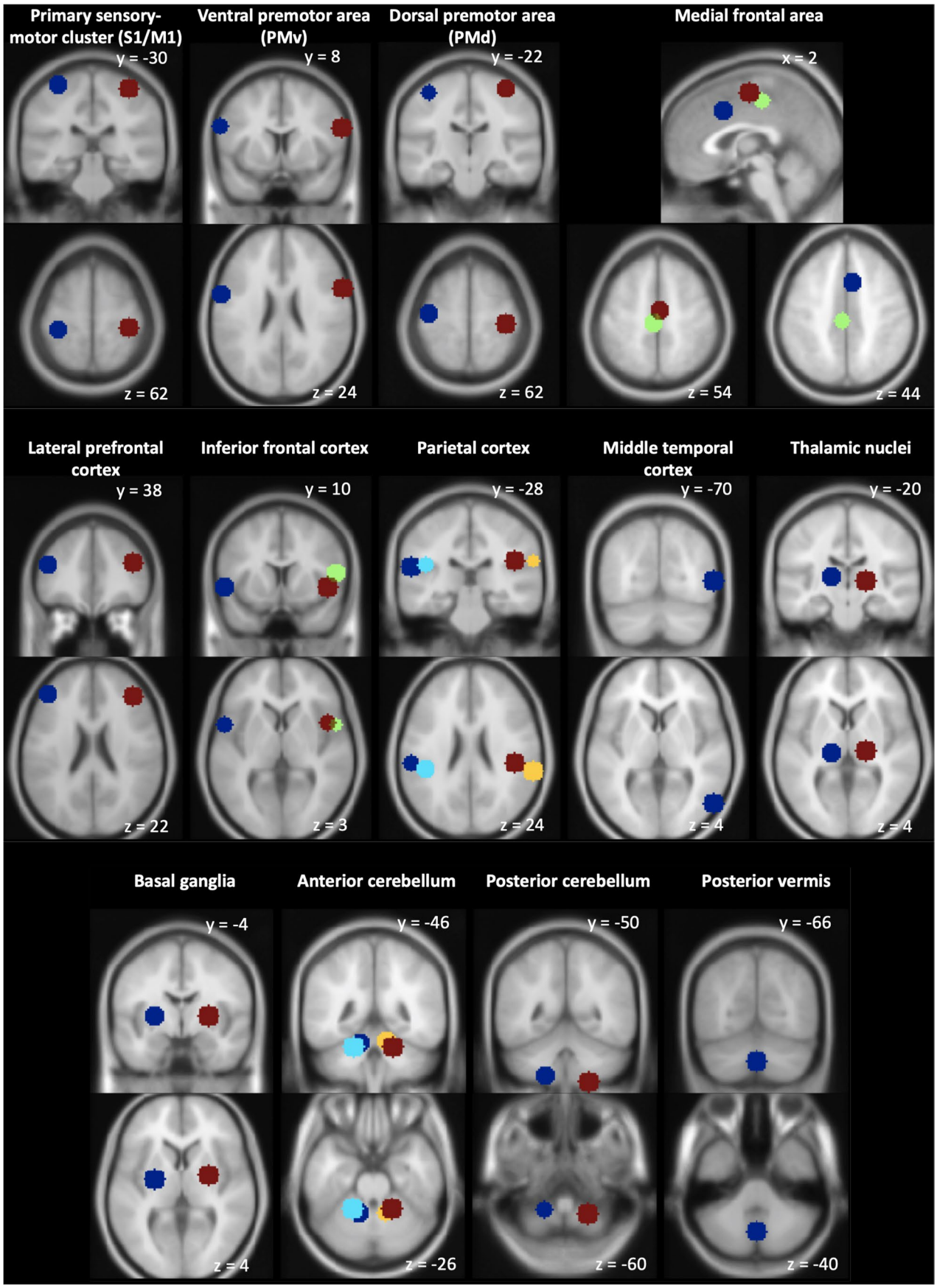
ALE Meta-analysis

The ALE meta-analysis was performed with GingerALE version 2.3.6 (www.brainmap.org/ale/), according to the methods described in [24, 25] and Turkeltaub et al. [26]. All coordinates were converted to MNI coordinates using GingerALE, depending on the software used in the article that reported the coordinates. Cluster-level inference was used with 5000 permutations, at a threshold of 0.05. The cluster-forming threshold was FDR pID < 0.001 [27]. Clusters with a size ≥ 50mm^3 and at least two different contributors (i.e., two different studies) were reported. This last requirement was implemented to avoid the inclusion of results that were primarily driven by one experiment and/or study. In total, four single dataset ALE analyses were performed: One general analysis, including all conditions, and one analysis per condition (IP, AP, and Complex BM coordination). The center coordinates of the clusters were reported, together with the local maxima. Due to lack of power, ALE contrast analyses between conditions were not possible. Only a visual comparison between conditions was performed. Cerebellar anatomy was identified using the SPM Anatomy toolbox (version 2.2b), which combines functional imaging data and probabilistic cytoarchitecture [28], and incorporates the SUIT template for the CB [29, 30].

Comparison with Previous Studies

Local maxima of the clusters found by the meta-analysis and in the three different conditions were visually compared to the general BM network as found by the fMRI study of Puttemans et al. [3], who used a complex cyclical BM coordination task. This network was the most extensive (32 foci) representation of BM coordination. Spheres of 10 mm diameter were created around the foci found by Puttemans et al. [3], using the SPM toolbox MarsBaR [31]. Figure 1 depicts the spheres around the foci. Note that results for the occipital lobe were not considered. Using MarsBaR, it was checked whether the local maxima of the clusters found by our analyses were inside one of the spheres around the foci of Puttemans et al. [3]. When a local maximum was part of two spheres, it was allocated to the sphere of which it was closest to the center.

Lastly, we also compared our results with the atlas of cerebellar and cerebral parcellations based on intrinsic functional connectivity by Buckner [32] and Thomas Yeo et al. [33]. The 7 network resting state cerebellar parcellation in FSL MNI152 space was used as provided by Freesurfer (http://www.freesurfer.net/fswiki/CerebellumParcellation_Buckner2011).


Primary sensory-motor cluster (S1/M1)
y = -30
z = 62
Ventral premotor area (PMv)
y = 8
z = 24
Dorsal premotor area (PMd)
y = -22
z = 62
Medial frontal area
x = 2
z = 54
z = 44
Lateral prefrontal cortex
y = 38
z = 22
Inferior frontal cortex
y = 10
z = 3
Parietal cortex
y = -28
z = 24
Middle temporal cortex
y = -70
z = 4
Thalamic nuclei
y = -20
z = 4
Basal ganglia
y = -4
z = 4
Anterior cerebellum
y = -46
z = -26
Posterior cerebellum
y = -50
z = -60
Posterior vermis
y = -66
z = -40

◂**Fig. 1** Regions of interest (ROIs) around the foci as found by Puttemans et al. [3] that were used for visual comparison with the foci found by our meta-analysis. Note that the occipital ROIs were not taken into account. The relevant MNI coordinate is indicated per slice

Results

Literature Review

The search yielded 188 articles after removal of duplicates. After exclusion based on abstract, 76 full-text articles were assessed. The flow chart is presented in Fig. 2.

In total, 30 studies were included, containing 68 contrasts. The number of foci, contrasts, subjects, individuals (i.e., total number of subjects that participated in the studies), and articles are shown in Table 1. IP contained 13 exclusive contrasts, AP had 20 exclusive contrasts, and Complex had 18 exclusive contrasts. Twelve contrasts were shared between IP and AP, and five were shared between all conditions. An overview of all included studies and contrasts is given in Table 7 of the Appendix.

ALE Meta-analysis

ALL The first ALE analysis included all contrasts and delineated 11 clusters (see Table 2 and Fig. 3). The three biggest clusters were located in the right and left precentral gyri (clusters 1 and 3), and in the anterior cerebellar vermis IV/V extending bilaterally into the hemispheres of lobules V and VI (cluster 2). Moreover, clusters in the SMA (cluster 4), in the right inferior frontal gyrus (cluster 7), and in the right and left thalamus extending into the globus pallidus (clusters 5 and 6) were identified. Two right lateralized clusters were found in the supramarginal gyrus (cluster 8) and the middle temporal gyrus (cluster 9). A posterior cerebellar cluster was located in the vermis of lobule VIIIa (cluster 10). The smallest cluster reflected activity in the left inferior parietal lobe (cluster 11).

IP The second ALE analysis, including contrasts examining the IP condition, identified 10 clusters (see Table 3 and Fig. 4). The largest cluster was observed in the anterior CB extending bilaterally into the hemispheres of lobules V and VI (cluster 1), followed by three clusters located in the right and left precentral gyrus (clusters 2 and 4) and the SMA (cluster 3). In addition, four subcortical clusters were found in the right and left thalamus and right and left globus pallidus (clusters 5 and 6, and clusters 7 and 8, respectively). The two smallest clusters were located in the left inferior parietal lobe (cluster 9) and the right inferior frontal gyrus (cluster 10).

AP The third ALE analysis consisted of contrasts investigating the AP condition (see Table 4 and Fig. 5). Here, the analysis resulted in nine clusters. The biggest cluster was in the anterior cerebellar vermis IV/V extending into the

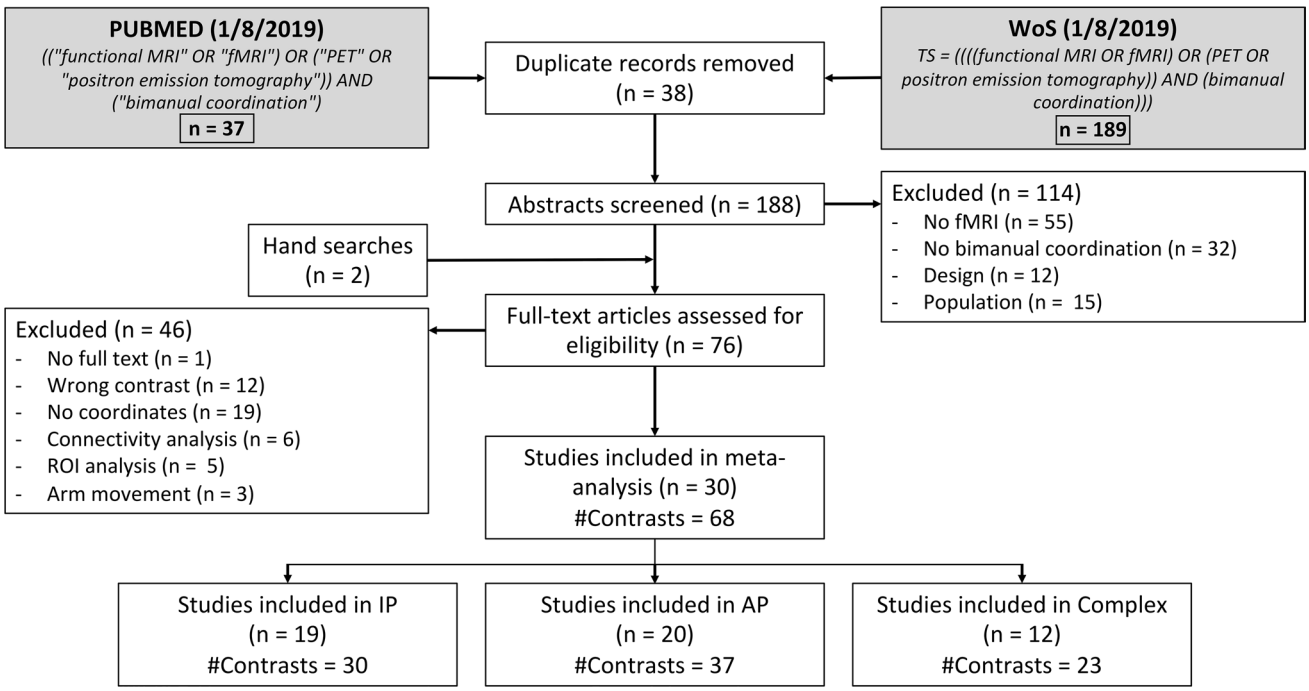


Fig. 2 CONSORT 2010 Flow Diagram. AP, anti-phase; IP, in-phase; WoS, Web of Science

Table 1 Number of foci, contrasts, subjects, individuals, and articles for each category

Category	Number of foci	Number of contrasts	Number of subjects	Number of individuals	Number of articles
All	757	68	875	441	30
IP	318	30	382	263	19
AP	420	37	473	277	20
Complex	312	23	321	197	12

AP anti-phase, *IP* in-phase

hemispheres of lobules V and VI (cluster 1) and the following three clusters in the SMA (cluster 2) and in the right and left precentral gyrus (clusters 3 and 4). Two subcortical clusters were delineated in the right and left thalamus extending into the globus pallidus (clusters 5 and 7), and one in the left anterior cerebellar hemisphere of lobule VI (cluster 6). The two smallest clusters were located in the right inferior frontal gyrus (cluster 8) and in the left supramarginal gyrus (cluster 9).

Complex The fourth and last ALE analysis using complex BM coordination contrasts revealed 13 clusters (see Table 5 and Fig. 6). Again, the largest cluster was found in the anterior cerebellar vermis IV/V extending into the vermis of lobule VI and the right hemisphere of lobule V (cluster 1). Additionally, a left and a right cluster were identified in lobule VI (clusters 4 and 6). Three clusters were located in the right and left precentral gyrus (cluster 2, and clusters 7 and 9), and two in the SMA (clusters 3 and 10). Subcortically, clusters were observed in the right and left thalamus (clusters 5 and 12), and in the right globus pallidus (cluster 11). In the posterior CB, a cluster was centered in the vermis of lobule VIIIa (cluster 8). Lastly, the smallest cluster was identified in the left inferior parietal lobule (cluster 13).

Comparison with Previous Studies

Most clusters found in Puttemans et al. [3] were also present in the All analysis of our study, with exception of the left inferior precentral gyrus, the anterior cingulate motor cortex, the left and right middle frontal gyrus, the left and right insula, and the left and right parietal operculum. The left and right activations in the lateral hemispheres of the posterior CB were also not replicated in our study. Additional clusters were found in the right superior frontal gyrus (somatomotor (integration) network [33]), the right superior (somatomotor integration network [33]), and left inferior parietal lobe (executive network [33]), and in the vermis of the anterior CB (somatomotor network [32]). All clusters can be found in Table 6.

When comparing the different conditions, two regions that were found in the All analysis were only present in the Complex condition on the cerebral level: the posterior cingulate zone (in the posterior part of the SMA) (somatomotor network [33]), and the left inferior parietal lobe (executive network [33]).

On the cerebellar level, the only differences were observed in the vermis. For the posterior vermis, a cluster was found only in the Complex condition. Concerning the anterior vermis, the local peak coordinate found in the Complex condition was slightly more posterior and inferior to the local peaks found in the AP and IP conditions. Moreover, the local peak coordinate found in the IP condition was situated just outside the anterior vermis according to the SPM anatomy toolbox (assigned to the left CB IV/V hemisphere). All cerebellar clusters were part of the somatomotor network [32].

Discussion

General Network

This ALE meta-analysis largely reproduced the general BM network as reported by Puttemans et al. [3] when all contrasts were included, with large clusters in the left and right precentral gyri, and the SMA, in addition to the subcortical clusters in the bilateral thalami and the anterior CB. The activations in the left precentral gyrus, the anterior cingulate motor cortex, the bilateral middle frontal gyri, the bilateral insulae, and the bilateral parietal opercula were not reproduced. This might be attributed to the specific experimental setup of Puttemans et al. [3], who studied the acquisition and automatization of a skilled motor task. They found that the activations in the premotor areas, the right supramarginal gyrus, the prefrontal cortex, the anterior cingulate motor cortex, the bilateral insulae, and the bilateral parietal opercular areas showed a learning-related decrease during the early acquisition of the task. Since most studies included in our meta-analysis first practiced the task outside the scanner until an established performance level was reached, this might explain the lack of activation in these areas.

Surprisingly, the activations in the bilateral hemispheres of the posterior CB were not replicated either. Lobule VIII has traditionally been associated with a secondary motor homunculus, which is bilaterally activated even during UM movements [17, 34]. However, activation of these areas was not always consistent across studies. For example, Habas et al. [35] only found activations in the posterior CB during out-of-phase and not during IP BM movements. They speculated that the level of activation in the posterior cerebellar

Table 2 Results of the ALE analysis including All contrasts. Coordinates of the center of the cluster are provided in bold, together with the local maxima in italic

Cluster	Local peaks	Anatomical label	MNI coordinates in mm				
			x	*y*	*z*	Cluster size in mm^3 (no. of contrasts)	CB assigned to
Cluster 1	*A*	**R PreCG**	**36.1**	**−24.4**	**56.1**	**11,600 (25)**	
	B	*R PreCG*	*36*	*−24*	*54*		
	C	*R PreCG*	*36*	*−12*	*58*		
	D	*R SPL*	*36*	*−44*	*58*		
	E	*R SFG*	*22*	*−8*	*64*		
	F	*R SPL*	*28*	*−54*	*62*		
		R SFG	*26*	*−2*	*58*		
Cluster 2	*A*	**CB vermis IV/V**	**.9**	**−54.3**	**−21.1**	**11,216 (20)**	**IV (hem)**
	B	*L CB IV/V*	*−16*	*−50*	*−22*		*V (hem)*
	C	*R CB IV/V*	*8*	*−54*	*−18*		*V (hem)*
	D	*R CB IV/V*	*20*	*−48*	*−26*		*VI (hem)*
		CB vermis IV/V	*2*	*−58*	*−18*		*V (hem)*
Cluster 3	*A*	**L PreCG**	**−35.5**	**−20.7**	**57.1**	**8368 (23)**	
	B	*L PreCG*	*−36*	*−20*	*58*		
	C	*L SPL*	*−36*	*−42*	*56*		
		L SMG	*−56*	*−22*	*42*		
Cluster 4	*A*	**L Post-Med Front**	**1**	**−4.3**	**56.2**	**7968 (23)**	
	B	*L Post-Med Front*	*−2*	*−8*	*58*		
	C	*R Post-Med Front*	*2*	*0*	*60*		
		L Post-Med Front	*−4*	−20	*50*		
Cluster 5	*A*	**R Thal**	**19.7**	**−13**	**4.3**	**4200 (14)**	
	B	*R Thal*	*16*	*−18*	*6*		
		R Put	*26*	*−6*	*4*		
Cluster 6	*A*	**L Thal**	**−20**	**−10.4**	**4.1**	**3328 (9)**	
	B	*L Pall/Thal*	*−22*	*−8*	*2*		
		L Thal	*−14*	*−18*	*6*		
Cluster 7	*A*	**R PreCG**	**58.5**	**9.1**	**19.7**	**1336 (10)**	
	B	*R IFG*	*60*	*10*	*14*		
	C	*R PreCG*	*60*	*8*	*24*		
		R IFG	*52*	*8*	*28*		
Cluster 8	*A*	**R SMG**	**59.6**	**−30.8**	**26.1**	**944 (6)**	
		R SMG	*60*	*-32*	*26*		
Cluster 9	*A*	**R MTG**	**49.1**	**−66.7**	**3.3**	**480 (3)**	
		R MTG	*50*	*−66*	*4*		
Cluster 10	*A*	**CB vermis VIII**	**2.1**	**−68.1**	**−37.9**	**368 (5)**	**VIIIa (verm)**
		CB vermis VIII	*2*	*−68*	*−38*		*VIIIa (verm)*
Cluster 11	*A*	**L IPL**	**−47**	**−40**	**45**	**96 (2)**	
		L IPL	*−46*	*−40*	*44*		

ALE analyses: cluster-level correction of $p < 0.05$, cluster-forming method (pID) with a cluster-forming value of $p < 0.001$, and 5000 random permutations. Only clusters with cluster size > 50 mm^3 and more than 2 different contributors are reported

ALE, activation likelihood estimation; *CB*, cerebellum; *hem*, hemisphere; *IFG*, inferior frontal gyrus; *IPL*, inferior parietal lobe; *L*, left; *MTG*, middle temporal gyrus; *MNI*, Montreal Neurological Institute; *Pall*, globus pallidus; *Post-Med Front*, posterior-medial frontal area; *PreCG*, precentral gyrus; *Put*, putamen; *R*, right; *SFG*, superior frontal gyrus; *SMG*, supramarginal gyrus; *SPL*, superior parietal lobe; *Thal*, thalamus; *verm*, vermis

hemispheres might be related to the complexity of the movement and that the lack of activation during IP movements in their study might be attributed to a threshold problem [35]. Interestingly, when looking at the unthresholded ALE images in our analyses, these lateral posterior cerebellar hemisphere activations were indeed present in all three conditions, and were visually stronger in the Complex condition. Unfortunately, our study lacked the power to statistically

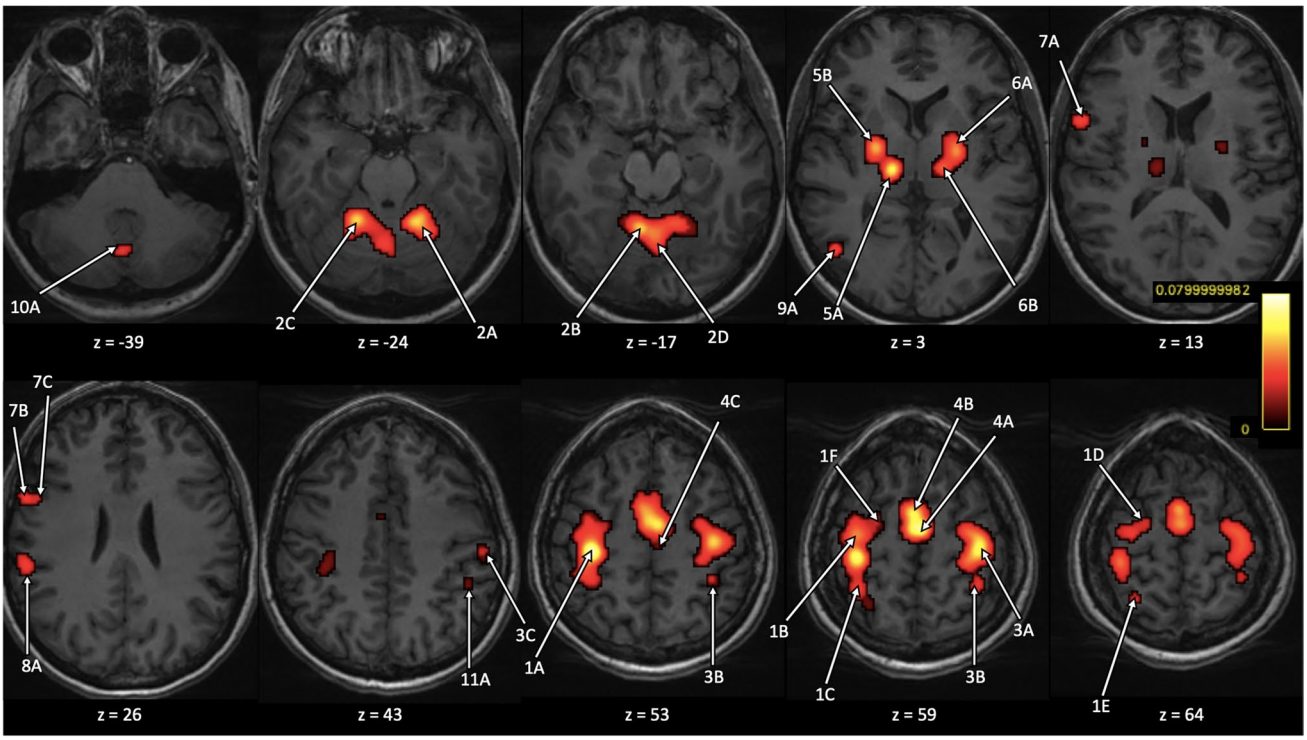


Fig. 3 ALE analysis, including ALL contrasts, resulting in 11 clusters (see Table 2) containing multiple peaks per cluster. MNI space *z* coordinates are indicated per axial slice. Numbers indicate the cluster and letters of the local maxima in the respective cluster. ALE scores are shown with a maximum of 0.08

validate this hypothesis, possibly due to the heterogeneity of included tasks (finger or wrist movements, flexion and extension, ab- and adduction, circular movements, etc.), the different manipulations of complexity (relative phase, relative interlimb frequency, and/or spatial characteristics), and the diversity of the included contrasts (contrasted with rest, UM movements, IP movements, etc.).

Our meta-analysis also found some activations in addition to the general BM network of Puttemans et al. [3]. Additional clusters were observed in the right superior frontal gyrus, the right superior and left inferior parietal lobe, and in the vermis of the anterior CB. Since the right superior frontal gyrus and the right superior parietal lobe were both part of the somatomotor network and were only found in the All analysis, these activations are probably linked to different types of coordinated movements that were required in the included studies. The activation in the anterior vermis, on the other hand, was more surprising. This area has been associated with increasing complexity and coordination demands [5, 15], and was observed in [5, 11] who used nearly the same task as Puttemans et al. [3] (flexion–extension of the wrist) but manipulated relative phase (90° out-of-phase in [5, 11]) instead of relative interlimb frequency (1:2 in [3]). It could be speculated that manipulating relative phase increased the coordination demands more than manipulating interlimb frequency.

Comparison Between Conditions

Cerebral Level On the cerebral level, two areas differed between conditions, showing activity exclusively in the Complex condition. First, the local peak analysis showed that the most posterior peak of the SMA cluster in the All analysis was not present in the IP and AP conditions. The main contributors to this posterior SMA activation were the general BM network of Puttemans et al. [3] and the study of Debaere et al. [5], who both used a complex cyclical wrist flexion–extension task. Activation of the SMA has been consistently linked to movement complexity, both in UM sequential tasks [36] and in BM coordination [37, 38]. The SMA was therefore activated in all conditions, even in the IP condition which still required some degree of coordination between both hands, but was more extended in the Complex condition due to the increased coordination complexity resulting in the posterior peak [5, 39].

The second cluster that was only present in the Complex condition was found in the left inferior parietal lobe, part of the executive network. Only two complex studies contributed

Table 3 Results of the ALE analysis including IP contrasts. Coordinates of the center of the cluster are provided in bold, together with the local maxima in italic

Cluster	Local peaks	Anatomical label	MNI coordinates in mm				
			x	*y*	*z*	Cluster size in mm^3 (no. of contrasts)	CB assigned to
Cluster 1	*A*	**CB vermis IV/V**	**−.1**	**−53.3**	**−21.1**	**5688 (12)**	**IV (hem)**
	B	*L CB IV/V*	*−18*	*−52*	*−22*		*VI (hem)*
	C	*R CB IV/V*	*20*	*−48*	*−26*		*VI (hem)*
	D	*R CB IV/V*	*10*	*−54*	*−18*		*V (hem)*
		L CB IV/V	*−4*	*−58*	*−16*		*V (hem)*
Cluster 2	*A*	**R PreCG**	**37.3**	**−23.4**	**56.4**	**4360 (12)**	
	B	*R PreCG*	*38*	*−26*	*56*		
		R PreCG	*36*	*−12*	*58*		
Cluster 3	*A*	**L Post-Med Front**	**.1**	**−6.8**	**55.8**	**3936 (13)**	
		L Post-Med Front	*−2*	*−8*	*56*		
Cluster 4	*A*	**L PreCG**	**−33.6**	**−20.6**	**58.1**	**3296 (10)**	
	B	*L PreCG*	*−28*	*−30*	*60*		
		L PreCG	*−36*	*−16*	*58*		
Cluster 5	*A*	**R Thal**	**15.2**	**−18.5**	**4.9**	**560 (4)**	
		R Thal	*14*	*−18*	*4*		
Cluster 6	*A*	**L Thal**	**−13.5**	**−17.9**	**4.9**	**552 (4)**	
		L Thal	*−14*	*−18*	*4*		
Cluster 7	*A*	**R Pall/Thal**	**24.4**	**−6.3**	**2.3**	**408 (4)**	
		R Pall/Thal	*24*	*−6*	*2*		
Cluster 8	*A*	**L Pall**	**−22.2**	**−7.4**	**.9**	**368 (3)**	
		L Pall	*−22*	*−8*	*0*		
Cluster 9	*A*	**L IPL**	**−55.3**	**−19.6**	**44.4**	**88 (2)**	
		L IPL	*−56*	*−20*	*44*		
Cluster 10	*A*	**R IFG**	**60.9**	**10.9**	**13.3**	**72 (2)**	
		R Rol Op	*62*	*10*	*12*		

ALE analyses: cluster-level correction of $p < 0.05$, cluster-forming method (pID) with a cluster-forming value of $p < 0.001$, and 5000 random permutations. Only clusters with cluster size > 50 mm^3 and more than 2 different contributors are reported

ALE, activation likelihood estimation; *CB*, cerebellum; *hem*, hemisphere; *IFG*, inferior frontal gyrus; *IPL*, inferior parietal lobe; *L*, left; *MNI*, Montreal Neurological Institute; *Pall*, globus pallidus; *Post-Med Front*, posterior-medial frontal area; *PreCG*, precentral gyrus; *R*, right; *Rol Op*, Rolandic operculum; *Thal*, thalamus; *verm*, vermis

to this cluster, which were both continuous goal-oriented tasks enforced by negative feedback [40, 41]. Duque et al. [40] required participants to follow the rotational speed of two white circling dots on the screen, either at a fixed relative interlimb frequency ratio (e.g., 1:2 where the right hand had to move twice as fast as the left hand) or in an independent manner (each hand followed their own speed indicator). In each trial, speed changes were introduced two times, either for both hands (maintaining the frequency ratio in the coordinated goal) or for one hand (maintaining the independent goal coordination). Movements were guided by the color of the screen, the left half of the screen corresponded to the left hand speed and the right half to the right hand speed. A white screen indicated an adequate speed, but when the hand moved too slow, the corresponding half of the screen turned green, when it moved too fast, it turned magenta. In Koeneke et al. [41], participants were asked to direct a moving cursor between two rotating parallel lines of fixed width, without touching the lines. When they touched or crossed the lines, the path turned red, within the lines, it stayed green. These were the only two tasks that requested a continuous movement with a clear goal that was enforced by negative (visual) feedback. Therefore, the activation of this cluster was probably not due to the complexity of the movement but rather due to the executive requirements of the visually enforced goal-oriented and/or continuous nature of the task.

Cerebellar Level On the cerebellar level, our study clearly showed that the posterior vermis activation was exclusively present in the Complex condition, while the anterior vermis was primarily observed in the AP and Complex conditions with no clear local maximum in the IP condition (only a peak in the vicinity of the vermis IV/V and no peak in vermis VI).

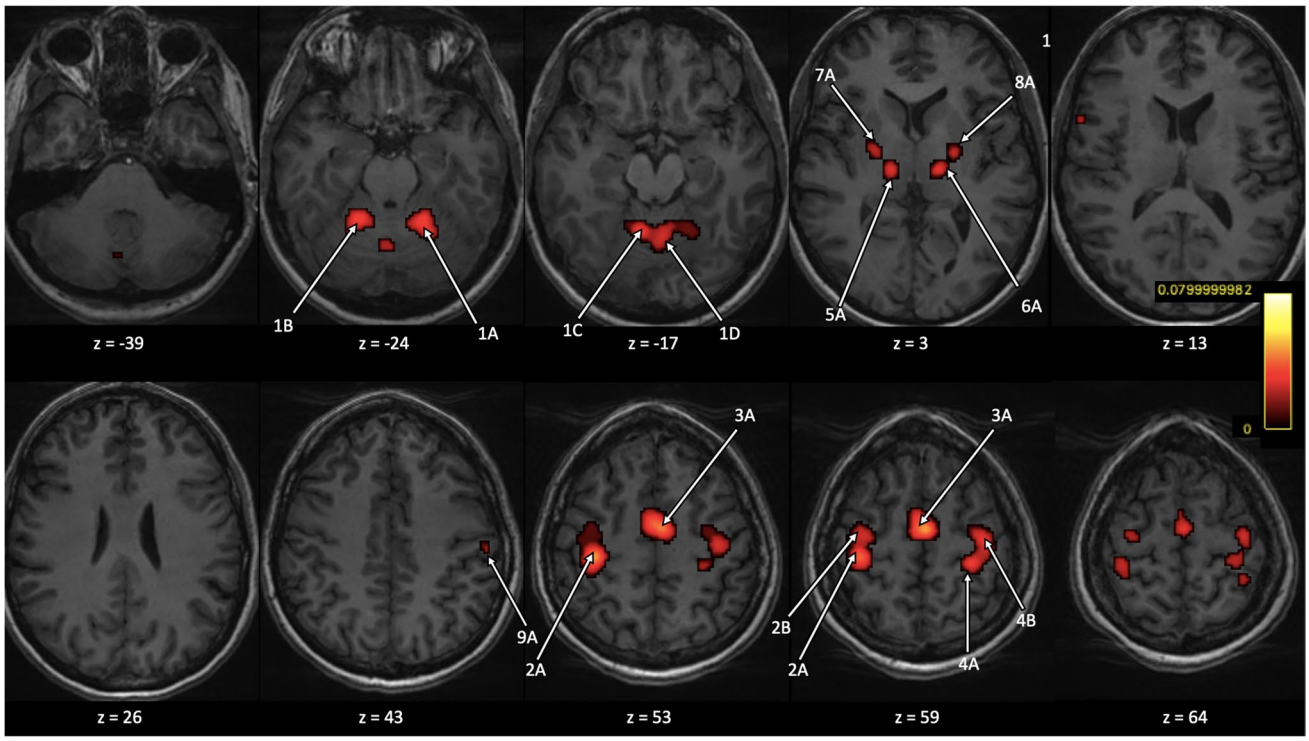


Fig. 4 ALE analysis, including IP contrasts, resulting in 10 clusters (see Table 3) containing multiple peaks per cluster. MNI space *z* coordinates are indicated per axial slice. Numbers indicate the cluster and letters of the local maxima in the respective cluster. ALE scores are shown with a maximum of 0.08

Tracy et al. [15] and Debaere et al. [5] already hypothesized that the posterior cerebellar vermis, together with the anterior vermis, is responsible for the integration of coordination complexity in BM movements, especially since Tracy et al. [15] only found these activations when contrasted with the UM condition. According to Swinnen and Wenderoth [8], an anterior/posterior division can be made in the cerebellar vermis based on the coordination effort. They speculated that the posterior vermis comes into play when limb movements are to be executed with an exact temporal delay in between, while the anterior vermis is more involved in preferred movements with a synchronized predictable rhythm (i.e., IP movements). This meta-analysis contradicts this specific theory about synchronization, since activation in the anterior vermis was primarily observed in the AP and Complex conditions, but it does reflect the general idea of the anterior/posterior division of the cerebellar vermis. While the anterior vermis was also clearly present in the AP condition, the posterior vermis only contributed to the more complex BM tasks requiring a higher coordination effort. However, several studies also suggest a differential role for the anterior and posterior vermis in complex BM coordination. Ullén et al. [16], for example, observed a posterior cerebellar vermis activation when contrasting polyrhythmic finger-tapping sequences (3:2 and 2:3) with IP and AP sequences, while a stronger anterior vermis activation was observed when performing the same BM finger-tapping serial sequence isochronously as compared to mirrored IP sequences. This might suggest a role for the anterior vermis in the sequential control of the (BM) movement (conducting the movements in the correct sequential order), while the posterior vermis is more involved in the (complex) temporal control of the (BM) movement (exact timing of the movements). This is supported by the observation that the posterior vermis is not activated in the IP and AP conditions, which require a minimum of temporal control over the movements, and by the minimal activation in the anterior vermis in IP movements, where the same movements have to be performed simultaneously (i.e., in a simultaneous sequential order).

However, other factors might also play a role. Spencer [42] already suggested a differential role for the CB in temporal control over continuous versus discontinuous UM movements. Based on their observations in patients with cerebellar lesions, they hypothesized that the CB is only involved in the temporal control of discontinuous movements [42], with a stronger activation in the vicinity of the anterior vermis (lobule VI) in timing discontinuous versus continuous UM movements [43]. Bo et al. [44] partially

Table 4 Results of the ALE analysis including AP contrasts. Coordinates of the center of the cluster are provided in bold, together with the local maxima in italic

Cluster	Local peaks	Anatomical label	MNI coordinates in mm				
			x	*y*	*z*	Cluster size in mm^3 (no. of contrasts)	CB assigned to
Cluster 1	*A*	**R CB IV/V**	**8**	**−54.5**	**−19.5**	**5200 (15)**	**V (hem)**
	B	*R CB IV/V*	*20*	*−50*	*−24*		*VI (hem)*
	C	*R CB IV/V*	*10*	*−54*	*−18*		*V (hem)*
	D	*L CB IV/V*	*−6*	*−54*	*−14*		*V (hem)*
	E	*CB Vermis IV/V*	*−2*	*−58*	*−16*		*V (hem)*
		CB Vermis VI	*2*	*−64*	*−20*		*VI (verm)*
Cluster 2	*A*	**L Post-Med Front**	**1.3**	**−4.8**	**57.2**	**5144 (16)**	
		L Post-Med Front	*−2*	*−8*	*58*		
Cluster 3	*A*	**R PreCG**	**35.9**	**−24.5**	**56.8**	**4192 (13)**	
	B	*R PreCG*	*36*	*−26*	*56*		
	C	*R PostCG*	*36*	*−34*	*66*		
		R PreCG	*34*	*−14*	*58*		
Cluster 4	*A*	**L PreCG**	**−33**	**−20.2**	**58.2**	**3096 (13)**	
	B	*L PreCG*	*−36*	*−22*	*58*		
	C	*L PreCG*	*−30*	*−28*	*60*		
	D	*L PreCG*	*−30*	*−10*	*56*		
	E	*L PreCG*	*−34*	*−14*	*64*		
		L PostCG	*−44*	*−18*	*52*		
Cluster 5	*A*	**R Thal**	**19.4**	**−13**	**3.8**	**2424 (10)**	
	B	*R Thal*	*16*	*−18*	*4*		
		R Pall	*24*	*−4*	*6*		
Cluster 6	*A*	**L CB VI**	**−20.2**	**−52.1**	**−22.9**	**2032 (10)**	**VI (hem)**
		L CB VI	*−22*	*−54*	*−22*		*VI (hem)*
Cluster 7	*A*	**L Thal**	**−19.1**	**−11.6**	**3.5**	**1792 (7)**	
	B	*L Thal*	*−14*	*−18*	*6*		
		L Pall	*−22*	*−8*	*0*		
Cluster 8	*A*	**R IFG**	**59.7**	**10**	**14.5**	**480 (6)**	
		R IFG	*60*	*10*	*14*		
Cluster 9	*A*	**L SMG**	**−56.5**	**−25.5**	**38.2**	**64 (2)**	
		L SMG	*−56*	*−26*	*38*		

ALE analyses: cluster-level correction of $p < 0.05$, cluster-forming method (pID) with a cluster-forming value of $p < 0.001$, and 5000 random permutations. Only clusters with cluster size > 50 mm^3 and more than 2 different contributors are reported

ALE, activation likelihood estimation; *CB*, cerebellum; *hem*, hemisphere; *IFG*, inferior frontal gyrus; *L*, left; *MNI*, Montreal Neurological Institute; *Pall*, globus pallidus; *Post-Med Front*, posterior-medial frontal area; *PostCG*, postcentral gyrus; *PreCG*, precentral gyrus; *R*, right; *SMG*, supramarginal gyrus; *Thal*, thalamus; *verm*, vermis

contradicted the results of Spencer [42]. Their results showed that patients with cerebellar lesions can be selectively impaired in the timing of either continuous or discontinuous movement. This suggests that temporal control over continuous and discontinuous movements might be located in different areas, with a specific role for the anterior vermis in temporal control over UM discontinuous movements [43]. However, translating these findings based on UM protocols to BM coordination tasks is not straightforward. Helmuth and Ivry [45] showed that deficits in a (discontinuous) finger-tapping task in patients with unilateral cerebellar lesions are improved when tapping IP with both hands, which might implicate involvement of different cerebellar regions in timing UM and BM coordination. Our meta-analysis included both discontinuous and continuous BM paradigms, which were generally auditorily or visually paced, unlike the UM synchronization-continuation experiments of Spencer [42], Spencer et al. [43], and Bo et al. [44]. Nevertheless, a distinction between continuous and discontinuous BM coordination in terms of temporal and sequential control might be needed to fully understand the specific role of different regions of the CB in BM coordination. Especially since in continuous movement, sequential control is sometimes difficult to define. For example, a continuous

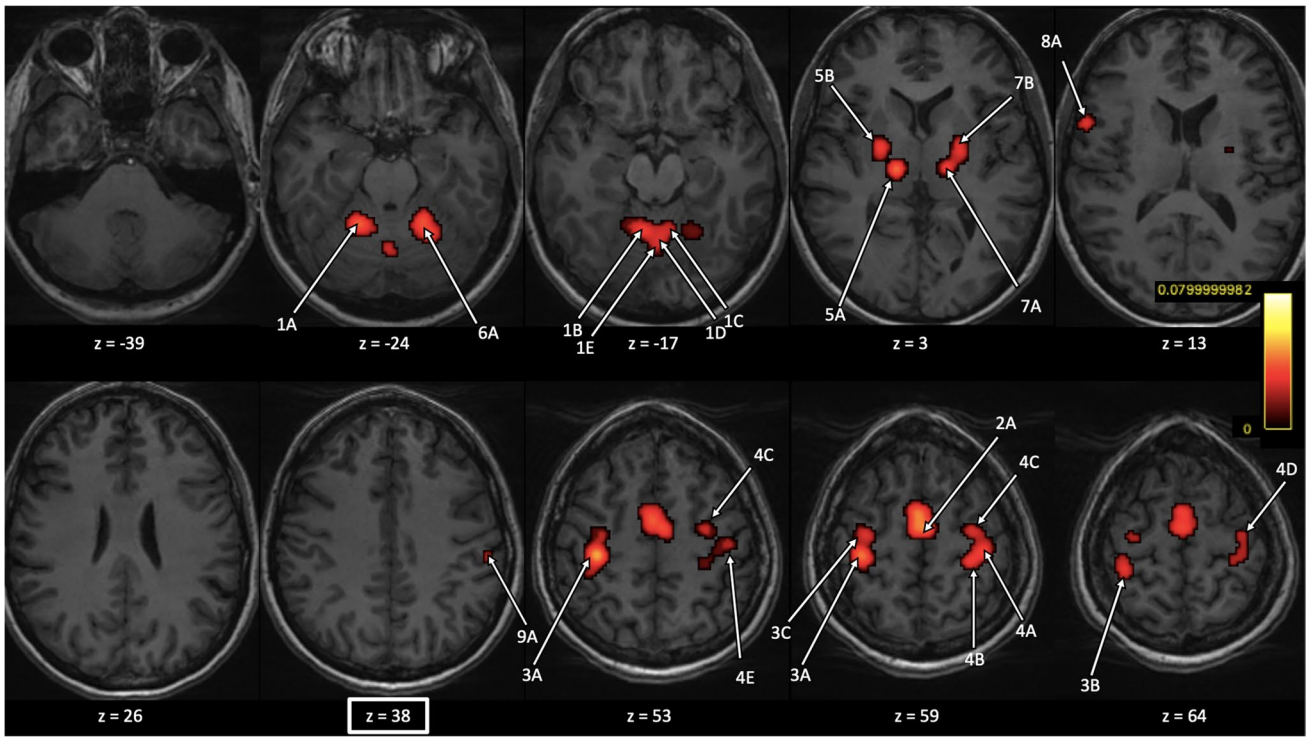


Fig. 5 ALE analysis, including AP contrasts, resulting in nine clusters (see Table 4) containing multiple peaks per cluster. MNI space z coordinates are indicated per axial slice. Numbers indicate the cluster and letters of the local maxima in the respective cluster. ALE scores are shown with a maximum of 0.08. Note the more inferior slice at $z = 38$ instead of $z = 43$ in the other figures

cyclical flexion–extension of the wrist was used by Puttemans et al. [3] with a differing interlimb frequency (1:2) and by Debaere et al. [5, 11] with a relative phase difference of 90°. While Debaere et al. [5, 11] found anterior and posterior vermis activations, Puttemans et al. [3] only found posterior vermis activation. You could argue that changing the interlimb frequency of the continuous movement primarily depends on adequate timing of the movements (i.e., posterior vermis), while changing the relative phase of the movements involves a more complex sequential/spatial (relative position of both hands in space) coordination of the movement (i.e., anterior vermis) which also requires an exact temporal control (i.e., posterior vermis). Here, sequential control relates to the kinematic landmarks where both hands have to change direction, or in other words, the sequence of the directional changes of both hands.

Wenderoth et al. [46] (not included in this meta-analysis) used a line and star drawing task, where participants had to draw vertical lines (Line condition) or had to change the orientation of the line 45° every eight trials (Star condition). When investigating spatial complexity by contrasting the StarLine/LineStar conditions (i.e., performing the Star condition with the left and the Line condition with the right hand or vice versa) with the symmetrical StarStar condition (i.e., performing the Star condition IP with both hands), they observed an anterior vermis activation which they related to directional interference [46]. This could also be interpreted as an involvement of the anterior vermis in sequential/spatial control since the LineStar and StarLine conditions required different sequences of directional changes for both hands, while the StarStar condition was symmetrical. In the LineStar and StarLine conditions, no changes of direction were required at the center of the linear movements for one hand, while the other hand had to change direction at the center every eight trials. Interestingly, Wenderoth et al. [46] also observed posterior vermis activation when contrasting the spatially complex StarLine/LineStar conditions with the symmetrical StarStar and the less complex LineLine condition (LineStar + StarLine > StarStar + LineLine). During the LineLine condition, only up and down movements were required with no changes of direction outside the vertical plane, and therefore also no timing of directional changes at the center of the linear movements. In the StarStar condition, although symmetrical, temporal control is still needed to time the directional changes at the center of the linear movements. This might explain the higher activation of the posterior vermis, involved in temporal control, when contrasted

Table 5 Results of the ALE analysis including Complex contrasts. Coordinates of the center of the cluster are provided in bold, together with the local maxima in italic

Cluster	Local peaks	Anatomical label	MNI coordinates in mm				
			x	*y*	*z*	Cluster size in mm^3 (no. of contrasts)	CB assigned to
Cluster 1	*A*	**CB vermis IV/V**	**3.6**	**−59.2**	**−19.4**	**1376 (4)**	**V (hem)**
	B	*CB vermis VI*	*2*	*−60*	*−20*		*V (hem)*
		R CB IV/V	*8*	*−56*	*−16*		*V (hem)*
Cluster 2	*A*	**R PreCG**	**35.4**	**−24.5**	**58.5**	**1248 (6)**	
	B	*R PreCG*	*36*	*−24*	*56*		
		R SFG	*32*	*−12*	*60*		
Cluster 3	*A*	**L Post-Med Front**	**−.8**	**−8.1**	**55.7**	**856 (4)**	
		L Post-Med Front	*−2*	*−8*	*56*		
Cluster 4	*A*	**L CB IV/V**	**−18.8**	**−50.9**	**−23**	**688 (3)**	**VI (hem)**
		L CB IV/V	*−18*	*−50*	*−22*		*VI (hem)*
Cluster 5	*A*	**R Thal**	**14.7**	**−17.9**	**5.2**	**688 (5)**	
		R Thal	*14*	*−18*	*6*		
Cluster 6	*A*	**R CB IV/V**	**19.1**	**−48.9**	**−24.6**	**640 (4)**	**VI (hem)**
		R CB IV/V	*20*	*−48*	*−26*		*VI (hem)*
Cluster 7	*A*	**L PreCG**	**−30.1**	**−9.6**	**58.2**	**592 (4)**	
	B	*L PreCG*	*−30*	*−8*	*56*		
		L PreCG	*−28*	*−10*	*64*		
Cluster 8	*A*	**CB Vermis VIII**	**2.8**	**−68.1**	**−39.1**	**456 (4)**	**VIIIa (verm)**
		CB Vermis VIII	*2*	*−68*	*−40*		*VIIIa (verm)*
Cluster 9	*A*	**L PreCG**	**−27.6**	**−28.2**	**60.2**	**312 (2)**	
		L PreCG	*−28*	*−28*	*60*		
Cluster 10	*A*	**L Post-Med Front**	**−2.9**	**−21**	**50.3**	**288 (2)**	
		L Post-Med Front	*−4*	*−22*	*50*		
Cluster 11	*A*	**R Pall**	**24.8**	**−5.3**	**1.8**	**136 (3)**	
		R Pall	*26*	*−6*	*2*		
Cluster 12	*A*	**L Thal**	**−13.6**	**−18.1**	**5.2**	**128 (2)**	
		L Thal	*−14*	*−18*	*6*		
Cluster 13	*A*	**L IPL**	**−47**	**−40.8**	**44.4**	**80 (2)**	
		L IPL	*−46*	*−40*	*44*		

ALE analyses: cluster-level correction of $p < 0.05$, cluster-forming method (pID) with a cluster-forming value of $p < 0.001$, and 5000 random permutations. Only clusters with cluster size > 50 mm^3 and more than 2 different contributors are reported

ALE, activation likelihood estimation; *CB*, cerebellum; *hem*, hemisphere; *IPL*, inferior parietal lobe; *L*, left; *MNI*, Montreal Neurological Institute; *Pall*, globus pallidus; *Post-Med Front*, posterior-medial frontal area; *PreCG*, precentral gyrus; *R*, right; *SFG*, superior frontal gyrus; *Thal*, thalamus; *verm*, vermis

with the LineLine and StarStar conditions, while this was not found when contrasted with the StarStar condition only.

However, an important factor that might affect vermal involvement is the presence, or absence, of (visual) feedback. A similar study of Wenderoth et al. [47] using the same task and the same contrast (LineStar + StarLine > 2 × StarStar), but taking together conditions without and with visual feedback, only found posterior vermis activation. They linked a cluster in the vicinity of the anterior vermis (lobule VI) to the presence of visual feedback during BM coordination (Visual feedback > No Visual feedback during LineStar, StarLine, and StarStar conditions). Therefore, the presence of visual feedback might eliminate the need for sequential/spatial control (anterior vermis), while increasing the dependence on temporal control (posterior vermis). Besides the presence of visual feedback, the amount of practice also differed slightly. Wenderoth et al. [47] did not investigate UM conditions, while Wenderoth et al. [46] also included UM Star and Line conditions. Wenderoth et al. [48] showed that both the anterior and posterior vermis are involved in not only the BM LineStar condition (LineStar > Rest) but also in the UM Line and Star conditions (Line > Rest and

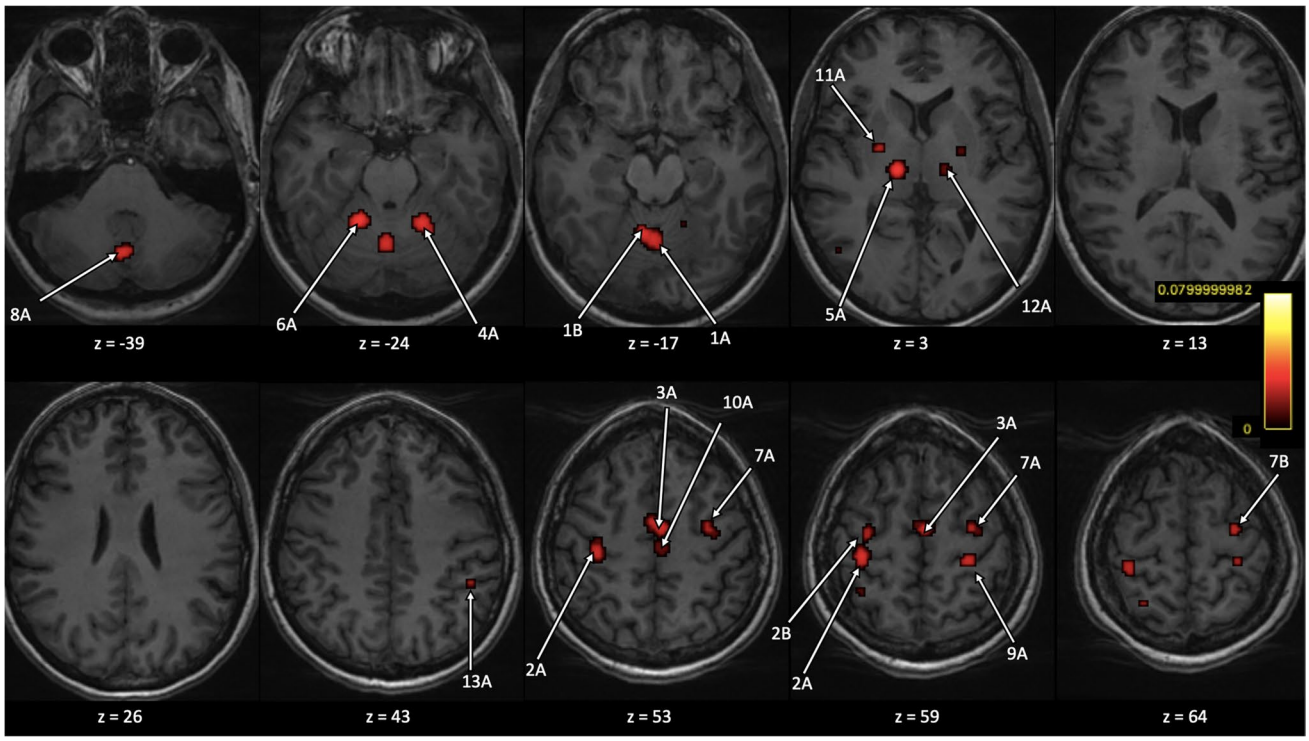


Fig. 6 ALE analysis, including Complex contrasts, resulting in 13 clusters (see Table 5) containing multiple peaks per cluster. MNI space *z* coordinates are indicated per axial slice. Numbers indicate the cluster and letters of the local maxima in the respective cluster. ALE scores are shown with a maximum of 0.08

Star > Rest). Therefore, practicing the Star and Line conditions with both hands separately might also have affected the neural network involved in the BM coordination of the StarLine and LineStar movements.

Both the timing and sequencing hypothesis have been used to explain cerebellar involvement in not only motor but also cognitive domains [49]. Keele and Ivry [50] first proposed the timing hypothesis, in which the CB closely monitored and compared the timing of movements with what was predicted by the CB, in order to correct when necessary. According to the sequencing hypothesis, on the other hand, the CB monitors the sequence of the movements [51]. Both timing and sequencing deficits have been observed in patients with cerebellar lesions (timing: [50], sequencing: [51]), which pleads for an involvement of the CB in both mechanisms. This meta-analysis suggests a topographical involvement with the anterior vermis responsible for the sequencing of BM movements, and the posterior vermis responsible for the timing of BM movements. However, other factors such as the continuity of the movement, (visual) feedback, or the amount of (UM) practice might also impact the involvement of the cerebellar vermis. Further studies are warranted to confirm this hypothesis in the motor domain, and investigate whether this topographical organization still holds in other domains.

Limitations and Future Studies

This meta-analysis encountered some limitations in terms of power. We made the decision to focus on BM coordination, and exclude motor learning- and visual feedback–related contrasts as much as possible, resulting in a limited number of contrasts. To increase this number, we also included "mixed" contrasts representing IP, AP, and/or Complex tasks, which were added to all the conditions that were represented in the contrast. ALE contrast analyses between conditions were therefore not possible. In addition, we included all contrasts that included (complex) BM coordination, i.e., contrasts versus a rest condition, but also contrasts versus UM tasks, or versus a similar BM task. As we have argued above, the nature of the contrast might also be crucial to reveal certain activations. Future meta-analyses could focus on specific contrasts to address other BM coordination-related topics.

According to the guidelines for neuroimaging meta-analyses of Müller et al. [52], at least 17 to 20 experiments are

Table 6 Comparison of the general BM network as found by Puttemans et al. [3] and the ALE analyses of the different conditions (All, IP, AP, Complex) in the cerebral regions

		Cluster	Local peaks	MNI coordinates in mm x	y	z
Primary sensory-motor cluster (S1/M1)						
R Central sulcus						
Puttemans et al. 2005				**36**	**-30**	**62**
-	All	Cluster 1	A	36	-24	54
		Cluster 1	C	36	-44	58
-	IP	Cluster 2	A	38	-26	56
-	AP	Cluster 3	A	36	-26	56
		Cluster 3	B	36	-34	66
-	Complex	Cluster 2	A	36	-24	56
L Central sulcus						
Puttemans et al. 2005				**-34**	**-32**	**66**
-	All	Cluster 3	B	-36	-42	56
-	IP	Cluster 4	A	-28	-30	60
		Cluster 9	A	-36	-40	64
-	AP	Cluster 4	B	-30	-28	60
-	Complex	Cluster 9	A	-28	-28	60
Ventral premotor area (PMv)						
R Inferior precentral gyrus						
Puttemans et al. 2005				**60**	**8**	**24**
-	All	Cluster 7	B	60	8	24
		Cluster 7	C	52	8	28
-	IP	None				
-	AP	None				
-	Complex	None				
L Inferior precentral gyrus						
Puttemans et al. 2005				**-60**	**2**	**26**
-	All	None				
-	IP	None				
-	AP	None				
-	Complex	None				

Table 6 (continued)

Dorsal premotor area (PMd)						
R Superior precentral gyrus						
Puttemans et al. 2005				**36**	**-26**	**62**
-	All	Cluster 1	B	36	-12	58
-	IP	Cluster 2	B	36	-12	58
-	AP	Cluster 3	C	34	-14	58
-	Complex	Cluster 2	B	32	-12	60
L Superior precentral gyrus						
Puttemans et al. 2005				**-40**	**-16**	**58**
-	All	Cluster 3	A	-36	-20	58
-	IP	Cluster 4	B	-36	-16	58
-	AP	Cluster 4	A	-36	-22	58
		Cluster 4	C	-30	-10	56
		Cluster 4	D	-34	-14	64
		Cluster 4	E	-44	-18	52
-	Complex	Cluster 7	A	-30	-8	56
		Cluster 7	B	-28	-10	64
R Superior frontal gyrus						
-	All	Cluster 1	D	22	-8	64
		Cluster 1	F	26	-2	58
-	IP	None				
-	AP	None				
	Complex	None				
Medial frontal area						
Cingulate motor zone; anterior cingulate zone						
Puttemans et al. 2005				**6**	**14**	**40**
-	All	None				
-	IP	None				
-	AP	None				
-	Complex	None				
Cingulate motor zone; posterior cingulate zone						
Puttemans et al. 2005				**-4**	**-24**	**50**
-	All	Cluster 4	C	-4	-20	50
-	IP	None				
-	AP	None				
-	Complex	Cluster 10	A	-4	-22	50

Table 6 (continued)

Supplementary motor area - proper						
Puttemans et al. 2005				**2**	**-12**	**58**
-	All	Cluster 4	A	-2	-8	58
		Cluster 4	B	2	0	60
-	IP	Cluster 3	A	-2	-8	56
-	AP	Cluster 2	A	-2	-8	58
-	Complex	Cluster 3	A	-2	-8	56
Lateral Prefrontal cortex						
R Middle frontal gyrus						
Puttemans et al. 2005				**40**	**38**	**22**
-	All	None				
-	IP	None				
-	AP	None				
-	Complex	None				
L Middle frontal gyrus						
Puttemans et al. 2005				**-44**	**40**	**20**
-	All	None				
-	IP	None				
-	AP	None				
-	Complex	None				
Inferior frontal cortex						
R Inferior frontal gyrus						
Puttemans et al. 2005				**54**	**8**	**12**
-	All	Cluster 7	A	60	10	14
-	IP	Cluster 11	A	62	10	12
-	AP	Cluster 8	A	60	10	14
-	Complex	None				
R operculum/short insular gyrus						
Puttemans et al. 2005				**46**	**10**	**-2**
-	All	None				
-	IP	None				
-	AP	None				
-	Complex	None				

Table 6 (continued)

L operculum/short insular gyrus						
Puttemans et al. 2005				**-56**	**8**	**-2**
-	All	None				
-	IP	None				
-	AP	None				
-	Complex	None				
Parietal cortex						
R parietal operculum						
Puttemans et al. 2005				**44**	**-28**	**24**
-	All	None				
-	IP	None				
-	AP	None				
-	Complex	None				
L parietal operculum						
Puttemans et al. 2005				**-44**	**-34**	**20**
-	All	None				
-	IP	None				
-	AP	None				
-	Complex	None				
R supramarginal gyrus						
Puttemans et al. 2005				**62**	**-36**	**24**
-	All	Cluster 8	A	60	-32	26
-	IP	None				
-	AP	None				
-	Complex	None				
L supramarginal gyrus						
Puttemans et al. 2005				**-58**	**-28**	**18**
-	All	Cluster 3	C	-56	-22	42
-	IP	Cluster 10	A	-56	-20	44
-	AP	Cluster 11	A	-56	-26	38
-	Complex	None				
R superior parietal lobe						
-	All	Cluster 1	E	28	-54	62
-	IP	None				
-	AP	None				
-	Complex	None				
L inferior parietal lobe						
-	All	Cluster 11	A	-46	-40	44
-	IP	None				
-	AP	None				
-	Complex	Cluster 13	A	-46	-40	44

Table 6 (continued)

Middle temporal cortex						
R middle temporal cortex						
Puttemans et al. 2005				**54**	**-70**	**4**
-	All	Cluster 9	A	50	-66	4
-	IP	None				
-	AP	None				
-	Complex	None				
Thalamic nuclei						
R Thalamus						
Puttemans et al. 2005				**18**	**-20**	**4**
-	All	Cluster 5	A	16	-18	6
-	IP	Cluster 5	A	14	-18	4
-	AP	Cluster 5	A	16	-18	4
-	Complex	Cluster 5	A	14	-18	6
L Thalamus						
Puttemans et al. 2005				**-16**	**-22**	**8**
-	All	Cluster 6	B	-14	-18	6
-	IP	Cluster 6	A	-14	-18	4
-	AP	Cluster 7	A	-14	-18	6
-	Complex	Cluster 12	A	-14	-18	6
Basal ganglia						
R Putamen/Globus Pallidus						
Puttemans et al. 2005				**26**	**-4**	**4**
-	All	Cluster 5	B	26	-6	4
-	IP	Cluster 7	A	24	-6	2
-	AP	Cluster 5	B	24	-4	6
-	Complex	Cluster 11	A	26	-6	2
L Putamen/Globus Pallidus						
Puttemans et al. 2005				**-26**	**-8**	**4**
-	All	Cluster 6	A	-22	-8	2
-	IP	Cluster 8	A	-22	-8	0
-	AP	Cluster 7	B	-22	-8	0
-	Complex	None				

Table 6 (continued)

Cerebellum							CB assigned to	Anatomical label
R Lobule IV/V								
Puttemans et al. 2005				**12**	**-50**	**-20**	R CB IV/V	V (hem)
-	All	Cluster 2	B	8	-54	-18	R CB IV/V	V (hem)
-	IP	Cluster 1	C	10	-54	-18	R CB IV/V	V (hem)
-	AP	Cluster 1	B	10	-54	-18	R CB IV/V	V (hem)
-	Complex	Cluster 1	B	8	-56	-16	R CB IV/V	V (hem)
L Lobule IV/V								
Puttemans et al. 2005				**-14**	**-50**	**-22**	L CB IV/V	V (hem)
-	*All*	*Cluster 2*	*A*	*-16*	*-50*	*-22*	*L CB IV/V*	*V (hem)*
-	*IP*	*Cluster 1*	*A*	*-18*	*-52*	*-22*	*L CB IV/V*	*VI (hem)*
-	AP	Cluster 1	C	-6	-54	-14	L CB IV/V	V (hem)
-	*Complex*	*Cluster 4*	*A*	*-18*	*-50*	*-22*	*L CB IV/V*	*VI (hem)*
R Lobule V/VI								
Puttemans et al. 2005				**18**	**-46**	**-26**	R CB IV/V	V (hem)
-	All	Cluster 2	C	20	-48	-26	R CB IV/V	VI (hem)
-	IP	Cluster 1	B	20	-48	-26	R CB IV/V	VI (hem)
-	AP	Cluster 1	A	20	-50	-24	R CB IV/V	VI (hem)
-	Complex	Cluster 6	A	20	-48	-26	R CB IV/V	VI (hem)
L Lobule V/VI								
Puttemans et al. 2005				**-20**	**-46**	**-26**	L CB IV/V	V (hem)
-	All	*Cluster 2*	*A*	*-16*	*-50*	*-22*	*L CB IV/V*	*V (hem)*
-	IP	*Cluster 1*	*A*	*-18*	*-52*	*-22*	*L CB IV/V*	*VI (hem)*
-	AP	Cluster 6	A	-22	-54	-22	L CB VI	VI (hem)
-	Complex	*Cluster 4*	*A*	*-18*	*-50*	*-22*	*L CB IV/V*	*VI (hem)*

Table 6 (continued)

R Lobule VIII B							
Puttemans et al. 2005			**22**	**-50**	**-60**	R CB VIII	VIIIb (hem)
- All	None						
- IP	None						
- AP	None						
- Complex	None						
L Lobule VIII B							
Puttemans et al. 2005			**-20**	**-46**	**-54**	L CB VIII	VIIIb (hem)
- All	None						
- IP	None						
- AP	None						
- Complex	None						
Vermis VIII B							
Puttemans et al. 2005			**0**	**-66**	**-40**	CB Vermis VIII	VIIIb (verm)
- All	Cluster 10	A	2	-68	-38	CB Vermis VIII	VIIIa (verm)
- IP	None						
- AP	None						
- Complex	Cluster 8	A	2	-68	-40	CB Vermis VIII	VIIIa (verm)
Vermis IV/V							
- All	Cluster 2	D	2	-58	-18	CB Vermis IV/V	V (hem)
- IP	Cluster 1	D	-4	-58	-16	L CB IV/V	V (hem)
- AP	Cluster 1	D	-2	-58	-16	CB Vermis IV/V	V (hem)
- Complex	None						
Vermis VI							
- All	None						
- IP	None						
- AP	Cluster 1	E	2	-64	-20	CB Vermis VI	VI (verm)
- Complex	Cluster 1	A	2	-60	-20	CB Vermis VI	V (hem)

Cluster < 50 mm^3 or with contributions of less than two different articles. Areas in gray are found in the meta-analysis but not in Puttemans et al. [3]. Areas in italic are assigned to more than 1 cluster found in Puttemans et al. [3]

ALE, activation likelihood estimation; *CB*, cerebellum; *hem*, hemisphere; *L*, left; *MNI*, Montreal Neurological Institute; *R*, right; *verm*, vermis

required for ALE meta-analyses in order to have sufficient power. Most of our single dataset analyses have included 19 or more articles, except for the Complex condition ($n = 12$). However, 23 contrasts or more were used for the analyses. Some studies therefore contributed multiple contrasts, creating a dependency across the data. This was corrected for by using cluster-level inference with an FDR pID cluster-forming threshold as recommended by Fox et al. [53]. This is, however, different than the currently recommended cluster-level FWE correction [52], which might have led to more false positives.

A general problem with fMRI meta-analyses targeting the CB concerns the field of view. Not all fMRI studies include the entire CB in their field of view. However, since only two studies [54, 55] explicitly mentioned that they included the entire CB, we did not set this as an exclusion criterion. This might have affected the results, especially concerning the posterior CB that is sometimes cut off. At least one study [56] only partially imaged the CB, but since 12 studies provided no information on the coverage of the CB, and 15 other studies only mentioned "entire cerebrum" or "whole brain," we cannot rule out that some of these included studies also only partially imaged the CB.

Motor learning literature reveals that the areas involved in (BM) motor tasks depend on the learning stage [3, 11]. We mostly included contrasts that were still in a relatively early learning phase. However, the amount of exercise before the scanning session differed between studies. Most studies aimed for a stable performance before scanning, but three studies only mentioned a short familiarization session [15, 41, 57], and two studies specifically aimed for automatization [56, 58]. In addition, the reported fMRI results of Debaere et al. [11] and Puttemans et al. [3] were collapsed across the different learning stages (before and after learning, and before, during, and after learning, respectively). This might have affected the results, especially since the amount of practice needed to acquire a new motor task also depends on the complexity of the task [59].

Environmental conditions can also have an impact on the cerebellar activations, as demonstrated by the studies of Wenderoth et al. [46–48], showing an impact of visual feedback [47], and/or of UM practice on the cerebellar vermal recruitment [46, 47]. Unfortunately, not many studies allowed for a direct comparison between different conditions. However, it is clear that these factors should be taken into account when studying the involvement of the (vermis of the) CB in BM coordination.

Due to the nature of the included tasks and contrasts, it was not possible to make a clear distinction between contrasts with a high sequential/spatial complexity and with a high temporal complexity. Future studies investigating the BM coordination might take this into account to confirm our hypothesis about the specific role of the anterior and posterior vermis. In addition, some involvement of the prefronto-cerebellar loop was expected in the Complex condition, especially given the activation in the inferior parietal lobe, which is also part of the executive network. During the execution of complex BM movements, executive functions can be involved. However, the diversity of the tasks included in the Complex condition and the fact that most tasks were trained until a stable performance level was reached might explain the lack of activation in the executive areas of the CB (e.g., lobule VII). It might also be that not all included BM tasks in the Complex condition were complex enough to recruit the prefronto-cerebellar loop.

Conclusion

BM coordination is supported by a large bilateral network in both the cortical and subcortical regions. The CB seems to play a crucial role in this type of movements requiring a high degree of coordination, with distinct roles for the anterior and posterior vermis. We hypothesize that the anterior vermis is more involved in sequential/spatial control, while the posterior vermis is responsible for temporal control. However, more studies are needed to confirm this hypothesis.

Appendix

Table 7 Overview of the included studies and contrasts

Article	#	RH/LH	Age	Task	Limb	Contrasts included	# of foci per contrast	AP/IP/Complex
Hanawa et al. [60]	37	RH	18–24 y	Imitation movements	Hand	Difficulty Rhythm	6 2	Complex (imitate) Complex (imitate)
Müller et al. [61]	15	LH	22–47y	Ab- and adduction	Index fingers, palms up or down	Motor > Rest	20	IP + AP
Duque et al. [40]	15	RH	19–32 y	Circling movements	Hands	Coordination BM > Rest Independent goal BM > Rest	25 30	Complex (cyclical) Complex (cyclical)
Müller et al. [62]	11	RH	35.5 ± 9.6 y	Ab- and adduction	Index fingers, palms up or down	Active > Rest	19	IP + AP
Wenderoth et al. [48]	10	RH	25 ± 5 y	Line and star drawing	Hand and wrist	BM LineStar > Rest Coordination effort > UM	18 6	Complex (drawing) Complex (drawing)
Wenderoth et al. [63]	12	RH	19–33 y	Line drawing	Hand and wrist	AmpInt DirInt DirInt × AmpInt	13 7 7	Complex (drawing) Complex (drawing) Complex (drawing)
Meister et al. [64]	13	RH	29.4 ± 6.1 y	Flexion and extension	Index finger	Same timing diff ampl > same timing same ampl Diff timing diff ampl > same timing diff ampl	2 8	Complex (drawing) Complex (drawing)
Hanakawa et al. [65]	10	RH	23–36 y	Tapping	Fingers	BM > Rest	11	IP
Aramaki et al. [54]	15	RH	24–31 y	Tapping	Fingers	Parallel > Rest Mirror > Rest Parallel > Mirror	18 7 19	AP IP AP
Aramaki et al. [55]	17	RH	25–38 y	Ab- and adduction	Finger	BM > left + right	2	IP + AP
Goerres et al. [56]	6	RH	59–68 y	Ballistic pressing	Index and pinky fingers	BM symm > Rest BM asymm > Rest BM symm > UM right index BM asymm > UM right index BM asymm > BM symm	18 20 3 6 3	IP AP IP AP AP
Sadato et al. [66]	12	RH	19–25 y	Sequential finger tapping	Fingers	Mirror > Rest Parallel > Rest Parallel > Mirror	13 15 4	IP AP AP
	9		22–27 y	Ab- and adduction	Index Finger	Mirror > Rest Parallel > Rest Parallel > Mirror	12 13 2	IP AP AP
Puttemans et al. [3]	11	RH	23.9 ± 1.58 y	Flexion–extension (freq 2:1)	Wrists	BM > Rest	32	Complex (cyclical)
Tracy et al. [15]	9	RH	21–43 y	Pronation-supination	Wrists	BM > Rest BM > UM	15 8	IP + AP IP + AP
Ullén et al. [16]	6	RH	21–27 y	Tapping	Index finger	Polyrhythmic > IP Polyrhythmic > AP	18 3	Complex (tapping) Complex (tapping)
	3	RH				AP > IP IP > AP Polyrhythmic > Iso Iso > IP	18 7 4 12	AP IP Complex (tapping) AP
Kraft et al. [58]	12	RH	53 ± 12 y	Grip force	Hands	BM sim > Rest BM alternate > Rest	10 10	IP AP
Theorin and Johansson [67]	16	RH	23–37 y	Force and twist task	Hands	BM > UM	7	Complex (pressing)

Table 7 (continued)

Article	#	RH/LH	Age	Task	Limb	Contrasts included	# of foci per contrast	AP/IP/Complex
Wenderoth et al. [47]	11	RH	22 ± 2 y	Line and star drawing	Hand and wrist	LineStar > StarStar (incomp > comp)	16	Complex (drawing)
						StarStar > LineStar (Comp > Incomp)	2	IP
Koeneke et al. [41]	14	RH	24.14 ± 5.8 y	Finger pressing, coordination task	Fingers	BM > Rest	20	Complex (pressing)
Debaere et al. [5]	12	RH	22–31 y	Cyclical flexion–extension (90° offset)	Wrists	BM > UM	23	IP/AP/Complex (cyclical)
						BM Frequency > Rest	12	IP/AP/Complex (cyclical)
						BM Complexity > Rest	15	IP/AP/Complex (cyclical)
						Frequency × Complexity > Rest	11	IP/AP/Complex (cyclical)
Debaere et al. [11]	20	RH	21–29 y	Cyclical flexion–extension (90° offset)	Wrists	FB + no FB > Vis + Rest	27	IP/AP/Complex (cyclical)
Kraft et al. [68]	11	RH	21–34 y	Tapping	Fingers	Mirror > Rest	9	IP
						Parallel > Rest	12	AP
Goble et al. [39]	32	RH	21–79 y	Flexion–extension	Wrist	Young + Old BM > Rest	21	IP + AP
Kiyama et al. [69]	20	RH	61–67 y	Button pressing	Fingers	Young BM IP > Rest	8	IP
						Young BM AP > Rest	8	AP
						Young AP > IP	2	AP
						Old BM IP > Rest	10	IP
						Old BM AP > Rest	10	AP
De Luca et al. [70]	12	RH	28 ± 6 y	Flexion and extension	Index finger	Preswitch coordination rate	6	IP + AP
						Preswitch pattern stability	6	IP + AP
						During switch preswitch pattern stability	3	IP + AP
						During switch switching time duration	1	IP + AP
						Postswitch	7	IP + AP
Dietz et al. [71]	20	RH	25–32 y	Flexion–extension or pronation-supination	Wrist	AP > IP + AP	7	AP
Christensen et al. [72]	11	RH	24.6 ± 3 y	Ab- and adduction	Index finger	Parallel > Symmetric	15	AP
						Symmetric > Parallel	3	IP
Haslinger et al. [57]	12	RH	23 ± 22.2 y	Tapping	Fingers	Parallel > Mirror	12	AP
Wu et al. [73]	15	RH	44–73 y	Flexion and extension	Index finger	AP > IP	8	AP
Meyer-Lindenberg et al. [14]	12	RH and LH	23–41 y	Cyclical flexion–extension	Hand and wrist	Movement pattern × Frequency > Rest	9	IP + AP

Declarations

Conflict of Interest The authors declare no competing interest.

References

1. Rinehart JK, Singleton RD, Adair JC, Sadek JR, Haaland KY. Arm use after left or right hemiparesis is influenced by hand preference. Stroke. 2009;40(2):545–50.
2. Vega-González A, Granat MH. Continuous monitoring of upper-limb activity in a free-living environment. Arch Phys Med Rehabil. 2005;86(3):541–8.
3. Puttemans V, Wenderoth N, Swinnen S. Changes in brain activation during the acquisition of a multifrequency bimanual coordination task: from the cognitive stage to advanced levels of automaticity. J Neurosci. 2005;25(17):4270–8. https://doi.org/10.1523/JNEUROSCI.3866-04.2005.
4. Swinnen S. Intermanual coordination: from behavioural principles to neural-network interactions. Nat Rev Neurosci. 2002;3(5):348–59. https://doi.org/10.1038/nrn807.
5. Debaere F, Wenderoth N, Sunaert S, Van Hecke P, Swinnen S. Cerebellar and premotor function in bimanual coordination: parametric neural responses to spatiotemporal complexity and cycling frequency. Neuroimage. 2004b;21(4):1416–27. https://doi.org/10.1016/j.neuroimage.2003.12.011.

6. Gooijers J, Swinnen S. Interactions between brain structure and behavior: the corpus callosum and bimanual coordination. Neurosci Biobehav Rev. 2014;43:1–19. https://doi.org/10.1016/j.neubiorev.2014.03.008.
7. Swinnen S, & Gooijers J (2015) Bimanual coordination. In Brain Mapping (pp. 475–482). Elsevier. https://doi.org/10.1016/B978-0-12-397025-1.00030-0
8. Swinnen S, Wenderoth N. Two hands, one brain: cognitive neuroscience of bimanual skill. Trends Cogn Sci. 2004;8(1):18–25. https://doi.org/10.1016/j.tics.2003.10.017.
9. Shih P-C, Steele CJ, Nikulin V, Villringer A, & Sehm B (2019) Kinematic profiles suggest differential control processes involved in bilateral in-phase and anti-phase movements. Sci Rep 9(1). https://doi.org/10.1038/s41598-019-40295-1
10. Kelso JA. Phase transitions and critical behavior in human bimanual coordination. Am J Physiol Regul Integr Comp Physiol. 1984;246(6):R1000–4.
11. Debaere F, Wenderoth N, Sunaert S, Van Hecke P, Swinnen S. Changes in brain activation during the acquisition of a new bimanual coordination task. Neuropsychologia. 2004a;42(7):855–67. https://doi.org/10.1016/j.neuropsychologia.2003.12.010.
12. Stoodley CJ, Schmahmann JD. Evidence for topographic organization in the cerebellum of motor control versus cognitive and affective processing. Cortex. 2010;46(7):831–44. https://doi.org/10.1016/j.cortex.2009.11.008.
13. Debaere F, Wenderoth N, Sunaert S, Van Hecke P, Swinnen S. Internal vs external generation of movements: differential neural pathways involved in bimanual coordination performed in the presence or absence of augmented visual feedback. Neuroimage. 2003;19(3):764–76. https://doi.org/10.1016/S1053-8119(03)00148-4.
14. Meyer-Lindenberg A, Ziemann U, Hajak G, Cohen L, Berman KF. Transitions between dynamical states of differing stability in the human brain. Proc Natl Acad Sci. 2002;99(17):10948–53. https://doi.org/10.1073/pnas.162114799.
15. Tracy JI, Faro SS, Mohammed FB, Pinus AB, Madi SM, Laskas JW. Cerebellar mediation of the complexity of bimanual compared to unimanual movements. Neurology. 2001;57(10):1862–9. https://doi.org/10.1212/WNL.57.10.1862.
16. Ullén F, Forssberg H, Ehrsson HH. Neural networks for the coordination of the hands in time. J Neurophysiol. 2003;89(2):1126–35. https://doi.org/10.1152/jn.00775.2002.
17. Schlerf JE, Verstynen TD, Ivry RB, Spencer RMC. Evidence of a novel somatopic map in the human neocerebellum during complex actions. J Neurophysiol. 2010;103(6):3330–6. https://doi.org/10.1152/jn.01117.2009.
18. Manto M, Bower JM, Conforto AB, Delgado-García JM, da Guarda SNF, Gerwig M, Habas C, Hagura N, Ivry RB, Mariën P, Molinari M, Naito E, Nowak DA, Taib OB, N., Pelisson, D., Tesche, C. D., Tilikete, C., & Timmann, D. . Consensus paper: roles of the cerebellum in motor control—the diversity of ideas on cerebellar involvement in movement. The Cerebellum. 2012;11(2):457–87. https://doi.org/10.1007/s12311-011-0331-9.
19. Halsband U, Lange RK. Motor learning in man: a review of functional and clinical studies. J Physiol Paris. 2006;99(4–6):414–24. https://doi.org/10.1016/j.jphysparis.2006.03.007.
20. Sisti HM, Geurts M, Gooijers J, Heitger MH, Caeyenberghs K, Beets IAM, Serbruyns L, Leemans A, Swinnen S. Microstructural organization of corpus callosum projections to prefrontal cortex predicts bimanual motor learning. Learn Mem. 2012;19(8):351–7. https://doi.org/10.1101/lm.026534.112.
21. Schmahmann JD, Guell X, Stoodley CJ, Halko MA. The theory and neuroscience of cerebellar cognition. Annu Rev Neurosci. 2019;42(1):337–64. https://doi.org/10.1146/annurev-neuro-070918-050258.
22. Houk JC, Buckingham JT, Barto AG. Models of the cerebellum and motor learning. Behav Brain Sci. 1996;19:368–83.
23. Ito M (2000) Mechanisms of motor learning in the cerebellum. Brain Res 9
24. Eickhoff SB, Bzdok D, Laird AR, Kurth F, Fox PT. Activation likelihood estimation revisited. Neuroimage. 2012;59:2349–61.
25. Eickhoff SB, Laird AR, Grefkes C, Wang LE, Zilles K, Fox PT. Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: a random-effects approach based on empirical estimates of spatial uncertainty. Hum Brain Mapp. 2009;30:2907–26.
26. Turkeltaub PE, Eickhoff SB, Laird AR, Fox M, Wiener M, Fox PT. Minimizing within-experiment and within-group effects in activation likelihood estimation meta-analyses. Hum Brain Mapp. 2012;33:1–13.
27. Laird AR, Fox M, Price CJ, Glahn DC, Uecker AM, Lancaster JL, Turkeltaub PE, Kochunov PV, Fox PT. ALE meta-analysis: controlling the false discovery rate and performing statistical contrasts. Hum Brain Mapp. 2005;25:155–64.
28. Eickhoff SB, Stephan KE, Grefkes C, Fink GR, Amunts K, Zilles K. A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. Neuroimage. 2005;25(4):1325–35. https://doi.org/10.1016/j.neuroimage.2004.12.034.
29. Diedrichsen J, Balsters JH, Flavell J, Cussans E & Ramnani N (2009) A probabilistic MR Atlas of the human cerebellum. 8
30. Diedrichsen J, Maderwald S, Küper M, Thürling M, Rabe K, Gizewski ER, Ladd ME, Timmann D. Imaging the deep cerebellar nuclei: a probabilistic atlas and normalization procedure. Neuroimage. 2011;54(3):1786–94. https://doi.org/10.1016/j.neuroimage.2010.10.035.
31. Brett M, Anton JL, Valabregue R, & Poline JB (2002) Region of interest analysis using an SPM toolbox. In 8th International Conference on Functional Mapping of the Human Brain 16(2), 497
32. Buckner RL. The cerebellum and cognitive function: 25 years of insight from anatomy and neuroimaging. Neuron. 2013;80(3):807–15. https://doi.org/10.1016/j.neuron.2013.10.044.
33. Thomas Yeo BT, Krienen FM, Sepulcre J, Sabuncu MR, Lashkari D, Hollinshead M, Roffman JL, Smoller JW, Zöllei L, Polimeni JR, Fischl B, Liu H, Buckner RL. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiol. 2011;106(3):1125–65. https://doi.org/10.1152/jn.00338.2011.
34. Grodd W, Hülsmann E, Lotze M, Wildgruber D, Erb M. Sensorimotor mapping of the human cerebellum: FMRI evidence of somatotopic organization. Hum Brain Mapp. 2001;13(2):55–73.
35. Habas C, Axelrad H, Nguyen TH. Specific neocerebellar activation during out-of-phase bimanual movements. Neuro Report. 2004;15(4):595–9.
36. Shibasaki H, Sadato N, Lyshkow H, Yonekura Y, Honda M, Nagamine T, Suwazono S, Magata Y, Ikeda A, Miyazaki M, Fukuyama H, Asato R, Konishi J. Both primary motor cortex and supplementary motor area play an important role in complex finger movement. Brain. 1993;116(6):1387–98. https://doi.org/10.1093/brain/116.6.1387.
37. Toyokura M, Muro I, Komiya T, Obara M. Relation of bimanual coordination to activation in the sensorimotor cortex and supplementary motor area: analysis using functional magnetic resonance imaging. Brain Res Bull. 1999;48(2):211–7. https://doi.org/10.1016/S0361-9230(98)00165-8.
38. Toyokura M, Muro I, Komiya T, Obara M. Activation of pre-supplementary motor area (SMA) and SMA proper during unimanual and bimanual complex sequences: an analysis using functional magnetic resonance imaging. J Neuroimaging. 2002;12(2):172–8. https://doi.org/10.1111/j.1552-6569.2002.tb00116.x.

39. Goble DJ, Coxon JP, Van Impe A, De Vos J, Wenderoth N, & Swinnen S (2010) The neural control of bimanual movements in the elderly: brain regions exhibiting age-related increases in activity, frequency-induced neural modulation, and task-specific compensatory recruitment. Human Brain Mapping, NA-NA. https://doi.org/10.1002/hbm.20943
40. Duque J, Davare M, Delaunay L, Jacob B, Saur R, Hummel F, Hermoye L, Rossion B, Olivier E. Monitoring coordination during bimanual movements: where is the mastermind? J CognNeurosci. 2010;22(3):526–42. https://doi.org/10.1162/jocn.2009.21213.
41. Koeneke S, Lutz K, Wüstenberg T, Jäncke L. Bimanual versus unimanual coordination: what makes the difference? Neuroimage. 2004;22(3):1336–50. https://doi.org/10.1016/j.neuroimage.2004.03.012.
42. Spencer RMC. Disrupted timing of discontinuous but not continuous movements by cerebellar lesions. Science. 2003;300(5624):1437–9. https://doi.org/10.1126/science.1083661.
43. Spencer RMC, Verstynen T, Brett M, Ivry R. Cerebellar activation during discrete and not continuous timed movements: an fMRI study. Neuroimage. 2007;36(2):378–87. https://doi.org/10.1016/j.neuroimage.2007.03.009.
44. Bo J, Block HJ, Clark JE, Bastian AJ. A cerebellar deficit in sensorimotor prediction explains movement timing variability. J Neurophysiol. 2008;100(5):2825–32. https://doi.org/10.1152/jn.90221.2008.
45. Helmuth LL, & Ivry RB (1996) When two hands are better than one: reduced timing variability during bimanual movements. 16
46. Wenderoth N, Debaere F, Sunaert S, van Hecke P, Swinnen S. Parieto-premotor areas mediate directional interference during bimanual movements. Cereb Cortex. 2004;14(10):1153–63. https://doi.org/10.1093/cercor/bhh075.
47. Wenderoth N, Toni I, Bedeleem S, Debaere F, Swinnen S. Information processing in human parieto-frontal circuits during goal-directed bimanual movements. Neuroimage. 2006;31(1):264–78. https://doi.org/10.1016/j.neuroimage.2005.11.033.
48. Wenderoth N, Debaere F, Sunaert S, Swinnen S. The role of anterior cingulate cortex and precuneus in the coordination of motor behaviour. Eur J Neurosci. 2005a;22(1):235–46. https://doi.org/10.1111/j.1460-9568.2005.04176.x.
49. van Dun K, Manto M, Mariën P. The language of the cerebellum. Aphasiology. 2016;30(12):1378–98. https://doi.org/10.1080/02687038.2015.1132297.
50. Keele SW, Ivry R. Does the cerebellum provide a common computation for diverse tasks? A timing hypothesis. Ann N Y Acad Sci. 1990;608(1):179–211.
51. Leggio MG, Chiricozzi FR, Clausi S, Tedesco AM, Molinari M. The neuropsychological profile of cerebellar damage: the sequencing hypothesis. Cortex. 2011;47(1):137–44. https://doi.org/10.1016/j.cortex.2009.08.011.
52. Müller VI, Cieslik EC, Laird AR, Fox PT, Radua J, Mataix-Cols D, Tench CR, Yarkoni T, Nichols TE, Turkeltaub PE, Wager TD, Eickhoff SB. Ten simple rules for neuroimaging meta-analysis. Neurosci Biobehav Rev. 2018;84:151–61. https://doi.org/10.1016/j.neubiorev.2017.11.012.
53. Fox PT, Laird AR, Eickhoff SB, Lancaster JL, Fox M, Uecker AM, & Ray KL (2013) User manual for GingerALE 2.3. UT Health Science Center San Antonio
54. Aramaki Y, Honda M, Okada T, Sadato N. Neural correlates of the spontaneous phase transition during bimanual coordination. Cereb Cortex. 2006;16(9):1338–48. https://doi.org/10.1093/cercor/bhj075.
55. Aramaki Y, Osu R, Sadato N. Resource-demanding versus cost-effective bimanual interaction in the brain. Exp Brain Res. 2010;203(2):407–18. https://doi.org/10.1007/s00221-010-2244-0.
56. Goerres GW, Samuel M, Jenkins IH, & Brooks DJ (1998) Cerebral control of unimanual and bimanual movements: An H 15O PET study. Neuro Report t9: 3631–3638
57. Haslinger B, Erhard P, Altenmüller E, Hennenlotter A, Schwaiger M, Gräfin von Einsiedel H, Rummeny E, Conrad B, Ceballos-Baumann AO. Reduced recruitment of motor association areas during bimanual coordination in concert pianists: Bimanual Coordination in Pianists. Hum Brain Mapp. 2004;22(3):206–15. https://doi.org/10.1002/hbm.20028.
58. Kraft E, Loichinger W, Diepers M, Lule D, Schwarz J, Ludolph AC, Storch A. Levodopa-induced striatal activation in Parkinson's disease: a functional MRI study. Parkinsonism Relat Disord. 2009;15(8):558–63. https://doi.org/10.1016/j.parkreldis.2009.02.005.
59. Smethurst CJ, Carson RG. The acquisition of movement skills: practice enhances the dynamic stability of bimanual coordination. Hum MovSci. 2001;20(4–5):499–529. https://doi.org/10.1016/S0167-9457(01)00065-3.
60. Hanawa S, Sugiura M, Nozawa T, Kotozaki Y, Yomogida Y, Ihara M, Akimoto Y, Thyreau B, Izumi S, Kawashima R. The neural basis of the imitation drive. Soc Cogn Affect Neurosci. 2016;11(1):66–77. https://doi.org/10.1093/scan/nsv089.
61. Müller K, Kleiser R, Mechsner F, Seitz RJ. Involvement of area MT in bimanual finger movements in left-handers: an fMRI study: bimanual coordination in left-handers. Eur J Neurosci. 2011;34(8):1301–9. https://doi.org/10.1111/j.1460-9568.2011.07850.x.
62. Müller K, Kleiser R, Mechsner F, Seitz RJ. Perceptual influence on bimanual coordination: an fMRI study. Eur J Neurosci. 2009;30(1):116–24. https://doi.org/10.1111/j.1460-9568.2009.06802.x.
63. Wenderoth N, Debaere F, Sunaert S, Swinnen SP. Spatial interference during bimanual coordination: differential brain networks associated with control of movement amplitude and direction. Hum Brain Mapp. 2005b;26(4):286–300. https://doi.org/10.1002/hbm.20151.
64. Meister IG, Foltys H, Gallea C, Hallett M. How the brain handles temporally uncoupled bimanual movements. Cereb Cortex. 2010;20(12):2996–3004. https://doi.org/10.1093/cercor/bhq048.
65. Hanakawa T, Dimyan MA, Hallett M. The representation of blinking movement in cingulate motor areas: a functional magnetic resonance imaging study. Cereb Cortex. 2008;18(4):930–7. https://doi.org/10.1093/cercor/bhm129.
66. Sadato N, Yonekura Y, Waki A, Yamada H, Ishii Y. Role of the supplementary motor area and the right premotor cortex in the coordination of bimanual finger movements. J Neurosci. 1997;17(24):9667–74. https://doi.org/10.1523/JNEUROSCI.17-24-09667.1997.
67. Theorin A, Johansson RS. Zones of bimanual and unimanual preference within human primary sensorimotor cortex during object manipulation. Neuroimage. 2007;36:T2–15. https://doi.org/10.1016/j.neuroimage.2007.03.042.
68. Kraft E, Chen AW, Flaherty AW, Blood AJ, Kwong KK, Jenkins BG. The role of the basal ganglia in bimanual coordination. Brain Res. 2007;1151:62–73. https://doi.org/10.1016/j.brainres.2007.01.142.
69. Kiyama S, Kunimi M, Iidaka T, & Nakai T (2014) Distant functional connectivity for bimanual finger coordination declines with aging: an fMRI and SEM exploration. Front Hum Neurosci 8. https://doi.org/10.3389/fnhum.2014.00251

70. De Luca C, Jantzen KJ, Comani S, Bertollo M, Kelso JAS. Striatal activity during intentional switching depends on pattern stability. J Neurosci. 2010;30(9):3167–74. https://doi.org/10.1523/JNEUROSCI.2673-09.2010.
71. Dietz V, Macauda G, Schrafl-Altermatt M, Wirz M, Kloter E, Michels L. Neural coupling of cooperative hand movements: a reflex and fMRI study. Cereb Cortex. 2015;25(4):948–58. https://doi.org/10.1093/cercor/bht285.
72. Christensen MS, Ehrsson HH, Nielsen JB. Seeing or moving in parallel: The premotor cortex does both during bimanual coordination, while the cerebellum monitors the behavioral instability of symmetric movements. Exp Brain Res. 2013;230(1):101–15. https://doi.org/10.1007/s00221-013-3633-y.
73. Wu T, Wang L, Hallett M, Li K, Chan P. Neural correlates of bimanual anti-phase and in-phase movements in Parkinson's disease. Brain. 2010;133(8):2394–409. https://doi.org/10.1093/brain/awq151.