

Functional neuroimaging correlates of finger-tapping task variations: An ALE meta-analysis

Suzanne T. Witt,^{a,*} Angela R. Laird,^b and M. Elizabeth Meyerand^{a,*}

^aDepartment of Medical Physics, University of Wisconsin, Madison, Wisconsin, USA

^bResearch Imaging Center, University of Texas Health Science Center, San Antonio, Texas, USA

Received 14 January 2008; revised 24 March 2008; accepted 1 April 2008
Available online 16 April 2008

Finger-tapping tasks are one of the most common paradigms used to study the human motor system in functional neuroimaging studies. These tasks can vary both in the presence or absence of a pacing stimulus as well as in the complexity of the tapping task. A voxel-wise, coordinate-based meta-analysis was performed on 685 sets of activation foci in Talairach space gathered from 38 published studies employing finger-tapping tasks. Clusters of concordance were identified within the primary sensorimotor cortices, supplementary motor area, premotor cortex, inferior parietal cortices, basal ganglia, and anterior cerebellum. Subsequent analyses performed on subsets of the primary set of foci demonstrated that the use of a pacing stimulus resulted in a larger, more diverse network of concordance clusters, in comparison to varying the complexity of the tapping task. The majority of the additional concordance clusters occurred in regions involved in the temporal aspects of the tapping task, rather than its execution. Tapping tasks employing a visual pacing stimulus recruited a set of nodes distinct from the results observed in those tasks employing either an auditory or no pacing stimulus, suggesting differing cognitive networks when integrating visual or auditory pacing stimuli into simple motor tasks. The relatively uniform network of concordance clusters observed across the more complex finger-tapping tasks suggests that further complexity, beyond the use of multi-finger sequences or bimanual tasks, may be required to fully reveal those brain regions necessary to execute truly complex movements.

© 2008 Elsevier Inc. All rights reserved.

Keywords: Meta-analysis; Finger tapping; Motor; Activation likelihood estimation; ALE; Paced finger tapping; Auditory stimulus; Visual stimulus; Self-paced movement; Movement complexity; Sequential finger movements; Bimanual

Introduction

Finger-tapping tasks are commonly used to study the human motor system in functional neuroimaging studies. Tapping tasks have the advantage of being simple enough to use in the study of both normal control subjects as well as those with neuropathologies affecting the motor system, while being flexible enough to accommodate numerous modifications. These tasks can vary across studies both by the use or lack of a pacing stimulus and in the relative complexity of the tapping task.

Pacing stimuli are used to ensure that all subjects uniformly perform a given finger-tapping task at a predetermined rate. The stimuli are usually in the form of a regularly paced, repetitive auditory or visual cue, such as that produced by a metronome (e.g. [Catalan et al., 1998](#); [Colebatch et al., 1991](#); [Sadato et al., 1996a](#)) or blinking light (e.g. [Indovina and Sanes, 2001](#); [Jäncke et al., 2000b](#)), respectively. Such finger-tapping tasks performed in the presence of a pacing stimulus are referred to as externally guided or externally generated. In contrast, the task can be performed in the absence of any pacing stimulus (i.e. self-paced). Such self-paced tapping tasks are referred to as internally guided or internally generated. The results from studies investigating the effects of auditory and visual pacing stimuli have reported different networks of active brain regions, however, these results are not consistent across different studies.

Pacing stimuli are also often used in conjunction with more complex finger-tapping tasks such as multi-finger sequential or bimanual tapping tasks. For the purposes of the ensuing analyses, multi-finger sequential tapping tasks were taken to be complex in terms of the increased number of fingers involved in the task; factors such as the rate of movement and the length of the sequence were not specifically considered. Bimanual tasks were taken to be any task involving the tapping of fingers on both hands, regardless of the symmetry. These types of complex finger-tapping tasks are often employed to elicit neural activation that is more representative of what would be observed in typical, everyday manual movements that may not be practical to complete within the confines of a MRI or PET scanner. The use of complex finger-tapping tasks also allows for the further study of secondary and tertiary neural motor regions

* Corresponding authors. Department of Medical Physics, University of Wisconsin, 1530 Medical Sciences Center, 1300 University Avenue, Madison, WI 53706, USA. Fax: +1 608 265 9840.

E-mail addresses: stwitt@wisc.edu (S.T. Witt), memeyerand@wisc.edu (M.E. Meyerand).

Available online on ScienceDirect (www.sciencedirect.com).

Table 1
Published studies employing finger-tapping tasks used in the meta-analyses

Publication	Contrast	Foci	Stimulus	Complexity	Bimanual
Aoki et al. (2005)	Index finger vs Rest	1	Auditory	RH index	Bimanual
	Ring finger vs Rest	7	Auditory		
	Double finger tapping vs Rest	12	Auditory		
Aramaki et al. (2006)	Parallel vs Rest	18	Auditory	Bimanual	Bimanual
	Mirror vs Rest	7	Auditory		
Blinkenberg et al. (1996)	Finger tapping vs Rest	10	Auditory	RH index	
Boecker et al. (1998)	Motor sequences vs Rest	20	Auditory	Sequence	
Calautti et al. (2001)	RH tapping vs Rest, young subjects	10	Auditory	RH index	
	LH tapping vs Rest, young subjects	10	Auditory		
	RH tapping vs Rest, older subjects	4	Auditory	RH index	
	LH tapping vs Rest, older subjects	10	Auditory		
	Sequence-12 vs Rest	9	Auditory	Sequence	
	Sequence-16 vs Rest, controls	12	Auditory	Sequence	
Colebatch et al. (1991)	Index vs Rest	3	Auditory	RH index	
De Luca et al. (2005)	Opposition vs Rest	8	Auditory	Sequence	
Denslow et al. (2005)	RH finger tapping, controls	4	Visual	RH index	
Fox et al. (2004)	Volitional movement vs sham TMS	18	Auditory	RH index	
Gelnar et al. (1999)	Finger movement vs sham TMS	1	Auditory	RH index	
Gerardin et al. (2000)	Finger opposition vs Rest	8	None	Sequence	
Gosain et al. (2001)	Motor Execution vs Rest	24	Auditory		
Hanakawa et al. (2003)	Finger tapping vs Rest	2	None	RH index	
Indovina and Sanes (2001)	Finger movement vs Rest	25	Visual	Sequence	
Jäncke et al. (1999)	Move vs Rest	15	Visual	RH index	
Jäncke et al. (2000a)	RH, 1 Hz vs Rest	2	Auditory	Sequence	
	RH, 3 Hz vs Rest	2	Auditory	Sequence	
	LH, 1 Hz vs Rest	2	Auditory	Sequence	
	LH, 3 Hz vs Rest	2	Auditory	Sequence	
	Both hands, 1 Hz vs Rest	2	Auditory	Sequence	Bimanual
	Both hands, 3 Hz vs Rest	2	Auditory	Sequence	
	Right fast, left slow	3	None		
	Right slow, left fast	3	None		
	Right fast	1	None	RH index	
	Right slow	2	None	RH index	
Jäncke et al. (2000b)	Left fast	1	None		
	Left slow	2	None		
	Auditory synchronization vs Rest	12	Auditory	RH index	
	Auditory continuation vs Rest	11	None	RH index	
	Visual synchronization vs Rest	13	Visual	RH index	
	Visual continuation vs Rest	12	None	RH index	
	Finger tapping vs Rest	13	None	RH index	
Joliot et al. (1998)	Finger tapping vs Rest — PET	11	None	RH index	
Joliot et al. (1999)	Finger tapping vs Rest — fMRI-average	16	None	RH index	
Kawashima et al. (1999)	Finger tapping vs Rest — fMRI-correlation	20	None	RH index	
	Finger movements vs Rest	3	None	RH index	
	Memory timed finger movement vs Rest	10	None	RH index	
Kawashima et al. (2000)	Visually cued finger movement vs Rest	14	Visual	RH index	
Kuhtz-Buschbeck et al. (2003)	Motor execution, complex RH vs baseline	8	Auditory	Sequence	
Larsson et al. (1996)	Motor execution, complex LH vs baseline	12	Auditory	Sequence	
Lehericy et al. (2006)	Self-paced movements vs Rest	12	None	RH index	
	Visually triggered movements vs Rest	14	Visual	RH index	
	Simple vs Rest	8	Auditory	RH index	
	Scale vs Rest	11	Auditory	Sequence	
Lerner et al. (2004)	Complex vs Rest	27	Auditory	Sequence	
	Tapping vs Rest, Normals	9	Auditory	RH index	
	Random vs Rest	17	Visual	RH index	
Mattay et al. (1998)	Regular vs Rest	7	Visual	RH index	
Müller et al. (2002)	Non-dominant hand, simple motor	8	None	Sequence	
	Dominant hand, simple motor	12	None	Sequence	
	Dominant hand, random motor	15	None	Sequence	
Ramsey et al. (1996)	Finger tapping vs Rest, healthy subjects	4	None		
	fMRI finger tapping vs Rest, Mean	1	None	Sequence	
	PET finger tapping vs Rest, Mean	1	None	Sequence	

Table 1 (continued)

Publication	Contrast	Foci	Stimulus	Complexity	Bimanual
Riecker et al. (2006)	Main effects during index finger movement, young subjects	6	Auditory	RH index	
	Main effects during index finger movement, older subjects	8	Auditory	RH index	
Rounis et al. (2005)	Main effects of movement	17	Auditory	RH index	
Sadato et al. (1996a)	Various length sequences	6	Auditory	Sequence	
Sadato et al. (1997)	Mirror vs Rest	13	Auditory	Sequence	Bimanual
	Parallel vs Rest	15	Auditory	Sequence	Bimanual
	Right unimanual vs Rest	3	Auditory	RH index	
	Left unimanual vs Rest	6	Auditory		
	Bimanual mirror vs Rest	12	Auditory		Bimanual
	Bimanual parallel vs Rest	13	Auditory		Bimanual
Seitz et al. (2000)	Irregularly paced right finger movement	4	Auditory	RH index	
Wilson et al. (2004)	Moving fingers	2	None	Sequence	Bimanual
Yoo et al. (2005)	Group-level finger-tapping activation	17	Auditory	Sequence	

A total of 38 studies with 74 contrasts and 685 foci was included in the finger-tapping meta-analyses (listed in alphabetical order by first author). The type or lack of pacing stimulus and the level of complexity as well as whether the task was bimanual are indicated for each contrast.

that may not be active during a simple, unimanual index finger-tapping task.

Results from studies employing finger-tapping tasks can be divergent due to variations in the experimental paradigms used, making them difficult to interpret across studies. Additionally, studies can choose to focus on a few specific neural regions (e.g. Jäncke et al., 2000a; Colebatch et al., 1991; De Luca et al., 2005), resulting in partial descriptions of the underlying neural network involved in a given tapping task. A quantitative meta-analysis technique, such as that proposed independently by Turkeltaub et al. (2002) and Chein et al. (2002) provides a method to assess the degree of concordance across multiple studies. The results of such an analysis can be useful in determining a more complete network of neural regions involved in a given task or paradigm as well as in forming new hypotheses and interpreting results from subjects with neurological impairments.

This present study was not the first to use quantitative meta-analysis techniques to assess concordance across studies examining the human motor system. Chouinard and Paus (2006) employed a similar technique to further elucidate the roles of the primary motor and premotor cortices in various motor tasks. Four motor-related tasks – movement response selection, movement response to a stimulus, execution of object-related hand movements, and observation of object-related hand movements – were chosen to map out the roles of the dorsal and ventral premotor cortices in these tasks. Chouinard and Paus were successful in utilizing meta-analysis to identify several distinct nonprimary motor areas within the motor cortex.

In the present meta-analysis, our aim was to isolate the corpus of published literature for simple hand movements (i.e., finger tapping), and identify the entire network of brain regions associated with this type of motor task. Our intent was to examine agreement across studies not only in the motor cortex, but also throughout all cortical, subcortical, and cerebellar regions. In addition, meta-analysis was used to differentiate the brain regions that are active during the most common variations of finger-tapping tasks: auditorily-paced, visually-paced, self-paced, single index finger, unimanual, dominant hand (RH) multi-finger sequence, and bimanual, as well as to compare these networks among the tapping task variations. We hypothesized that the choice of finger-tapping task variation would have a strong influence on the observed network of active brain regions.

Methods

Several literature searches were performed in Medline to find the published corpus of literature prior to July 2006 involving finger-tapping tasks in unimpaired, right-handed subjects. References from all relevant papers were also examined. From these search results, only those papers which reported activations as coordinates in stereotactic space (x,y,z) were considered. Papers directly addressing motor learning or using over-trained subjects such as professional musicians were excluded. Results from 38 papers (22 fMRI and 16 PET; Table 1) were selected (685 foci), and three analyses were performed. The first pooled the results from all of the included studies. For the second, studies were divided into three groups based on the type or lack of pacing stimulus employed: auditory stimulus (22 papers; 403 foci), visual stimulus (7 papers; 109 foci), and no stimulus (13 papers; 173 foci). The final analysis divided the studies into three groups determined by the complexity of the tapping task used: right hand index finger (23 papers; 311 foci), RH multi-finger sequence (15 papers; 242 foci), and bimanual (5 papers; 90 foci). All MNI coordinates were transformed to Talairach space using the *icbm2tal* transform (Lancaster et al., 2007), which has shown to provide improved fit over the *mni2tal* transform (Brett et al., 2001, 2002). When applying the Lancaster transform, software-specific versions were used for FSL (*icbm_fsl2tal*) and SPM (*icbm_spm2tal*) coordinates, to correct for varying normalization methods within each software package. Activation likelihood estimate (ALE) maps were created for each grouping by modeling each focus as a three-dimensional Gaussian function with a FWHM of 12 mm (Turkeltaub et al., 2002). Statistical significance was assessed using a permutation test with 5000 permutations, corrected for multiple comparisons using the false discovery rate (FDR) (Laird et al., 2005). The resultant maps were thresholded at $P < 0.05$.

Results

The ALE map for the main effects of all finger-tapping task variations included in this study is shown in Fig. 1. Common, robust concordance was seen in bilateral sensorimotor cortices (L: -38, -26,50; R: 36, -22,54), supplementary motor area (SMA) (-4, -8,52), left ventral premotor cortex (-54, -2,32), bilateral inferior

parietal cortices (L: -50,-26,20; R: 40,-42,44), bilateral basal ganglia (L: -22,-8,4; R: 22,-10,6), and bilateral anterior cerebellum (L: -22,-52,22; R: 16,-50,-20). Smaller clusters of concordance were seen in the right dorsolateral prefrontal cortex (34,32,34), right inferior frontal gyrus (54,4,22), and left occipital lobe (-44,-66,4). The appearance of this latter trio of brain regions will later be shown to have more to do with the inclusion of visually-paced finger-tapping tasks, than in these regions playing a role in the performance of finger-tapping tasks in general.

Figs. 2A–G show representative axial slices of the combined ALE map for the three groups of studies involving the use or absence of pacing stimuli — auditorily-paced, visually-paced, and self-paced. In addition to the executive areas noted above for the main effects, the ALE map for the pacing stimulus group showed clusters of concordance, which were unique to one or more of the task variations in this grouping. All three variations within this group showed

concordance within the dorsal premotor cortices (R: 47,1,50; 38, -10,54), with laterality depending on task variation. The visually- and self-paced groups exhibited concordance within the right dorsolateral prefrontal cortex (42,34,32; 32,30,32) and right inferior parietal lobe (46,-44,44). The auditorily- and self-paced groups shared concordance in bilateral claustrum (L: -32,-4,6; R: 34,-8,14), again with laterality depending on task variation. The visually-paced group had exclusive concordance in bilateral insula (L: -48,10,0; R: 48,10,2), right inferior frontal gyrus (50,8,32), bilateral occipital lobe (L: -42,-66,4; -10,-82,-2; R: 44,-66,-2; 4,-76,0), and left posterior cerebellum (-28,-62,-28). Finally, the auditorily-paced group had exclusive concordance in Brodmann's area 44 (56,3,20) and the self-paced group in the left ventral premotor cortex (-52,-2,10) and right posterior cerebellum (10,-66,-32).

In order to determine the relative effect of tapping rate in the meta-analytic comparisons of stimulus modality, we performed a comparison

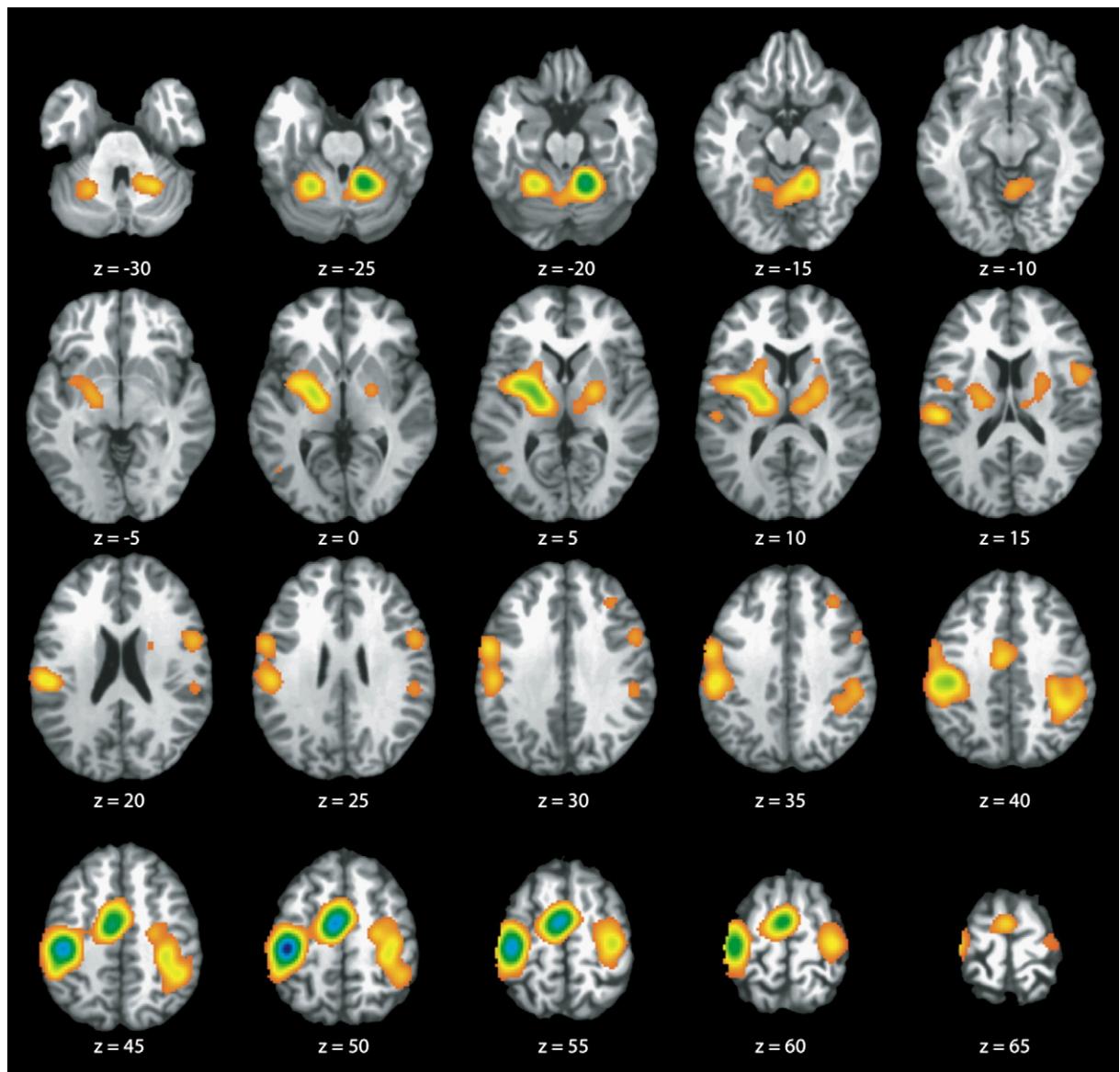


Fig. 1. ALE map of the main effects (all finger-tapping task variations). Axial slices representing full brain coverage are shown ($P < 0.05$; FDR corrected). Robust concordance is seen in bilateral sensorimotor cortices, supplementary motor area, left ventral premotor, bilateral inferior parietal cortices, bilateral basal ganglia, and bilateral anterior cerebellum.

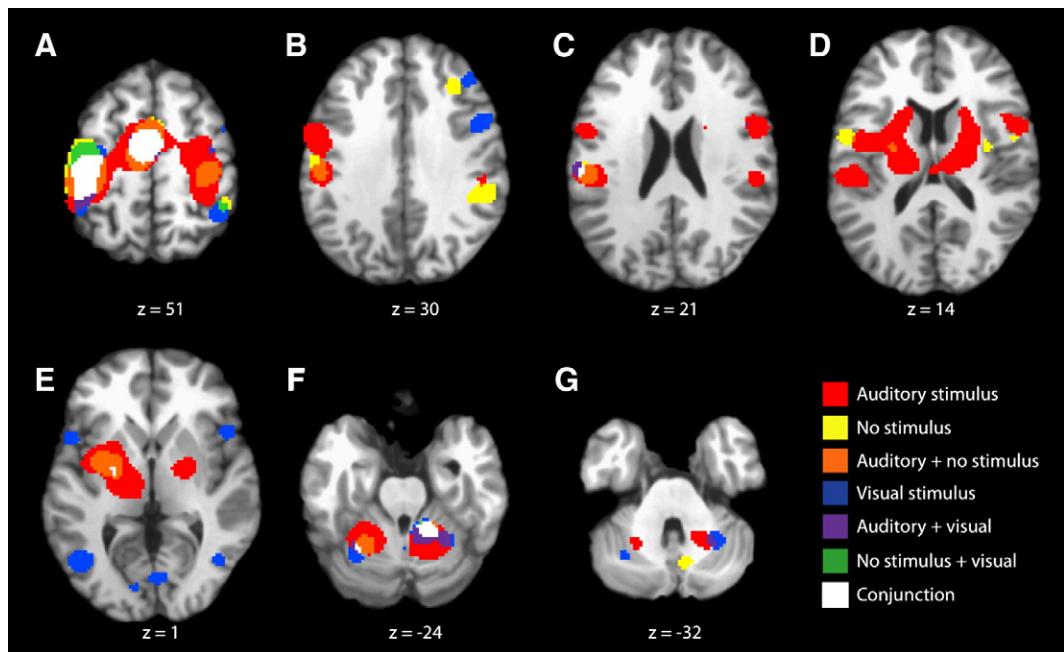


Fig. 2. ALE results segregated by pacing stimuli. Representative axial slices are shown ($P < 0.05$; FDR corrected) for finger-tapping activations when paced by auditory, visual, or no stimuli. Overlap (conjunction) among all three task variations is seen in the same executive regions noted for the main effects in Fig. 1, except the basal ganglia. The results also show many clusters of concordance that are unique to one or more of the task variations.

of study characteristics for auditory vs visual stimuli and paced vs self-paced tapping tasks. The tapping rate was recorded for each experiment that was included in the meta-analyses. An unpaired *t* test was performed on the tapping rates for auditory (mean rate = 1.716 Hz) and visual (mean rate = 1.241 Hz) studies in which no statistical difference was found between groups ($P = 0.182$). A subsequent test was performed to determine if a rate effect existed between paced (mean rate = 1.642 Hz) and self-paced (mean rate = 1.795 Hz) studies; however, this test also revealed no difference ($P = 0.5301$). Note that this result may potentially be biased by the fact that no observed tapping rate was reported in 6 of 24 self-paced experiments; however, given the high P value this is unlikely.

To determine the effect of tapping difficulty on the observed meta-analysis results, studies were reviewed and assigned scores of tapping difficulty according to a five-point rating system: 1 — unimanual single finger, 2 — bimanual single finger or unimanual simple sequence, 3 — bimanual simple sequence or unimanual complex sequence, 4 — bimanual mirrored tapping of a complex sequence, and 5 — bimanual parallel tapping of a complex sequence. Unpaired *t* tests were carried out on comparisons of auditory (mean score = 1.919) vs visual (mean score = 1.125) studies and paced (mean score = 1.794) vs self-paced (mean score = 1.708) studies. Again, no difference was found between either group ($P = 0.059$ and $P = 0.760$, respectively). Arguably, the test of auditory vs visual nearly achieved significance, and therefore some potential bias may have been introduced into the meta-analysis as a result of this. Future imaging studies will be useful in dissociating the degree of interaction between auditory vs visual stimuli and tapping difficulty.

Figs. 3A–G show representative axial slices of the combined ALE map for the three groups of studies involving tapping task complexity — RH index finger, RH multi-finger sequence, and bimanual. Unlike for the meta-analyses results for the pacing stimulus group, the combined ALE map for the complexity group

suggested that there are fewer unique brain regions required to complete more complex finger-tapping tasks that are not already active during the execution of finger-tapping tasks of all variations. All three task variations within this grouping shared concordance within the dorsal (L: -16, -20, 48; R: 34, -8, 52; 46, 1, 51) and ventral (-56, -4, 34; -54, 2, 10; -50, 0, 34) premotor cortices. The RH multi-finger sequence and RH index finger-tapping task variations showed concordance in the right inferior parietal cortex (46, -44, 44; 38, -40, 44). The RH multi-finger sequence tapping task group exhibited concordance within bilateral posterior parietal cortices (L: -26, -62, 48; R: 16, -72, 42), and the bimanual group within the left posterior cerebellum (-4, -66, -18). The RH index finger-tapping task group showed a small cluster of concordance within the left DLPFC (-37, 30, 32), in addition to sharing several clusters of concordance with the externally paced tasks, including the right insula (48, 12, 4), right inferior frontal gyrus (52, 6, 28), bilateral claustra (L: -32, -4, 4; R: 34, 14, 6), and right DLPFC (34, 30, 32).

Discussion

An ALE meta-analysis was performed to quantify the motor system during finger tapping, a common task used in functional imaging studies. Results allowed for detailed description of the motor networks involved in single finger, unimanual, dominant hand multi-finger, and bimanual movement sequences, varying in the presence or absence of a pacing (auditory or visual) stimulus.

Main effects

The results for the main effects analysis across all finger-tapping tasks exhibited clusters of concordance in regions commonly associated with the performance of motor tasks, including the

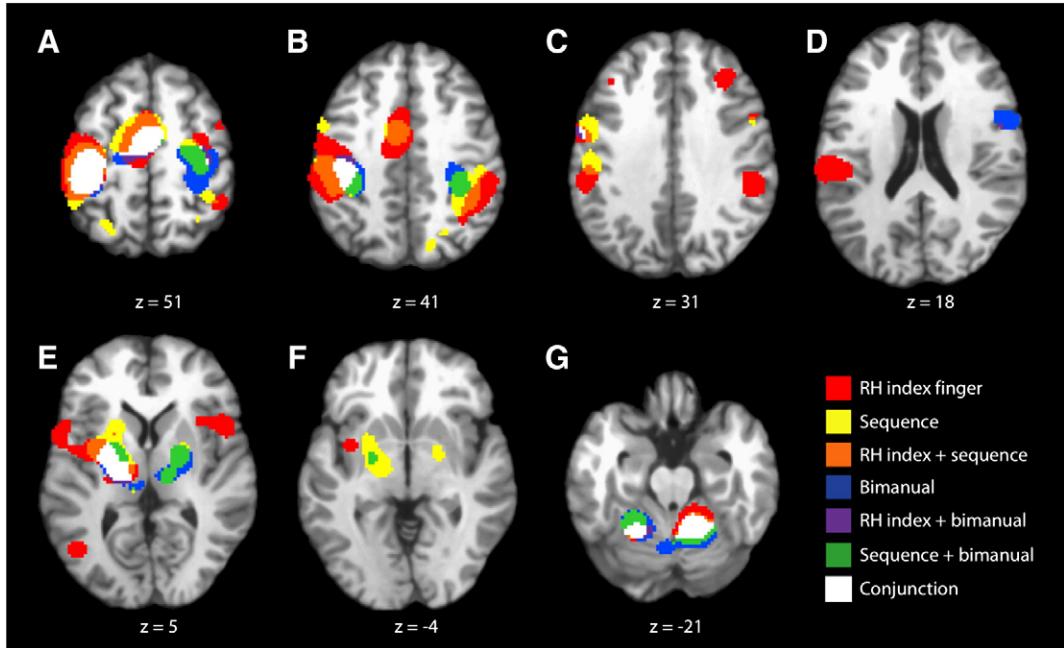


Fig. 3. ALE results segregated by task complexity. Representative axial slices are shown ($P < 0.05$; FDR corrected). Overlap (conjunction) among all three task variations (RH index, RH multi-finger sequence, and bimanual tapping) is seen in the same executive regions noted for the main effects in Fig. 1. Compared with the results from the effects of a pacing stimulus, there are fewer concordance clusters that are unique to one or more of the task variations, not observed in the main effects.

primary sensorimotor cortex (SM1), supplementary motor area (SMA), basal ganglia (BG), and cerebellum. The primary sensorimotor cortex has traditionally been considered the main executive locus for simple voluntary movements (Gerloff et al., 1998), however, recent studies have implicated this region in the processing of complex sequential tapping tasks (Kawashima et al., 1993; Kawashima and Fukuda, 1994; Kawashima et al. 1994; Kim et al., 1993a,b; Rao et al., 1993; Chen et al., 1997) as well as the processing of bimanual movements (Kermadi et al., 2000). The SMA has also been found to be an executive area for simple voluntary movements (Colebatch et al., 1991; Matelli et al., 1993; Sadato et al., 1995). Additionally, activity in the SMA has been linked to higher motor processing functions such as the initiation of movement, motor programming (Roland et al., 1980b), motor planning (Orgogozo and Larsen, 1979; Grafton et al., 1992a; Rao et al., 1993), readiness to move (Fox et al., 1985), motor learning (Roland et al., 1989; Seitz et al., 1990; Grafton et al., 1992a), complexity of movement (Shibasaki et al., 1993), bimanual coordination (Goerres et al., 1998; Immisch et al., 2001; Jäncke et al., 2000a; Meyer-Lindenberg et al., 2002; Sadato et al., 1997; Stephan et al., 1999a,b; Toyokura et al., 1999, 2002; Ullén et al., 2003), and responsiveness to internal cueing of movement (Halsband et al., 1993) or to the selection of movement (Deiber et al., 1991). Activation in the basal ganglia has been associated with both the performance of simple repetitive movements (Lehéricy et al., 1998; Maillard et al., 2000), as well as more complex sequential movements (Roland et al., 1982; Shibasaki et al., 1993; Jenkins et al., 1994a; Jueptner et al., 1997; Gordon et al., 1998; Boecker et al., 1998; Catalan et al., 1998; Haslinger et al., 2002). Activity in both the SMA and BG has been preferentially linked to internally generated movements over externally generated movements in non-human primates (Mushiake et al., 1990, 1991; Tanji, 1994; Tanji and Shima, 1994, 1996; Brinkman, 1984; Chen et al.,

1995; Taniwaki et al., 2003; Romo and Schultz, 1987; Middleton and Strick, 2000), however this distinction has not been consistently reported in humans (Menon et al., 1998; Cunningham et al., 2002). Regions in the cerebellum have been shown to be active during the preparation, execution, and timing of both simple and complex movements (Habas et al., 2004a), and while cerebellar activity has been traditionally associated with externally cued movements, it has been observed in motor tasks driven by both external and internal cues (Grafton et al., 1992b).

In addition to the above regions, clusters of concordance are observed in regions that have been traditionally reported to be preferentially active during one or more specific finger-tapping task variations, namely the premotor and parietal cortices. For both the externally cued and complex tapping tasks, activity has been reported within the premotor and parietal cortices. The premotor cortex has been shown to play an important role in the transformation of sensory information into appropriate motor behavior (Crammond and Kalaska, 1996; Godschalk et al., 1981; Johnson et al., 1996; Mushiake et al., 1991; Wise et al., 1997; Halsband et al., 1993; Harrington et al., 2000; Grafton et al., 1993; Kawashima et al., 1995; Passingham, 1985; Samuel et al., 1997; Roland, 1984), especially in regards to sequential movements (Harrington et al., 2000; Catalan et al., 1998; Grafton et al., 1992a; Shibasaki et al., 1993). The parietal cortex has also been shown to be active during both auditorily- and visually-cued movements (Deiber et al., 1991; Grafton et al., 1992b; Jenkins et al., 1994b; Huttunen et al., 1996; Forss and Jousmaki, 1998; Linn and Forss, 2002), also particularly during both the execution and production of complex, sequential motor tasks (Gordon et al., 1998; Sadato et al., 1996a; Honda et al., 1998; Jenkins et al., 1994b; Rauch et al., 1995; Sakai et al., 1998; Boecker et al., 1998). The observed concordance in these two regions suggests that they may play a more general, executive role in motor tasks, in addition to their more task variation specific roles discussed below.

Pacing stimulus effects

In line with the ALE map for the main effects of all finger-tapping task variations (Fig. 1), conjunction analysis revealed that the three groups (auditorially-, visually-, and self-paced) shared common, robust concordance in the primary sensorimotor cortex, supplementary motor area, and anterior cerebellum (Fig. 2). This shared concordance is in agreement with the body of literature on externally and internally generated motor tasks, suggesting that these areas are involved in the execution motor tasks under both conditions (Weeks et al., 2001; Grafton et al., 1992b). Within the basal ganglia, there was no robust concordance among all three groups. The auditorily- and self-paced groups demonstrated concordance within the putamen and thalamus. The use of visually-paced tapping tasks only revealed concordance within the left globus pallidus external (GPe). These results suggest that the basal ganglia may be active during both externally and internally generated motor tasks but only for those externally generated tasks driven by an auditory cue.

The concordance within the dorsal premotor cortex (PMd; BA 6) was lateralized based on task variation, with the visually-paced group showing bilateral concordance, the auditorily-paced group in the right PMd, and the self-paced group in the left PMd. With the exception of the visually-paced group's clusters in the right PMd, none showed distinct clusters of concordance in this region. Rather, the clusters comprising the primary sensorimotor cortices extended anterior enough to encompass the cortical region usually defined as the dorsal premotor cortex, and the location of this extension in the left hemisphere was in agreement with the region of the left PMd identified through a previous meta-analysis study (Chouinard and Paus, 2006) as being involved in the execution of simple movements in response to an external stimulus. The premotor cortex, in general, has traditionally been associated with the execution of movements under sensory guidance (Goldberg, 1985). Removal of the PMd in humans, in particular, has been shown to disrupt the ability to use arbitrary cues to withhold or perform a particular movement (Petrides, 1982, 1985; Halsband and Passingham, 1982, 1985). More recently, Schubotz and von Cramon (2003) posited a general trend for lateral premotor cortex dominance over externally guided movements and medial premotor cortex dominance over internally guided movements, implying that the premotor cortex is involved in movement execution regardless of the presence or absence of an external cue, which is confirmed by concordance within this region for both the externally and internally paced tasks.

From Fig. 2B, one can observe a definite somatotopy to the concordance cluster within the right dorsolateral prefrontal cortex (DLPFC; BA 9), with the visually-paced group exhibiting concordance in the lateral aspect and the self-paced group in the more medial aspect. The DLPFC has been consistently linked to self-paced movements. Jahanshahi et al. (1995) found greater activation within the DLPFC during self-initiated movements. This study also noted, in line with previous results (Deiber et al., 1991; Frith et al., 1991; Playford et al., 1992) that the DLPFC was the area that significantly distinguished internally generated movements from externally triggered movements, especially in regards to internal temporal processing (Rao et al., 2001; Thaut, 2003), so its observed concordance for visually-paced movements is not in line with previous results. However, this area is also associated with sustained attention (Pardo et al., 1991). It may be that externally generated finger-tapping tasks that use a visual pacing stimulus may not be as automatic as those that make use of an auditory pacing stimulus.

The inferior parietal lobe (LPI; BA 40) has been linked to the encoding of sequence-specific information (Honda et al., 1998; Jenkins

et al., 1994b; Rauch et al., 1995; Sakai et al., 1998) as well as sensorimotor integration processes (Huttunen et al., 1996; Forss and Jousmaki, 1998; Linn and Forss, 2002). Vaillancourt et al. (2006) showed increased activation in right LPI, in conjunction with right PMd and right PMv, in the presence of frequent visual pacing stimulus during a visuomotor task. Its increased activity observed during internally generated movements has been hypothesized to be a consequence of increased attentional demands directed towards somatosensory input from the limbs (Debaere et al., 2003).

As with the dorsal premotor cortices, the concordance in the bilateral claustra was also lateralized based on task variation, with the cluster in the left hemisphere corresponding to the auditorily-paced group and that in the right hemisphere to the self-paced group. Activity in the claustrum has been linked to sensorimotor integration (Edelstein and Denaro, 2004). Neuroanatomical studies have shown that the non-human primate claustrum shares reciprocal connections with structures in the frontal lobe, including the motor, premotor, and cingulate cortices; the visual cortices in the occipital lobe; the temporal cortex; the parieto-occipital and posterior parietal cortices; and somatosensory areas (Crick and Koch, 2005). A prior PET study in humans revealed involvement of the claustrum, along with the insula, in cross-modal matching tasks that require the simultaneous evaluation of information from more than one sensory domain (Hadjikhani and Roland, 1998). The results from this study, in particular, lend support to the hypothesis that the claustrum serves to combine and bind different attributes of objects, both within and across modalities. Crick and Koch (2005) further suggest that the claustrum may contain specialized mechanisms that permit information within its own extent to synchronize different perceptual, cognitive, and motor modalities. That these two different pacing modalities activated the left and right claustra separately suggest a potential segregation of sensory processing within the claustrum.

The concordance seen in bilateral insula, right inferior frontal gyrus (IFG), Brodmann's areas 18 and 37, and left posterior cerebellum, specifically Crus I (Schmahmann et al., 1999) can all be related to the processing of the visual pacing stimuli. Areas 18 and 37 are commonly associated with the processing of visual information, and activity in Crus I has been linked to visuomotor processing in the presence of frequent but not infrequent visual stimuli (Vaillancourt et al., 2006). Anatomic studies have shown that the insular cortex (BA 13) has numerous afferent and efferent connections with a diverse array of brain structures including the motor and somatosensory cortices (Augustine, 1996). With regard to its motor-related connections, researchers have suggested that the insula plays an important role as a motor association area involved in the movement of the upper limbs, including the hands (Chollet et al., 1991; Weiller et al., 1992) and in saccadic movements of the eyes (Petit et al., 1993). This region has also been shown to be involved in a variety of timing tasks including interval sequence encoding (Schubotz et al., 2000) and sensorimotor synchronization (Rubia et al., 2000). Cerasa et al. (2006) proposed that this region, along with the right IFG (BA 9), may guide the timing of sequential movements through both the internal subvocalization of the interval duration and multi-modal integration. This hypothesis is supported by observed insular and right IFG activity during both acoustically (Rao et al., 1997; Riecker et al., 2002) and visually (Cerasa et al., 2005; Penhune et al., 1998) stimulated timing tasks.

The self-paced group exhibited small clusters of concordance within the left inferior ventral premotor cortex (BA 6) and the right cerebellar pyramis (VIII–IX; Schmahmann et al., 1999). The role of the ventral premotor cortex is discussed more fully below in relation to its observed concordance for the complex finger-tapping tasks, but as it is most often associated with the execution of

visually guided movements (Kurata, 1993, 1994a; Rizzolatti et al., 1996; Debaere et al., 2003), its apparent concordance for the self-paced tapping task group represents a deviation from the accepted role of the PMv. This suggests a role of the PMv in movement beyond sensorimotor integration. There is little published about the right cerebellar pyramis, however, Rijntjes et al. (1999) provided evidence that it may be the location of a third homunculus. If this is true, it is uncertain why activation was not seen in this area for all finger-tapping task variations.

Brodmann's area 44 (frontal opercular cortex; inferior frontal gyrus) has been connected to finger movements (Binkofski et al., 1999; Harrington et al., 2000; Schlaug et al., 1994), motor imagination (Decety et al., 1994; Grafton et al., 1996; Stephan et al., 1995), motor learning (Seitz, 1992), and motor observation (Haslinger et al., 2002; Chouinard and Paus, 2006). Rao et al. (1997) found this region to be active during auditory continuation tasks, suggesting that it may play a role in the internal timing of movements. Studies have further found the right inferior frontal gyrus along with the right superior temporal gyrus form a network associated with the retrieval and rehearsal of auditory information, particularly in the absence of any external stimulus (Zatorre et al., 1996), making this network key in the subvocal rehearsal systems (Paulesu et al., 1993). Additional studies have proposed that this region, along with the lateral aspect of BA 6, forms the human ventral premotor cortex (Tomaiuolo et al., 1999). Activity in the frontal opercular and ventral premotor cortices has been linked to the learning of implicit and explicit motor sequences (Hazeltine et al., 1997; Rauch et al., 1995; Seitz, 1992) and novel visuomotor associations (Toni et al., 2001; Toni et al., 2002). In non-human primates, studies have shown that the ventral premotor cortex plays an important role during visually guided movements (Kurata and Hoffman, 1994), so its concordance for the auditorily-paced tasks – many of which are sequential tapping tasks – may have more to do with the performance of the sequential task as opposed to the modality of the pacing sequence.

The use or lack of a pacing stimulus has an effect on the network of brain regions observed to be active during finger-tapping tasks. The use of a visual stimulus requires the recruitment of a number of brain regions distinct from either the use of an auditory stimulus or no stimulus. This network includes the bilateral insula, right inferior frontal gyrus (IFG), Brodmann's areas 18 and 37, and left posterior cerebellum. The self-paced tasks appear to be more demanding than the auditorily-paced tasks, necessitating more complex cognitive control, as evidenced by observed concordance in several frontal and prefrontal regions including more lateral aspects of the premotor and parietal cortices, as well as the dorsolateral prefrontal cortex. The auditorily-paced tasks did not appear to recruit many additional regions beyond those observed in the main effects (Fig. 1). However, the observed concordance in Brodmann's Area 44 is of interest, as while in this region has previously been associated with the internal timing system, its observed concordance during the auditorily-paced tasks, suggests a role in both the internal timing system as well as the sensorimotor integration of external, auditory pacing stimuli. Taken together, these results suggest that there is a stronger distinction between the visually-paced tasks and either the auditorily- or self-paced tasks than between the auditorily- and self-paced tasks, as evidenced by greater overlap of the ALE results for the auditorily- and self-paced tasks.

Task complexity effects

Comparing the studies based on the complexity of the tapping task employed – RH index finger, RH multi-finger sequence, and

bimanual – conjunction analysis yielded common concordance in the primary sensorimotor cortex, SMA, basal ganglia, and anterior cerebellum. The concordance was contralateral to the dominant hand for the RH index finger-tapping task group in all areas except the anterior cerebellum, in which case it was bilateral. The concordance within these executive regions was bilateral for the bimanual tapping group, which was expected. It was also bilateral for the sequence tapping group, even though the majority of the studies included in this group used unimanual sequence tasks.

Concordance within the dorsal premotor cortices was again lateralized based on task variation, with the RH index finger group exhibiting bilateral clusters of concordance, the sequence group right hemispherical, and the bimanual group left hemispherical. The PMd, in addition to its afore-described role in integrating sensory information into movements, has also been shown to be involved in modulating movement frequency and complexity (Nakai et al., 2003; Debaere et al., 2004; Ullén et al., 2003). Kermadi et al. (2000) demonstrated that this region contains bimanual specific neurons, with the left PMd playing a fundamental role in the control of bimanual movements in right-handed subjects (Hlustik et al., 2002). The right PMd has been shown to play a role in the execution of motor sequences, even those performed with the dominant hand in right-handed subjects (Sadato et al., 1996a). The cluster of concordance centered on the right primary sensorimotor cortex for the sequence tapping task group extended anterior into the cortical area traditionally considered to be the PMd, supporting this conclusion. However, the only definite concordance within the right PMd was seen in the results for the RH index finger-tapping group. Since the two clusters of concordance were in similar locations to those seen for the auditorily- and visually-paced groups (and likewise with the anterior extension of the left sensorimotor cluster), their appearance in the RH index finger results may have more to do with that group's inclusion of externally paced tapping tasks, as opposed to the region's role in simple, dominant hand index finger tapping. Particularly, the location of the anterior extension of the left sensorimotor cortex into the left PMd – as discussed above for in reference to the use of pacing stimuli – is in agreement with the locus for simple movements in response to an external stimulus (Chouinard and Paus, 2006).

The clusters of concordance in the ventral aspect of the premotor cortex were located in the left hemisphere (BA 6) for the RH index finger and sequence groups; the bimanual group also exhibited a small cluster in the left hemisphere (BA 6), in addition to a larger cluster in the right hemisphere (BA 44), where the role of BA 44 in motor tasks and the PMv has been previously addressed in reference to its observed concordance for the auditorily-paced tapping task group. As stated above, the ventral premotor cortex has consistently been shown to be active during visually guided movements (Kurata, 1993, 1994a; Rizzolatti et al., 1996; Debaere et al., 2003), especially during reaching and grasping tasks (Kurata, 1994b; Kurata and Hoffman, 1994; Kurata and Hoshi, 1999; Rizzolatti et al., 1987, 1990). Fogassi et al. (1992) posited that the PMv represents a body-centered frame of reference which is involved in manipulating movement direction towards a target location. Since all of the studies used in these meta-analyses involved finger-tapping tasks, it is more likely that the observed concordance within this region supports the results of Stephan et al. (1995) who found activation within the left PMv, in particular, during the execution of upper limb movements. This suggests that PMv activity may constitute part of the normal physiologic processes during finger movement. In addition to its role in sensorimotor integration, the left PMv in particular has been

implicated speech and language production, as its extent has been shown to encompass part of Broca's region (Binkofski and Buccino, 2004), and as one of the key structures in the human mirror neuron system, demonstrating activation during observation, execution, and imitation of action (Iacoboni et al., 1999; Iacoboni and Dapretto, 2006).

As mentioned above, the inferior parietal lobe has been implicated in the performance of sequential finger movements (Jenkins et al., 1994a), confirmed by the concordance observed in the right hemisphere for the RH multi-finger sequence group. A large cluster of concordance was also observed in the right LPI for the RH index finger-tapping group, suggesting that, in addition to this region's role in sensorimotor integration and sequence performance, it may play a role in the execution of movements in general. There was also an apparent somatotopy within the right LPI, with the region controlling sequence production and performance located more anteriorly to that controlling sensorimotor integration and general movement production. Such a functional dichotomy within this region has not yet, to the best of the authors' knowledge, been reported.

The roles of the insular cortex, right inferior frontal gyrus, claustrum, and right dorsolateral prefrontal cortex have been previously discussed in terms of their roles in externally paced finger-tapping tasks. The observed concordance within these regions for the RH index finger group is more likely due to the inclusion of these studies using external pacing cues in the RH index finger-tapping task group, as opposed any specific role these regions have in simple, right hand index finger tapping. However in regards to the insular cortex, its role in movement timing would seem to suggest that this region should exhibit concordance for more than just the visually-paced studies and RH index finger studies, especially since this region is also implicated in such timing tasks as interval sequence encoding (Schubotz et al., 2000) and sensorimotor synchronization (Rubia et al., 2000). The concordance cluster within the left DLPFC, observed for the RH index finger group, cannot be fully explained, as this region has been implicated in motor preparation for imitative tasks as well as in the selection and combination of individual motor elements into new motor tasks (Buccino et al., 2004), and the RH index finger-tapping tasks employed by the studies were neither imitative nor novel.

Only the ALE maps for the RH multi-finger sequence tapping task group showed concordance within bilateral posterior parietal cortex (BA7, precuneus). Neurons in the posterior parietal cortex (PPC) have been shown to be responsive to hand manipulation and movements in extra-personal space (Mountcastle et al., 1975), and the region itself is thought of as an integrative system involved in the processing of spatial aspects of movements (Boecker et al., 1998; Sadato et al., 1996a; Roland et al., 1980a). Since finger-tapping tasks do not necessitate extensive movements in extra-personal space, the observed concordance within the PPC may suggest that this area is also involved in the temporal aspects of the task, the integration of sensory information into the movement sequence, as well as the production of movement sequences in general (Gordon et al., 1998). Studies have shown that this region, particularly the right PPC, is active during complex sequential motor tasks (Boecker et al., 1998; Jenkins et al., 1994a; Wenderoth et al., 2005; Grafton et al., 1992b). Further studies have demonstrated the role of the PPC in the integration of both auditory and visual cues into movement selection and execution (Deiber et al., 1991; Grafton et al., 1992b; Jenkins et al., 1994a). In addition to serving as a higher-order motor structure, activity within the PPC has been linked to the executive

processing of working memory, in particular, updating, order, and manipulation tasks (Wager and Smith, 2003). Further studies have also demonstrated this region to be active during memory retrieval (Buckner et al., 1996; Smith and Jonides, 1997; Krause et al., 1999; Schmidt et al., 2002; Shannon and Buckner, 2004), suggesting that activity in the posterior parietal cortex may be related to the retrieval of a memorized sequence and its translation into a plan of execution (Sakai et al., 1998) in addition to its above described role in the temporal aspects and sensory integration of movement sequences.

Concordance for the bimanual tapping task group is observed in the posterior cerebellum, vermal lobe VI/declive (Schmahmann et al., 1999). Activity in the posterior cerebellum has been most often linked to the temporal aspects of motor and visuospatial working memory tasks (Geier et al., 2007; Jantzen et al., 2007; Simmonds et al., 2007). Additionally, Habas et al. (2004b) demonstrated, specifically, that vermal lobe VI may play a role in both simple and complex bimanual movements. These results suggest that bimanual movements may require additional temporal processing compared with unimanual tasks.

Effects of tapping rate and proficiency

Although we included coordinates from studies specifically employing tapping tasks of varying rates (Aramaki et al., 2006; Blinkenberg et al., 1996; Jäncke et al., 1999; Jäncke et al., 2000a; Kawashima et al., 1999; Lehéricy et al., 2006; Riecker et al., 2006; Rounis et al., 2005), and previous studies have shown that the so called "rate effect" can have an impact on the degree of both cortical (Deiber et al., 1999; Jäncke et al., 1998; Lutz et al., 2005) and subcortical (Lutz et al., 2005) activations, it would be difficult for us to draw any conclusions regarding the effect of varying the frequency of a tapping task would have on the observed clusters of concordance. For all studies reporting a movement frequency, the frequencies ranged from 0.25 to 4 Hz (average=1.73 Hz; mode=2 Hz). There, as yet, does not appear to be a consensus as to at what frequency or frequencies of movement the rate effect becomes important (Deiber et al., 1999). Sadato et al. (1996b) found peak SMA activation at 0.5 Hz, with decreasing activation at higher frequencies. Blinkenberg et al. (1996), in contrast, found peak SMA activation at 1 Hz, with decreasing activation at higher frequencies less than 2 Hz; a second peak was reported at 4 Hz. Finally, in regards to self-paced, repetitive simple movements in young, healthy subjects, Diciotti et al. (2007) demonstrated that the rate effect did was not a relevant source of variability in fMRI signal for task frequencies ranging from 0.2 to 2 Hz. Since the average and mode frequencies of movement reported were both approximately 2 Hz, it is unlikely that the rate effect had any significant impact on the results of our meta-analyses.

Enhanced training on motor tasks has also been shown to have an effect on the level of activation observed in cortical motor structures, particularly the primary sensorimotor cortex (Jäncke et al., 2000c; Koeneke et al., 2006a,b). Prior functional neuroimaging studies have demonstrated an initial decrease in primary sensorimotor cortical activation contralateral to the moving hand during motor skill acquisition, followed by an enlargement in activation in this same region during the course of motor training, which has been shown to be sustained for up to 4 weeks post-training (Jäncke et al., 2000c). Motor skill acquisition has been suggested to occur in two discrete stages: the first being a fast learning, initial, within-session improvement phase and the second being a slow learning phase, consisting of delayed, incremental gains in performance during

continued practice (Koeneke et al., 2006a). Only one study included (Boecker et al., 1998) reported using an extended training period of 2 weeks, in an effort to allow the complex tapping sequences employed to become more automatic. Of the remaining studies who reported training (21 studies), all used training sessions just prior to scanning. Although the majority of these studies merely indicated that training had occurred, several studies did report the duration of these training sessions, which lasted from a few minutes to up to an hour. As there is no conclusive neurophysiological data demonstrating a clear effect of the first stage of motor skill learning (Koeneke et al., 2006a), the lack of consistency in reporting details on pre-scan training makes it again difficult to assess what effect, if any this may have had on our results.

Conclusions

From the results of the meta-analyses performed, it appears that the choice or lack of a pacing stimulus has a greater effect on the network of brain regions consistently reported to be active than the choice of a more complex tapping task. For all of the task variations considered, though, the additional regions reported to be active, beyond those involved in the general motor execution, seem to be involved preferentially in the temporal aspects of the tapping task. The use of a visual pacing stimulus seems to require a network of brain regions that is distinct from either that observed during the use of an auditory or no pacing stimulus. This suggests that the network of brain regions necessary to integrate a visual pacing stimulus into a simple motor task is separate from that for an auditory pacing stimulus, however, further study examining the effects of pacing stimuli on the performance of simple motor tasks is warranted. The lack of diversity in brain networks consistently reported during the two complex finger-tapping task variations examined here suggests that further complexity, such as movement in extra-personal space, may be required to fully elucidate the network of brain regions necessary to execute truly complex motor tasks.

Acknowledgments

ARL was supported by the Human Brain Project of the NIMH (R01-MH074457-01A1; PI: Peter T. Fox). STW was supported by the Vilas (William F) Trust Estate: Vilas Life Cycle Professorship and NIH (R01-CA118365-01; PI: M. Elizabeth Meyerand).

References

- Aoki, T., Tsuda, H., Takasawa, M., Osaki, Y., Oku, N., Hatazawa, J., Kinoshita, H., 2005. The effect of tapping finger and mode differences on cortical and subcortical activities: a PET study. *Exp. Brain Res.* 160, 375–383.
- Aramaki, Y., Honda, M., Okada, T., Sadato, N., 2006. Neural correlates of the spontaneous phase transition during bimanual coordination. *Cereb. Cortex* 16, 1338–1348.
- Augustine, J.R., 1996. Circuitry and functional aspects of the insular lobe in primates including humans. *Brain Res. Brain Res. Rev.* 22, 229–244.
- Binkofski, F., Buccino, G., 2004. Motor functions of the Broca's region. *Brain Lang.* 89, 362–369.
- Binkofski, F., Buccino, G., Posse, S., Seitz, R.J., Rizzolatti, G., Freund, H., 1999. A fronto-parietal circuit for object manipulation in man: evidence from an fMRI-study. *Eur. J. Neurosci.* 11, 3276–3286.
- Blinkenberg, M., Bonde, C., Holm, S., Svarer, C., Andersen, J., Paulson, O.B., Law, I., 1996. Rate dependence of regional cerebral activation during performance of a repetitive motor task: a PET study. *J. Cereb. Blood Flow Metab.* 16, 794–803.
- Boecker, H., Dagher, A., Ceballos-Baumann, A.O., Passingham, R.E., Samuel, M., Friston, K.J., Poline, J., Dettmers, C., Conrad, B., Brooks, D.J., 1998. Role of the human rostral supplementary motor area and the basal ganglia in motor sequence control: investigations with H₂ 15O PET. *J. Neurophysiol.* 79, 1070–1080.
- Brett, M., Christoff, K., Cusack, R., Lancaster, J., 2001. Using the Talairach atlas with the MNI template. *NeuroImage* 13, S85.
- Brett, M., Johnsrude, I.S., Owen, A.M., 2002. The problem of functional localization in the human brain. *Nat. Rev. Neurosci.* 3, 243–249.
- Brinkman, C., 1984. Supplementary motor area of the monkey's cerebral cortex: short- and long-term deficits after unilateral ablation and the effects of subsequent callosal section. *J. Neurosci.* 4, 918–929.
- Buccino, G., Vogt, S., Ritzl, A., Fink, G.R., Zilles, K., Freund, H.J., Rizzolatti, G., 2004. Neural circuits underlying imitation learning of hand actions: an event-related fMRI study. *Neuron* 42, 323–334.
- Buckner, R.L., Raichle, M.E., Miezin, F.M., Petersen, S.E., 1996. Functional anatomic studies of memory retrieval for auditory words and visual pictures. *J. Neurosci.* 16, 6219–6235.
- Calautti, C., Serrati, C., Baron, J.C., 2001. Effects of age on brain activation during auditory-cued thumb-to-index opposition: A positron emission tomography study. *Stroke* 32, 139–146.
- Catalan, M.J., Honda, M., Weeks, R.A., Cohen, L.G., Hallett, M., 1998. The functional neuroanatomy of simple and complex sequential finger movements: a PET study. *Brain* 121, 253–264.
- Catalan, M.J., Ishii, K., Honda, M., Samii, A., Hallett, M., 1999. A PET study of sequential finger movements of varying length in patients with Parkinson's disease. *Brain* 122, 483–495.
- Cerasa, A., Hagberg, G.E., Bianciardi, M., Sabatini, U., 2005. Visually cued motor synchronization: modulation of fMRI activation patterns by baseline condition. *Neurosci. Lett.* 373, 32–37.
- Cerasa, A., Hagberg, G.E., Peppe, A., Bianciardi, M., Gioia, M.C., Costa, A., Castriona-Scanderbeg, A., Caltagirone, C., Sabatini, U., 2006. Functional changes in the activity of cerebellum and frontostriatal regions during externally and internally timed movement in Parkinson's disease. *Brain Res. Bull.* 71, 259–269.
- Chein, J.M., Fissell, K., Jacobs, S., Fiez, J.A., 2002. Functional heterogeneity within Broca's area during verbal working memory. *Physiol. Behav.* 77, 635–639.
- Chen, Y.C., Thaler, D., Nixon, P.D., Stern, C.E., Passingham, R.E., 1995. The functions of the medial premotor cortex. II. The timing and selection of learned movements. *Exp. Brain Res.* 102, 461–473.
- Chen, R., Gerloff, C., Hallett, M., Cohen, L.G., 1997. Involvement of the ipsilateral motor cortex in finger movements of different complexities. *Ann. Neurol.* 41, 247–254.
- Chollet, F., DiPiero, V., Wise, R.J., Brooks, D.J., Dolan, R.J., Frackowiak, R.S., 1991. The functional anatomy of motor recovery after stroke in humans: a study with positron emission tomography. *Ann. Neurol.* 29, 63–71.
- Chouinard, P.A., Paus, T., 2006. The primary motor and premotor areas of the human cerebral cortex. *Neurosci.* 12, 143–152.
- Colebatch, J.G., Deiber, M.P., Passingham, R.E., Friston, K.J., Frackowiak, R.S., 1991. Region cerebral blood flow during voluntary arm and hand movements in human subjects. *J. Neurophysiol.* 65, 1392–1401.
- Crammond, D.J., Kalaska, J.F., 1996. Differential relation of discharge in primary motor cortex and premotor cortex to movements versus actively maintained postures during a reaching task. *Exp. Brain Res.* 108, 45–61.
- Crick, F.C., Koch, C., 2005. What is the function of the claustrum? *Philos. Trans. R. Soc. Lond., B Bio. Sci.* 360, 1271–1279.
- Cunnington, R., Windischberger, C., Deecke, L., Moser, E., 2002. The preparation and execution of self-initiated and externally-triggered movement: a study of event-related fMRI. *NeuroImage* 15, 373–385.
- De Luca, M., Smith, S., De Stefano, N., Federico, A., Matthews, P.M., 2005. Blood oxygenation level dependent contrast resting state networks are relevant to functional activity in the neocortical sensorimotor system. *Exp. Brain Res.* 167, 587–594.

- Debaere, F., Wenderoth, N., Sunaert, S., Van Hecke, P., Swinnen, S.P., 2003. Internal vs. external generation of movements: differential neural pathways involved in bimanual coordination performed in the presence or absence of augmented visual feedback. *NeuroImage* 19, 764–776.
- Debaere, F., Wenderoth, N., Sunaert, S., Van Hecke, P., Swinnen, S.P., 2004. Cerebellar and premotor function in bimanual coordination: parametric neural response to spatiotemporal complexity and cycling frequency. *NeuroImage* 21, 1416–1427.
- Decety, J., Perani, D., Jeannerod, M., Bettinardi, V., Tadary, B., Woods, R., Mazzotta, J.C., Fazio, F., 1994. Mapping motor representations with positron emission tomography. *Nature* 371, 600–602.
- Deiber, M.P., Passingham, R.E., Colebatch, J.G., Friston, K.J., Nixon, P.D., Frackowiak, R.S., 1991. Cortical areas and the selection of movement: a study with positron emission tomography. *Exp. Brain Res.* 84, 393–402.
- Deiber, M.P., Honda, M., Ibáñez, V., Sadato, N., Hallett, M., 1999. Mesial motor areas in self-initiated versus externally triggered movements examined with fMRI: effect of movement type and rate. *J. Neurophysiol.* 81, 3065–3077.
- Denslow, S., Lomarev, M., George, M.S., Bohning, D.E., 2005. Cortical and subcortical brain effects of transcranial magnetic stimulation (TMS)-induced movement: an interleaved TMS/functional magnetic resonance imaging study. *Biol. Psychiatry* 57, 752–760.
- Diciotti, S., Gavazzi, C., Della Nave, R., Boni, E., Ginestroni, A., Paoli, L., Cecchi, P., De Stefano, N., Mascalchi, M., 2007. Self-paced frequency of a simple motor task and brain activation: an fMRI study in healthy subjects using an on-line monitor device. *NeuroImage* 38, 402–412.
- Edelstein, L.R., Denaro, F.J., 2004. The clastrum: a historical review of its anatomy, physiology, cytochemistry and functional significance. *Cell. Mol. Biol. (Noisy-le-grand)* 50, 675–702.
- Fogassi, L., Gallesse, V., di Pellegrino, G., Fadiga, L., Gentilucci, J., Luppino, G., Matelli, M., Pedotti, A., Rizzolatti, G., 1992. Space coding by premotor cortex. *Exp. Brain Res.* 89, 686–690.
- Forss, N., Jousmaki, V., 1998. Sensorimotor integration in human primary and secondary somatosensory cortices. *Brain Res.* 781, 259–267.
- Fox, P.T., Raichle, M.E., Thach, W.T., 1985. Functional mapping of the human cerebellum with positron emission tomography. *Proc. Natl. Acad. Sci. U. S. A.* 82, 7462–7466.
- Fox, P.T., Narayana, S., Tandon, N., Sandoval, H., Fox, S.P., Kochunov, P., Lancaster, J.L., 2004. Column-based model of electric field excitation of cerebral cortex. *Hum. Brain Mapp.* 22, 1–14.
- Frith, C.D., Friston, K., Liddle, P.F., Frackowiak, R.S., 1991. Willed action and prefrontal cortex in man: a study with PET. *Proc. Biol. Sci.* 244, 241–246.
- Geier, C.F., Garver, K.E., Luna, B., 2007. Circuitry underlying temporally extended spatial working memory. *NeuroImage* 35, 904–915.
- Gelnar, P.A., Krauss, B.R., Sheehe, P.R., Szeverenyi, N.M., Apkarian, A.V., 1999. A comparative fMRI study of cortical representations for thermal painful, vibrotactile, and motor performance tasks. *NeuroImage* 10, 460–482.
- Gerardin, E., Sirigu, A., Lehéricy, S., Poline, J.B., Gaymard, B., Marsault, C., Agid, Y., Le Bihan, D., 2000. Partially overlapping neural networks for real and imagined hand movements. *Cereb. Cortex* 10, 1093–1104.
- Gerloff, C., Corwell, B., Chen, R., Hallett, M., Cohen, L.G., 1998. The role of the human motor cortex in the control of complex and simple finger movement sequences. *Brain* 121, 1695–1709.
- Godschalk, M., Lemon, R.N., Nijs, H.G., Kuypers, H.G., 1981. Behaviour of neurons in monkey peri-arcuate and precentral cortex before and during visually guided arm and hand movements. *Exp. Brain Res.* 44, 113–116.
- Goerres, G.W., Samuel, M., Jenkins, I.H., Brooks, D.J., 1998. Cerebral control of unimanual and bimanual movements: an H₂(15)O PET study. *Neuroreport* 9, 3631–3638.
- Goldberg, G., 1985. Supplementary motor area structure and function: review and hypotheses. *Behav. Brain Sci.* 8, 567–616.
- Gordon, A.M., Lee, J.H., Flament, D., Ugurbil, K., Ebner, T.J., 1998. Functional magnetic resonance imaging of motor, sensory, and posterior parietal cortical areas during performance of sequential typing movements. *Exp. Brain Res.* 121, 153–166.
- Gosain, A.K., Birn, R.M., Hyde, J.S., 2001. Localization of the cortical response to smiling using new imaging paradigms with functional magnetic resonance imaging. *Plast. Reconstr. Surg.* 108, 1136–1144.
- Grafton, S.T., Mazzotta, J.C., Woods, R.P., Phelps, M.E., 1992a. Human functional anatomy of visually guided finger movements. *Brain* 115, 565–587.
- Grafton, S.T., Mazzotta, J.C., Presky, S., Friston, K.J., Frackowiak, R.S., Phelps, M.E., 1992b. Functional anatomy of human procedural learning determined with regional cerebral blood flow and PET. *J. Neurosci.* 12, 2542–2548.
- Grafton, S.T., Woods, R.P., Tyszka, M., 1993. Functional imaging of procedural motor learning: Relating cerebral blood flow with individual subject performance. *Hum. Brain Mapp.* 1, 221–234.
- Grafton, S.T., Fagg, A.H., Woods, R.P., Arbib, M.A., 1996. Functional anatomy of pointing and grasping in humans. *Cereb. Cortex* 6, 226–237.
- Habas, C., Axelrad, H., Cabanis, E.A., 2004a. The cerebellar second homunculus remains silent during passive bimanual movements. *Neuroreport* 15, 1571–1574.
- Habas, C., Axelrad, H., Nguyen, T.H., Cabanis, E.A., 2004b. Specific neocerebellar activation during out-of-phase bimanual movements. *Neuroreport* 15, 595–599.
- Hadjikhani, N., Roland, P.E., 1998. Cross-modal transfer of information between the tactile and the visual representations in the human brain: a positron emission tomographic study. *J. Neurosci.* 18, 1072–1084.
- Halsband, U., Passingham, R.E., 1982. The role of premotor and parietal cortex in the direction of action. *Brain Res.* 240, 368–372.
- Halsband, U., Passingham, R.E., 1985. Premotor cortex and the conditions for movement in monkeys (*Macaca fascicularis*). *Behav. Brain Res.* 18, 269–277.
- Halsband, U., Ito, N., Tanji, J., Freund, H.J., 1993. The role of premotor cortex and the supplementary motor area in the temporal control of movement in man. *Brain* 116, 243–266.
- Hanakawa, T., Immisch, I., Toma, K., Dimyan, M.A., Van Gelderen, P., Hallett, M., 2003. Functional properties of brain areas associated with motor execution and imagery. *J. Neurophysiol.* 89, 989–1002.
- Harrington, D.L., Rao, S.M., Haaland, K.Y., Bobholz, J.A., Mayer, A.R., Binder, J.R., Cox, R.W., 2000. Specialized neural systems underlying representations of sequential movements. *J. Cogn. Neurosci.* 12, 56–77.
- Haslinger, B., Erhard, P., Weilke, F., Ceballos-Baumann, A.O., Bartenstein, P., von Einsiedel, H.G., Schwaiger, M., Conrad, B., Boecker, H., 2002. The role of lateral premotor-cerebellar-parietal circuits in motor sequence control: a parametric fMRI study. *Brain Res. Cogn. Brain Res.* 13, 159–168.
- Hazeltine, E., Grafton, S.T., Ivry, R., 1997. Attention and stimulus characteristics determine the locus of motor-sequence encoding. A PET study. *Brain* 120, 123–140.
- Hubl, P., Solodkin, A., Gullapalli, R.P., Noll, D.C., Small, S.L., 2002. Functional lateralization of the human premotor cortex during sequential movements. *Brain Cogn.* 49, 54–62.
- Honda, M., Deiber, M.P., Ibáñez, V., Pascual-Leone, A., Zhuang, P., Hallett, M., 1998. Dynamic cortical involvement in implicit and explicit motor sequence learning. A PET study. *Brain* 121, 2159–2173.
- Huttunen, J., Wikström, H., Korvenoja, A., Seppäläinen, A.M., Aronen, H., Ilmoniemi, R.J., 1996. Significance of the second somatosensory cortex in sensorimotor integration: enhancement of sensory responses during finger movements. *NeuroReport* 7, 1009–1012.
- Iacoboni, M., Dapretto, M., 2006. The mirror neuron system and the consequence of its dysfunction. *Nat. Rev. Neurosci.* 7, 942–951.
- Iacoboni, M., Woods, R.P., Brass, M., Bekkering, H., Mazzotta, J.C., Rizzolatti, G., 1999. Cortical mechanisms of human imitation. *Science* 286, 2526–2528.
- Immisch, I., Walvgogel, D., van Gelderen, P., Hallett, M., 2001. The role of the medial wall and its anatomical variations for bimanual antiphase and in-phase movements. *NeuroImage* 14, 674–684.
- Indovina, I., Sanes, J.N., 2001. Combined visual attention and finger movement effects on human brain representations. *Exp. Brain Res.* 140, 265–279.

- Jahanshahi, M., Jenkins, I.H., Brown, R.G., Marsden, C.D., Passingham, R.E., Brooks, D.J., 1995. Self-initiated versus externally triggered movements. I. An investigation using measurement of regional cerebral blood flow with PET and movement-related potentials in normal and Parkinson's disease subjects. *Brain* 118, 913–933.
- Jantzen, K.J., Oullier, O., Marshall, M., Steinberg, F.L., Kelso, J.A.S., 2007. A parametric fMRI investigation of context effects in sensorimotor timing and coordination. *Neuropsychologia* 45, 673–684.
- Jäncke, L., Specht, K., Mirzazade, S., Loose, R., Himmelbach, M., Lutz, K., Shah, N.J., 1998. A parametric analysis of the 'rate effect' in the sensorimotor cortex: a functional magnetic resonance imaging analysis in human subjects. *Neurosci. Lett.* 252, 37–40.
- Jäncke, L., Specht, K., Mirzazade, S., Peters, M., 1999. The effect of finger-movement speed of the dominant and the subdominant hand on cerebellar activation: a functional magnetic resonance imaging study. *NeuroImage* 9, 497–507.
- Jäncke, L., Peters, M., Himmelbach, M., Nösselt, T., Shah, J., Steimetz, H., 2000a. fMRI study of bimanual coordination. *Neuropsychologia* 38, 164–174.
- Jäncke, L., Loose, R., Lutz, K., Specht, K., Shah, N.J., 2000b. Cortical activations during paced finger-tapping applying visual and auditory pacing stimuli. *Brain Res. Cogn. Brain Res.* 10, 51–66.
- Jäncke, L., Shah, N.J., Peters, M., 2000c. Cortical activations in primary and secondary motor areas for complex bimanual movements in professional pianists. *Cogn. Brain Res.* 10, 177–183.
- Jenkins, I.H., Brooks, D.J., Nixon, P.D., Frackowiak, R.S., Passingham, R.E., 1994a. Motor sequence learning: a study with positron emission tomography. *J. Neurosci.* 14, 3775–3790.
- Jenkins, I.H., Jahanshahi, M., Brown, R., Frackowiak, R.S.J., Marsden, C.D., Passingham, R.E., Brooks, D.J., 1994b. Impaired activation of mesial frontal-cortex during self-paced movements in Parkinsons-disease. *Neurology* 44, A353.
- Johnson, P.B., Ferraina, S., Bianchi, L., Caminti, R., 1996. Cortical networks for visual reaching: physiological and anatomical organization of frontal and parietal lobe arm regions. *Cereb. Cortex* 6, 102–119.
- Joliot, M., Crivello, F., Badier, J.M., Diallo, B., Tzourio, N., Mazoyer, B., 1998. Anatomical congruence of metabolic and electromagnetic activation signals during a self-paced motor task: a combined PET-MEG study. *NeuroImage* 7, 337–351.
- Joliot, M., Papathanassiou, D., Mellet, E., Quinton, O., Mazoyer, N., Courtheoux, P., Mazoyer, B., 1999. FMRI and PET of self-paced finger movement: comparison of intersubject stereotaxic averaged data. *NeuroImage* 10, 430–447.
- Jueptner, M., Frith, C.D., Brooks, D.J., Frackowiak, R.S., Passingham, R.E., 1997. Anatomy of motor learning. II. Subcortical structures and learning by trial and error. *J. Neurophysiol.* 77, 1325–1337.
- Kawashima, R., Fukuda, H., 1994. Functional organization of the human primary motor area: an update on current concepts. *Rev. Neurosci.* 5, 347–354.
- Kawashima, R., Roland, P.E., O'Sullivan, B.T., 1994. Activity in the human primary motor cortex related to ipsilateral hand movements. *Brain Res.* 663, 251–256.
- Kawashima, R., Yamada, K., Kinomura, S., Yamaguchi, T., Matsui, H., Yoshioka, S., Fukuda, H., 1993. Regional cerebral blood flow changes of cortical motor areas and prefrontal areas in humans related to ipsilateral and contralateral hand movement. *Brain Res.* 623, 33–40.
- Kawashima, R., Roland, P.E., O'Sullivan, B.T., 1995. Functional anatomy of reaching and visuomotor learning: a positron emission tomography study. *Cereb. Cortex* 5, 111–122.
- Kawashima, R., Inoue, K., Sugiura, M., Okada, K., Ogawa, A., Fukuda, H., 1999. A positron emission tomography study of self-paced finger movements at difference frequencies. *Neuroscience* 92, 107–112.
- Kawashima, R., Okuda, J., Umetsu, A., Sugiura, M., Inoue, K., Suzuki, K., Tabuchi, M., Tsukiura, T., Narayan, S.L., Nagasaka, T., Yanagawa, I., Fujii, T., Takahashi, S., Fukuda, H., Yamadori, A., 2000. Human cerebellum plays an important role in memory-timed finger movement: an fMRI study. *J. Neurophysiol.* 83, 1079–1087.
- Kermadi, I., Liu, Y., Rouiller, E.M., 2000. Do bimanual motor actions involve the dorsal premotor (PMd), cingulated (CMA) and posterior parietal (PPC) cortices? Comparison with primary and supplementary motor cortical areas. *Somatos. Mot. Res.* 17, 255–271.
- Kim, S.G., Ashe, J., Georgopoulos, A.P., Merkle, H., Ellermann, J.M., Menon, R.S., Ogawa, S., Ugurbil, K., 1993a. Functional imaging of human motor cortex at high magnetic field. *J. Neurophysiol.* 69, 297–302.
- Kim, S.G., Ashe, J., Hendrich, K., Ellermann, J.M., Merkle, H., Ugurbil, K., Georgopoulos, A.P., 1993b. Functional magnetic resonance imaging of motor cortex: hemispheric asymmetry and handedness. *Science* 261, 615–617.
- Koeneke, S., Lutz, K., Herwig, U., Ziemann, U., Jäncke, L., 2006a. Extensive training of elementary finger tapping movements changes the pattern of motor cortex excitability. *Exp. Brain Res.* 174, 199–209.
- Koeneke, S., Lutz, K., Esslen, M., Jäncke, L., 2006b. How finger tapping practice enhances efficiency of motor control. *NeuroReport* 17, 1565–1569.
- Krause, B.J., Schmidt, D., Mottaghay, F.M., Taylor, J., Halsband, U., Herzog, H., Tellmann, L., Müller-Gärtner, H.W., 1999. Episodic retrieval activates the precuneus irrespective of the imagery content of word pair associates. A PET study. *Brain* 122, 255–263.
- Kuhtz-Buschbeck, J.P., Mahnkopf, C., Holzknecht, C., Siebner, H., Ulmer, S., Jansen, O., 2003. Effector-independent representations of simple and complex imagined finger movements: a combined fMRI and TMS study. *Eur. J. Neurosci.* 18, 3375–3387.
- Kurata, K., 1993. Premotor cortex of monkeys: set- and movement-related activity reflecting amplitude and direction of wrist movements. *J. Neurophysiol.* 69, 187–200.
- Kurata, K., 1994a. Information processing for motor control in primate premotor cortex. *Behav. Brain Res.* 61, 135–142.
- Kurata, K., 1994b. Site of origin of projections from the thalamus to dorsal versus ventral aspects of the premotor cortex of monkeys. *Neurosci. Res.* 21, 71–76.
- Kurata, K., Hoffman, D.S., 1994. Differential effects of muscimol microinjection into dorsal and ventral aspects of the premotor cortex of monkeys. *J. Neurophysiol.* 71, 1151–1164.
- Kurata, K., Hoshi, E., 1999. Reacquisition deficits in prism adaptation after muscimol microinjection into the ventral premotor cortex of monkeys. *J. Neurophysiol.* 81, 1927–1938.
- Laird, A.R., Fox, P.M., Price, C.J., Glahn, D.C., Uecker, A.M., Lancaster, J.L., Turkeltaub, P.E., Kochunov, P., Fox, P.T., 2005. ALE meta-analysis: controlling the false discovery rate and performing statistical contrasts. *Hum. Brain Mapp.* 25, 155–164.
- Lancaster, J.L., Tordesillas-Gutiérrez, D., Martinez, M., Salinas, F., Evans, A., Zilles, K., Mazziotta, J.C., Fox, P.T., 2007. Bias between MNI and Talairach coordinates analyzed using the ICBM-152 brain template. *Hum. Brain Mapp.* 28, 1194–1205.
- Larsson, J., Gulyás, B., Roland, P.E., 1996. Cortical representation of self-paced finger movement. *Neuroreport* 7, 463–468.
- Lehéricy, S., van de Moortele, P.F., Lobel, E., Paradis, A.L., Vidailhet, M., Frouin, V., Neveu, P., Agid, Y., Marsault, C., Le Bihan, D., 1998. Somatotopical organization of striatal activation during finger and toe movement: a 3-T functional magnetic resonance imaging study. *Ann. Neurol.* 44, 398–404.
- Lehéricy, S., Bardinet, E., Tremblay, L., van de Moortele, P.F., Pochon, J.B., Dormont, D., Kim, D.S., Yelnik, J., Ugurbil, K., 2006. Motor control in basal ganglia circuits using fMRI and brain atlas approaches. *Cereb. Cortex* 16, 149–161.
- Lerner, A., Shill, H., Hanakawa, T., Bushara, K., Goldfine, A., Hallett, M., 2004. Regional cerebral blood flow correlates of the severity of writer's cramp symptoms. *NeuroImage* 21, 904–913.
- Lin, Y.Y., Forss, N., 2002. Functional characterization of human second somatosensory cortex by magnetoencephalography. *Behav. Brain Res.* 135, 141–145.
- Lutz, K., Specht, K., Shah, N.J., Jäncke, L., 2000. Tapping movements according to regular and irregular visual timing signals investigated with fMRI. *NeuroReport* 11, 1301–1306.

- Lutz, K., Koeneke, S., Wüstenberg, T., Jäncke, L., 2005. Asymmetry of cortical activation during maximum and convenient tapping speed. *Neurosci. Lett.* 373, 61–66.
- Maillard, L., Ishii, K., Bushara, K., Waldvogel, D., Schulman, A.E., Hallett, M., 2000. Mapping the basal ganglia: fMRI evidence for somatotopic representation of face, hand, and foot. *Neurology* 55, 377–383.
- Matelli, M., Rizzolatti, G., Bettinardi, V., Gilardi, M.C., Perani, D., Rizzo, G., Fazio, F., 1993. Activation of precentral and mesial motor areas during the execution of elementary proximal and distal arm movements: a PET study. *Neuroreport* 4, 1295–1298.
- Mattay, V.S., Callicott, J.H., Bertolino, A., Santha, A.K., Van Horn, J.D., Tallent, K.A., Frank, J.A., Weinberger, D.R., 1998. Hemispheric control of motor function: a whole brain echo planar fMRI study. *Psychiatry Res.* 83, 7–22.
- Menon, V., Glover, G.H., Pfefferbaum, A., 1998. Differential activation of dorsal basal ganglia during externally and self paced sequences of arm movements. *NeuroReport* 9, 1567–1573.
- Meyer-Lindenberg, A., Ziemann, U., Hajak, G., Cohen, L., Berman, K.F., 2002. Transitions between dynamical states of differing stability in the human brain. *Proc. Natl. Acad. Sci. U. S. A.* 99, 10948–10953.
- Middleton, F.A., Strick, P.L., 2000. Basal ganglia and cerebellar loops: motor and cognitive circuits. *Brain Res. Brain Res. Rev.* 31, 236–250.
- Mountcastle, V.B., Lynch, J.C., Georgopoulos, A., Sakata, H., Acuna, C., 1975. Posterior parietal association cortex of the monkey: command functions for operations within extrapersonal space. *J. Neurophysiol.* 38, 871–908.
- Mushiake, H., Inase, M., Tanji, J., 1990. Selective coding of motor sequence in the supplementary motor area of the monkey cerebral cortex. *Exp. Brain Res.* 82, 208–210.
- Mushiake, H., Inase, M., Tanji, J., 1991. Neuronal activity in the primate premotor, supplementary, and precentral motor cortex during visually guided and internally determined sequential movements. *J. Neurophysiol.* 66, 705–718.
- Müller, J.L., Röder, C.H., Schuierer, G., Klein, H., 2002. Motor-induced brain activation in cortical, subcortical and cerebellar regions in schizophrenic inpatients. A whole brain fMRI fingertapping study. *Prog. Neuro-psychopharmacol. Biol. Psychiatry* 26, 421–426.
- Nakai, T., Kato, C., Glover, G.H., Toma, K., Moriya, T., Matsuo, K., 2003. A functional magnetic resonance imaging study of internal modulation of an external visual cue for motor execution. *Brain Res.* 968, 238–247.
- Orgogozo, J.M., Larsen, B., 1979. Activation of the supplementary motor area during voluntary movement in man suggests it works as a supramotor area. *Science* 206, 847–850.
- Pardo, J.V., Fox, P.T., Raichle, M.E., 1991. Localization of a human system for sustained attention by positron emission tomography. *Nature* 349, 61–64.
- Passingham, R.E., 1985. Premotor cortex: sensory cues and movement. *Behav. Brain Res.* 18, 175–185.
- Paulesu, E., Frith, C.D., Frackowiak, R.S., 1993. The neural correlates of the verbal component of working memory. *Nature* 362, 342–345.
- Penhune, V.B., Zattore, R.J., Evans, A.C., 1998. Cerebellar contributions to motor timing: a PET study of auditory and visual rhythm reproduction. *J. Cogn. Neurosci.* 10, 752–765.
- Petit, L., Orssaud, C., Tzourio, N., Salamon, G., Mazoyer, B., Berthoz, A., 1993. PET study of voluntary saccadic eye movements in humans: basal ganglia-thalamocortical system and cingulated cortex involvement. *J. Neurophysiol.* 69, 1009–1017.
- Petrides, M., 1982. Motor conditional associative-learning after selective prefrontal lesions in the monkey. *Behav. Brain Res.* 5, 407–413.
- Petrides, M., 1985. Deficits in non-spatial conditional associated learning after periarculate lesions in the monkey. *Behav. Brain Res.* 1985, 95–101.
- Playford, E.D., Jenkins, I.H., Passingham, R.E., Nutt, J., Frackowiak, R.S., Brooks, D.J., 1992. Impaired mesial frontal and putamen activation in Parkinson's disease: a positron emission tomography study. *Ann. Neurol.* 32, 151–161.
- Ramsey, N.F., Kirkby, B.S., van Gelderen, P., Berman, K.F., Duyn, J.H., Frank, J.A., Mattay, V.S., Van Horn, J.D., Esposito, G., Moonen, C.T., Weinberger, D.R., 1996. Functional mapping of human sensorimotor cortex with 3D BOLD fMRI correlates highly with H₂(15)O PET rCBF. *J. Cereb. Blood Flow Metab.* 16, 755–764.
- Rao, S.M., Binder, J.R., Bandettini, P.A., Hammek, T.A., Yetkin, F.Z., Jesmanowicz, A., Lisk, L.M., Morris, G.L., Mueller, W.M., Estkowski, L.D., 1993. Functional magnetic resonance imaging of complex human movements. *Neurology* 43, 2311–2318.
- Rao, S.M., Harrington, D.L., Haaland, K.Y., Bobholz, J.A., Cox, R.W., Binder, J.R., 1997. Distributed neural systems underlying the timing of movements. *J. Neurosci.* 17, 5528–5535.
- Rao, S.M., Mayer, A.R., Harrington, D.L., 2001. The evolution of brain activation during temporal processing. *Nat. Neurosci.* 4, 317–323.
- Rauch, S.L., Savage, C.R., Brown, H.D., Curran, T., Alpert, N.M., Kendrick, A., Fischman, A.J., Kosslyn, S.M., 1995. A PET investigation of implicit and explicit sequence learning. *Hum. Brain Mapp.* 3, 271–286.
- Riecker, A., Wildgruber, D., Dogil, G., Grodd, W., Ackermann, H., 2002. Hemispheric lateralization effects of rhythm implementation during syllable repetitions: an fMRI study. *NeuroImage* 16, 169–176.
- Riecker, A., Gröschel, K., Ackermann, H., Steinbrink, C., Witte, O., Kastrup, A., 2006. Functional significance of age-related differences in motor activation patterns. *NeuroImage* 32, 1345–1354.
- Rijntjes, M., Dettmers, C., Büchel, C., Kiebel, S., Frackowiak, R.S., Weiller, C., 1999. A blueprint for movement: functional and anatomical representations in the human motor system. *J. Neurosci.* 19, 8043–8048.
- Rizzolatti, G., Gentilucci, M., Fogassi, L., Luppino, G., Matelli, M., Ponzo, S., 1987. Neurons related to goal-directed motor acts in inferior act 6 of the macaque monkey. *Exp. Brain Res.* 67, 220–224.
- Rizzolatti, G., Gentilucci, M., Camarda, R.M., Gallese, V., Luppino, G., Metelli, M., Fogassi, L., 1990. Neurons related to reaching-grasping arm movements in the rostral part of 6 (area 6a beta). *Exp. Brain Res.* 82, 337–350.
- Rizzolatti, G., Fadiga, L., Gallese, V., Fogassi, L., 1996. Premotor cortex and the recognition of motor actions. *Brain Res. Cogn. Brain Res.* 3, 1131–1141.
- Roland, P.E., 1984. Organization of motor control by the normal human brain. *Hum. Neurobiol.* 2, 205–216.
- Roland, P.E., Skinhøj, E., Lassen, N.A., Larsen, B., 1980a. Different cortical areas in man in organization of voluntary movements in extrapersonal space. *J. Neurophysiol.* 43, 137–150.
- Roland, P.E., Larsen, B., Lassen, N.A., Skinhøj, E., 1980b. Supplementary motor area and other cortical areas in organization of voluntary movements in man. *J. Neurophysiol.* 43, 118–136.
- Roland, P.E., Meyer, E., Shibasaki, T., Yamamoto, Y.L., Thompson, C.J., 1982. Region cerebral blood flow changes in cortex and basal ganglia during voluntary movements in normal human volunteers. *J. Neurophysiol.* 48, 467–480.
- Roland, P.E., Eriksson, L., Widén, L., Stone-Elander, S., 1989. Changes in regional cerebral oxidative metabolism induced by tactile learning and recognition in man. *Eur. J. Neurosci.* 1, 3–18.
- Romo, R., Schultz, W., 1987. Neuronal activity preceding self-initiated or externally timed arm movements in area 6 of monkey cortex. *Exp. Brain Res.* 67, 656–662.
- Rounis, E., Lee, L., Siebner, H.R., Rowe, J.B., Friston, K.J., Rothwell, J.C., Frackowiak, R.S.J., 2005. *NeuroImage* 26, 164–176.
- Rubia, K., Overmeyer, S., Taylor, E., Brammer, M., Williams, S.C., Simmons, A., Andrew, C., Bullmore, E.T., 2000. Functional frontalisatation with age: mapping neurodevelopmental trajectories with fMRI. *Neurosci. Biobehav. Rev.* 24, 13–19.
- Sadato, N., Zeffl, T.A., Campbell, G., Konishi, J., Shibasaki, H., Hallett, M., 1995. Regional cerebral blood flow changes in motor cortical areas after transient anesthesia of the forearm. *Ann. Neurol.* 37, 74–81.
- Sadato, N., Campbell, G., Ibáñez, V., Deiber, M., Hallett, M., 1996a. Complexity affects regional cerebral blood flow change during sequential finger movements. *J. Neurosci.* 16, 2691–2700.
- Sadato, N., Ibáñez, V., Deiber, M.P., Campbell, G., Leonardo, M., Hallett, M., 1996b. Frequency-dependent changes in regional cerebral blood flow during finger movements. *J. Cereb. Blood Flow Metab.* 16, 23–33.

- Sadato, N., Yonekura, Y., Waki, A., Yamada, H., Ishii, Y., 1997. Role of the supplementary motor area and the right premotor cortex in the coordination of bimanual finger movements. *J. Neurosci.* 17, 9667–9674.
- Sakai, K., Hikosaka, O., Miyauchi, S., Takino, R., Sasaki, Y., Pütz, B., 1998. Transition of brain activation from frontal to parietal areas in visuomotor sequence learning. *J. Neurosci.* 18, 1827–1840.
- Samuel, M., Ceballos-Baumann, A.O., Blin, J., Uema, T., Boecker, H., Passingham, R.E., Brooks, D.J., 1997. Evidence for lateral premotor and parietal overactivity in Parkinson's disease during sequential and bimanual movements. A PET study. *Brain* 120, 963–976.
- Schlaug, G., Knott, U., Seitz, R., 1994. Inter-subject variability of cerebral activations in acquiring a motor skill: a study with positron emission tomography. *Exp. Brain Res.* 98, 523–534.
- Schmahmann, J.D., Doyon, J., McDonald, D., Holmes, C., Lavoie, K., Hurwitz, A.S., Kabani, N., Toga, A., Evans, A., Petrides, M., 1999. Three-dimensional MRI atlas of the human cerebellum in proportional stereotaxic space. *NeuroImage* 10, 233–260.
- Schmidt, D., Krause, B.J., Mottaghy, F.M., Halsband, U., Herzog, H., Tellmann, L., Müller-Gärtner, H.W., 2002. Brain systems engaged in encoding and retrieval of word-pair associates independent of their imagery content or presentation modalities. *Neuropsychologia* 40, 457–470.
- Schubotz, R.I., von Cramon, D.Y., 2003. Functional-anatomical concepts of human premotor cortex: evidence from fMRI and PET studies. *NeuroImage* 20, S5120–S5131.
- Schubotz, R.I., Friederici, A.D., von Cramon, D.Y., 2000. Time perception and motor timing: a common cortical and subcortical basis revealed by fMRI. *NeuroImage* 11, 1–12.
- Seitz, R.J., 1992. Learning of sequential finger movements in man: a combined kinematic and positron emission tomography (PET) study. *Eur. J. Neurosci.* 4, 154–165.
- Seitz, R.J., Roland, E., Bohm, C., Greitz, T., Stone-Elander, S., 1990. Motor learning in man: a positron emission tomographic study. *Neuroreport* 1, 57–60.
- Seitz, R.J., Stephan, K.M., Binkofski, F., 2000. Control of action as mediated by the human frontal lobe. *Exp. Brain Res.* 133, 71–80.
- Shannon, B.J., Buckner, R.L., 2004. Functional-anatomic correlates of memory retrieval that suggest nontraditional processing roles for multiple distinct regions within posterior parietal cortex. *J. Neurosci.* 24, 10084–10092.
- Shibasaki, H., Sadato, N., Lyshkov, H., Yonekura, Y., Honda, M., Nagamine, T., Suwazono, S., Magata, Y., Ikeda, A., Miyazaki, M., 1993. Both primary motor cortex and supplementary area play an important role in complex finger movement. *Brain* 116, 1387–1398.
- Simmonds, D.J., Fotedar, S.G., Suskauer, S.J., Pekar, J.J., Denckla, M.B., Mostofsky, S.H., 2007. Functional brain correlates of response time variability in children. *Neuropsychologia* 45, 2147–2157.
- Smith, E.E., Jonides, J., 1997. Working memory: a view from neuroimaging. *Cogn. Psychol.* 33, 5–42.
- Stephan, K.M., Fink, G.R., Passingham, R.E., Silbersweig, D., Ceballos-Baumann, A.O., Frith, C.D., Frackowiak, R.S., 1995. Functional anatomy of the mental representation of upper extremity movements in healthy subjects. *J. Neurophysiol.* 73, 373–386.
- Stephan, K.M., Binkofski, F., Halsband, U., Dohle, C., Wunderlich, G., Schnitzler, A., Tass, P., Posse, S., Herzog, H., Surm, V., Zilles, K., Seitz, R.J., Freund, H.J., 1999a. The role of ventral medial wall motor areas in bimanual coordination. A combined lesion and activation study. *Brain* 122, 351–368.
- Stephan, K.M., Binkofski, F., Posse, S., Seitz, R.J., Freund, H.J., 1999b. Cerebral midline structures in bimanual coordination. *Exp. Brain Res.* 128, 243–249.
- Taniwaki, T., Okayama, A., Yoshiura, T., Nakamura, Y., Goto, Y., Kira, J., Tobiomatsu, S., 2003. Reappraisal of the motor role of basal ganglia: a functional magnetic resonance image study. *J. Neurosci.* 23, 3432–3438.
- Tanji, J., 1994. The supplementary motor area in the cerebral cortex. *Neurosci. Res.* 19, 251–268.
- Tanji, J., Shima, K., 1994. Role for supplementary motor area cells in planning several movements ahead. *Nature* 371, 413–416.
- Tanji, J., Shima, K., 1996. Contrast of neuronal activity between the supplementary motor area and other cortical motor areas. In: Lüders, H.O. (Ed.), *Advances in Neurology. Supplementary Sensorimotor Area*. Lippincott-Raven, Philadelphia, pp. 95–103.
- Thaut, M.H., 2003. Neural basis of rhythmic timing networks in the human brain. *Ann. N.Y. Acad. Sci.* 999, 364–373.
- Tomaiauolo, F., MacDonald, D., Caramanos, Z., Posner, G., Chiavaras, M., Evans, A.C., Petridis, M., 1999. Morphology, morphometry and probability mapping of the pars opercularis of the inferior frontal gyrus: an in vivo MRI analysis. 1999. *Eur. J. Neurosci.* 11, 3033–3046.
- Toni, I., Ramnani, H., Josephs, O., Ashburner, J., Passingham, R.E., 2001. Learning arbitrary visuomotor association: temporal dynamic of brain activity. *NeuroImage* 14, 1048–1057.
- Toni, I., Rowe, J., Stephan, K.E., Passingham, R.E., 2002. Changes of cortico-striatal effect connectivity during visuomotor learning. *Cereb. Cortex* 12, 1040–1047.
- Toyokura, M., Muro, I., Komiya, T., Obara, M., 1999. Relation of bimanual coordination to activation in the sensorimotor cortex and supplementary motor area: analysis using functional magnetic resonance imaging. *Brain Res. Bull.* 48, 211–217.
- Toyokura, M., Muro, I., Komiya, T., Obara, M., 2002. 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* 12, 172–178.
- Turkeltaub, P.E., Eden, G.F., Jones, K.M., Zeffiro, T.A., 2002. Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. *NeuroImage* 16, 765–780.
- Ullén, F., Forssberg, H., Ehrsson, H.H., 2003. Neural networks for the coordination of the hands in time. *J. Neurophysiol.* 89, 1126–1135.
- Vaillancourt, D.E., Mayka, M.A., Corcos, D.M., 2006. Intermittent visuomotor processing in the human cerebellum, parietal cortex, and premotor cortex. *J. Neurophysiol.* 95, 922–931.
- Wager, T.D., Smith, E.E., 2003. Neuroimaging studies of working memory: a meta-analysis. *Cogn. Affect. Behav. Neurosci.* 3, 255–274.
- Weeks, R.A., Honda, M., Catalan, M.J., Hallett, M., 2001. Comparison of auditory, somatosensory, and visually instructed and internally generated finger movements: a PET study. *NeuroImage* 14, 219–230.
- Weiller, C., Chollet, F., Friston, K.J., Wise, R.J., Frackowiak, R.S., 1992. Functional reorganization of the brain in recovery from striatocapsular infarction in man. *Ann. Neurol.* 31, 463–472.
- Wenderoth, N., Debaere, F., Sunaert, S., Swinnen, S.P., 2005. The role of anterior cingulate cortex and precuneus in the coordination of motor behaviour. *Eur. J. Neurosci.* 22, 235–246.
- Wilson, S.M., Saygin, A.P., Sereno, M.I., Iacoboni, M., 2004. Listening to speech activates motor areas involved in speech production. *Nature Neuroscience* 7, 701–702.
- Wise, S.P., Boussaoud, D., Johnson, P.B., Caminiti, R., 1997. Premotor and parietal cortex: corticocortical connectivity and combinatorial computations. *Ann. Rev. Neurosci.* 20, 25–42.
- Yoo, S.S., Wei, X., Dickey, C.C., Guttmann, C.R., Panych, L.P., 2005. Long-term reproducibility analysis of fMRI using hand motor task. *Int. J. Neurosci.* 115, 55–77.
- Zatorre, R.J., Halpern, A.R., Perry, D.W., Meyer, E., Evans, A.C., 1996. Hearing in the mind's ear: a PET investigation of musical imagery and perception. *J. Cogn. Neurosci.*, 8, 29–46.