


Functional Brain Changes Following Cognitive and Motor Skills Training: A Quantitative Meta-analysis

Neurorehabilitation and
Neural Repair
27(3) 187–199
© The Author(s) 2013
Reprints and permission: <http://www.sagepub.com/journalsPermissions.nav>
DOI: 10.1177/1545968312461718
<http://nnr.sagepub.com>


Ronak Patel, MA¹, R. Nathan Spreng, PhD², and Gary R. Turner, PhD^{3,4}

Abstract

Background. Functional neuroimaging is increasingly used in rehabilitation research to map the neural mechanisms subserving training targets. These data can inform intervention design and improve evaluation of treatment outcomes. Reliable neural markers may provide standard metrics of treatment impact and allow consideration of behavioral outcomes in the context of functional brain changes. **Objective.** To identify common patterns of functional brain changes associated with training across a diverse range of intervention protocols. Reliable brain changes could inform development of candidate neural markers to guide intervention research. **Methods.** Taking a quantitative meta-analytic approach, we review the functional neuroimaging studies of cognitive and motor skills training interventions in healthy young adults ($N = 38$). **Results.** Reliable decreases in functional brain activity from pretraining to posttraining were observed in brain regions commonly associated with cognitive control processes, including lateral prefrontal, left anterior inferior parietal lobule, and dorsal anterior cingulate cortex. Training-related increases were observed in the medial prefrontal cortex and posterior cingulate and angular gyrus, core regions of the default network. Activity within the subcortical striatum also showed reliable increases pretraining to posttraining. **Conclusions.** These data suggest that altered engagement of large-scale, spatially distributed cortical brain networks and subcortical striatal brain regions may serve as candidate neural markers of training interventions. The development of reliable metrics based on activity and functional connectivity among large-scale brain networks may prove fruitful in identifying interactions between domain-general and -specific changes in brain activity that affect behavioral outcomes.

Keywords

meta-analysis, default mode, dorsal attention, frontoparietal control, network, neuroimaging, training

Introduction

Functional brain data are increasingly used to inform rehabilitation research, with early evidence suggesting a role for neuroimaging in the design and evaluation of more targeted intervention protocols.¹ Studies of functional brain changes associated with training intervention vary widely with respect to training design (eg, repeated practice, guided skill learning, problem-solving techniques) and targeted behavior (eg, motor skills, cognition, and sensory-perceptual abilities). As a result, the neural basis of training-related performance gains is typically characterized as patterns of functional changes in localized brain regions known to be engaged by the training target.² Variability across studies and training methods pose a significant challenge for identifying broadly applicable and reliable neural markers of training. The purpose of the current meta-analysis is to investigate whether common patterns of functional brain changes may be associated with cognitive and motor skills

training across a diverse range of intervention protocols. If reliable patterns emerge, this would provide preliminary evidence for overlapping neural mechanisms subserving training-related performance gains and inform the development of reliable metrics for measuring functional brain changes. Such domain-general markers would complement intervention- or domain-specific markers to better elucidate large-scale and localized functional brain changes associated with training across a wide array of training and rehabilitation interventions.

¹Ryerson University, Toronto, ON, Canada

²Cornell University, Ithaca, NY, USA

³York University, Toronto, ON, Canada

⁴Sunnybrook Health Sciences Centre, Toronto, ON, Canada

Corresponding Author:

Gary R. Turner, PhD, Department of Psychology, York University, 4700 Keele Street, Toronto, ON M3J 1P3, Canada
Email: gturner.ca@gmail.com

Although several qualitative reviews of studies examining functional brain changes associated with training have been published,²⁻⁸ we are aware of only 1 review⁹ that has used quantitative meta-analytic methods. Previous reviews have revealed both increases and decreases in activity across multiple, spatially distributed brain regions; however, there is mounting evidence for more global or domain-general brain changes. Kelly and Garavan² reported that patterns of functional brain change differed for motor versus cognitive training interventions. They observed activation decreases in executive control and attention-related areas (prefrontal cortex [PFC], anterior cingulate cortex [ACC], and posterior parietal cortex) in the initial stages of motor-related training, whereas later stages of training (ie, well-learned motor behavior) were associated with increases or “expansions” in motor/sensory areas (eg, primary motor cortex, the supplementary motor area [SMA], and the basal ganglia). In contrast, cognitive training was associated with a general pattern of activation decreases across a more distributed network of brain regions. Indeed, posttraining decreases in activation have been consistently emphasized as a neural marker for well-automated or highly trained performance.^{2,10} The “scaffolding framework” put forth by Peterson et al¹¹ proposes that early learning is supported by a set of regions that come online to support novel task demands. After extensive practice, these scaffolding regions disengage, whereas a set of different regions are recruited to store representations of the trained skill.¹¹ Posttraining decreases have been reliably observed in prefrontal and other attention-related regions across both motor and cognitive domains, suggesting that these regions provide important control resources to support novel and effortful performance (see Chein and Schneider⁹).

More recent qualitative reviews^{3,4,6} suggest that there may be less of a divergence between patterns of functional brain change across motor and cognitive training interventions. Within the motor domain, Doyon et al⁴ posited that 2 pathways—a corticostriatal and corticocerebellar pathway—contribute to the early acquisition of motor skills. Together, these pathways engage the striatum, cerebellum, and motor cortical regions (eg, primary motor cortex, SMA, pre-SMA) as well as the PFC, parietal cortex, and the hippocampus during initial learning. As task performance reaches asymptotic levels, activity in the corticocerebellum pathway—typically associated with intentional motor skill acquisition—decreases, whereas activity in the striatum (caudate/putamen) remains steady, suggesting that the striatum may be critical for long-term retention of well-learned motor sequences. Similarly, Dahlin et al³ reported that working memory training led to decreases in cortical areas typically related to working memory and attention (eg, frontal and parietal regions) and increases in the subcortical striatum. These data suggest that for both motor and cognitive training, there is lesser involvement of control-related

cortical areas (eg, PFC) and an increase in the recruitment of subcortical striatum as training progresses.

Quantitative evidence for more domain-general or global patterns of neural change associated with training was also reported by Chein and Schneider,⁹ who developed in-house quantitative methods to analyze brain imaging findings from 29 training studies. The authors contrasted activation maps showing training-related increases and decreases across both motor and cognitive domains. Training was associated with decreases across a broad network of regions implicated in executive and attentional control, whereas increases were limited primarily to posterior brain regions. Unlike these other reviews, training-related changes in the subcortical striatum were not reported. However, a majority of studies reviewed by Chen and Schneider contrasted “trained” versus “untrained” conditions during scanning; thus, training-related differences may have been at least partially obscured by differences in task characteristics.

Recently, evidence for training-related changes in large-scale functional brain networks has begun to emerge, providing further support for efforts to derive global markers of training efficacy. The default network is an interconnected set of brain regions, including medial PFC (mPFC), posterior cingulate cortex, superior and inferior frontal gyri, medial and lateral temporal lobes, and the posterior extent of the inferior parietal lobule.¹² These regions are typically suppressed during externally oriented, attention-demanding tasks.¹² Activation increases in the default network have been reported following problem-solving training in young adults¹³ and visuospatial attention training following traumatic brain injury.¹⁴ Changes following training have also been reported in frontoparietal control and dorsal attention networks, which are engaged during tasks requiring externally focused attention¹⁵ and rapid adaptation of thoughts and behaviors to changing internal states and external environments.^{16,17} Regions of the frontoparietal control network include lateral PFC, precuneus, the anterior extent of the inferior parietal lobule, dorsal ACC, and the anterior insula.¹⁶⁻¹⁸ The dorsal attention encompasses the dorsolateral PFC, frontal eye fields, inferior precentral sulcus, superior occipital gyrus, middle temporal motion complex, and superior parietal lobule.^{15,19} Reduced activity in the frontoparietal control and dorsal attention networks has been observed following cognitive training.^{14,20,21} Dynamic changes in the connectivity profiles of large-scale functional brain networks was also shown during a motor learning task.²² Moreover, these brain changes predicted future learning ability, highlighting the potential of functional brain data to inform intervention research.

Here we used quantitative meta-analytic methods, the activation likelihood estimation (ALE²³) technique to review all studies investigating functional brain changes associated with cognitive and motor skills training using a

longitudinal, within-subject experimental design. Our aim was to identify common patterns of functional brain changes associated with training across a diverse range of intervention protocols within these broader training domains. If reliable patterns emerge, these could provide the basis for establishing global markers of functional brain changes that could be used, in combination with more localized, domain-specific training markers, to inform intervention design and provide brain-based outcome measures for evaluating treatment efficacy.

Methods

Study Selection

A systematic literature search was conducted to identify neuroimaging studies of cognitive and motor skills training for inclusion in the meta-analysis. Peer-reviewed articles, published in English up until June 2012, were selected from the search results of 2 separate databases: MEDLINE and PsycINFO. The literature search was conducted using the following search words: (1) keywords: “train*[†]” <OR> “learn*” <OR> “rehab*” <OR> “practic*” >; AND (2) keywords: “fMRI” <OR> “neuroimaging”; AND (3) keywords: “cognit*” <OR> “motor” <OR> “memory” <OR> “attention” <OR> “executive function*” <OR> “language” <OR> “vision” <OR> “percept.*”

Studies were selected based on the following inclusion criteria: (1) inclusion of a healthy, young adult participant group, (2) neuroimaging data acquired during the same task pretraining and posttraining, and (3) reporting of voxelwise, whole-brain data. Studies investigating functional brain changes during repeated task practice within a single scan session²⁴⁻²⁷ were excluded as were those comparing performance on a “trained” versus “control” task.^{28,29} Studies that reported region-of-interest analyses³⁰⁻³² or did not report activation foci as 3D coordinates in stereotaxic space³³ were also excluded because these were incompatible with the ALE analysis methods.

For studies that reported results for multiple task contrasts using the same group of participants,³⁴ the contrast reporting the greatest number of foci was selected. This was done to limit the contribution of any 1 set of participants to the pool of foci. For studies containing more than 1 independent sample, peak activation foci from each sample were included.³⁵ Articles that reported results for pretraining and posttraining phases separately (ie, no direct pretraining vs posttraining comparison) were omitted because GingerALE v 2.0.4 does not compute between-group comparisons with random-effects analysis. As a final step to ensure the comprehensiveness of the review, reference lists

of all included articles were searched for additional studies that fit these criteria. In total, 38 appropriate articles were identified for the ALE analysis (a complete list of references for all included studies can be found in the appendix).

ALE Method

ALE was performed using BrainMap Ginger ALE v 2.0.4,²³ a coordinate-based, random-effects meta-analysis for functional neuroimaging data. The ALE method uses a series of permutations to differentiate statistically significant patterns of brain activity from random clustering (ie, noise) of foci, across multiple independent experiments.²³ ALE maps are derived based on foci of interest, which comprise statistically significant peak activation locations from multiple studies.³⁶

We conducted 2 separate ALE analyses, each yielding an ALE map and corresponding cluster report: (A) posttraining < pretraining and (B) posttraining > pretraining. All studies included in the analysis are listed in Table 1.

All study coordinates were entered in GingerALE in the stereotaxic space of Talairach and Tournoux.³⁷ Those studies that originally reported coordinates in Montreal Neurological Institute (MNI) space were transformed into Talairach space using *icbm2tal*³⁸ as implemented in GingerALE 2.0.4. Studies that originally reported coordinates in Talairach space derived from Statistical Parametric Mapping (SPM) were transformed back to MNI space using *tal2mni* and then retransformed into Talairach space using *icbm2tal*. Additional details regarding these transformations can be found on the BrainMap Web site (www.brainmap.org). Across all studies, activation likelihood estimates (ALE statistics) were computed for each voxel in the brain, reflecting the likelihood that a given voxel was activated across studies in each respective analysis. All reported data survived $P < .05$ significance, false discovery rate corrected for multiple comparisons, as determined by permutation testing,²³ with a spatial extent greater than 150 mm³. All the data in the figures are presented on a standard template in Talairach space. ALE results images were rendered to cortical surface maps using Caret³⁹ for presentation.

Results

Behavior

The majority of studies (29/38; 76%) reported statistically significant improvements in task performance following training. All remaining studies reported qualitative data indicating that performance improved with training.

[†]The “wildcard” asterisk (*) was used to retrieve search words with multiple endings (train, training, trained, etc).

Table 1. Details of Included Studies in the Meta-analysis

Study	First Author	Year	Modality	Domain	n	Age	Foci	Posttraining > Pretraining	Posttraining < Pretraining
1	Arima	2011	fMRI	Motor	13	27.3	11	6	5
2	Dahlin	2008	fMRI	Cognitive	15	23.67	7	4	3
3	Debaere	2004	fMRI	Motor	12	21-29	24	15	9
4	Floyer-Lea	2005	fMRI	Motor	7	28.6	3	3	—
5	Gaab	2006	fMRI	Cognitive	7	19-24	2	1	1
6	Golestani	2004	fMRI	Cognitive	10	20-29	2	2	—
7	Ilg	2008	fMRI	Cognitive	20	20-32	3	2	1
8	Jäncke	2001	fMRI	Cognitive	6	25	6	—	6
9	Jolles	2010	fMRI	Cognitive	15	22.0	12	12	—
10	Katiuscia	2009	fMRI	Motor	8	27	9	5	4
11	Kim	2004	fMRI	Motor	8	20-22	24	12	12
12	Kondo	2005	fMRI	Cognitive	14	22.3	6	6	—
13	Kwon	2009	fMRI	Cognitive	9	20-25	10	1	9
14	Miotto	2006	fMRI	Cognitive	15	38.8	9	9	—
15	Newman-Norlund	2006	fMRI	Cognitive	18	18-21	30		
	Auditory group				8			13	—
	Visual group				10			17	—
16	Nyberg	2003	PET	Cognitive	8	25.75	2	2	—
17	Nyberg	2006	fMRI	Motor	16	29.9	3		
	Motor group				8			2	—
	Mental group				8			1	—
18	Olesen	2004	fMRI	Cognitive	8		15		
	Experiment 1				3	21-23		4	1
	Experiment 2				5	29.3		8	3
19	Parsons	2005	fMRI	Motor	12	24.8	17	3	14
20	Penhune	2002	PET	Motor	9	23.5	18	11	7
21	Petersson	2001	PET	Cognitive			54		
	Experiment 1				16	25		16	17
	Experiment 2				10	26		13	8
22	Poldrack	1998	fMRI	Cognitive	6	NA ^a	19	5	14
23	Poldrack	2001	fMRI	Cognitive	16	20.3	12	10	2
24	Puttemans	2005	fMRI	Motor	11	23.9	7	4	3
25	Raboyeau	2004	PET	Cognitive	10	35.5	9	9	—
26	Raboyeau	2010	fMRI	Cognitive	10	22.7	9	4	5
27	Rémy	2008	fMRI	Motor	12	23.6	7	2	5
28	Ronsse	2011	fMRI	Motor	34	23.0	27		
	Auditory group				17			—	19
	Visual group				17			8	—
29	Sacco	2006	fMRI	Motor	12	27.5	13	9	4
30	Schiltz	1999	PET	Cognitive	6	21-24	4	—	4
31	Schiltz	2001	PET	Cognitive	6	23-28	5	1	4
32	Schmidt-Wilcke	2010	fMRI	Cognitive	16	30.1	7	7	—
33	Takeuchi	2011	fMRI	Cognitive	23	22.0	1	1	—
34	Thomas	2009	fMRI	Cognitive	12	32.5	14	3	11
35	Tracy	2003	fMRI	Motor	15	28.9	2	2	—
36	Wong	2007	fMRI	Cognitive	17	20.65	18	18	—
37	Wu	2004	fMRI	Motor	12	23-38	13	—	13
38	Zhang	2011	fMRI	Motor	14	22	12	3	9

Abbreviations: fMRI, functional magnetic resonance imaging; PET, positron emission tomography.

^aDemographics unavailable. First author confirmed young adult participation.

Table 2. Brain Regions Showing Reliable Decreases in Activity Across Studies Following Training ($P < .05$, FDR Corrected)

Lat	Region	BA	Volume (mm ³)	ALE (10-3)	x	y	z	Studies Contributing to Each Cluster
L	Cerebellum, anterior lobe, dentate	—	2240	16.25	-18	-56	-20	31 (C), 3 (M), 23 (C), 21 (C), 10 (M), 19 (M), 20 (M)
L	Cerebellum, pyramis	—		15.27	-4	-66	-24	
LR	Dorsal anterior cingulate cortex	6	1648	18.32	-2	2	48	18 (C), 37 (M), 34 (C), 20 (M), 38 (M), 24 (M)
R	Superior parietal lobule	7	1504	14.83	32	-60	56	5 (C), 2 (C), 22 (C), 28 (M)
L	Dorsolateral prefrontal cortex	9/46	616	15.59	-32	34	26	37 (M), 34 (C), 38 (M)
L	Inferior frontal gyrus	9	584	14.96	-44	2	22	34 (C), 1 (M), 38 (M)
R	Dorsolateral prefrontal cortex	9/46	336	13.37	28	38	30	34 (C), 28 (M)
R	Superior parietal lobule	7	320	13.03	12	-74	40	20 (M), 38 (M)
R	Inferior frontal gyrus	9	296	12.49	46	4	32	3 (M), 1 (M)
R	Premotor cortex	6	272	11.37	30	-10	60	37 (M), 27 (M)
R	Anterior insula	14	264	10.51	32	20	12	28 (M), 38 (M), 24 (M)
L	Middle occipital gyrus	19	240	11.89	-30	-80	16	21 (C), 34 (C)
R	Insula	13	240	9.76	46	-20	24	1 (M), 28 (M)
R	Frontal pole	10	232	12.15	30	54	16	2 (C), 21 (C)
R	Cerebellum, anterior lobe, culmen	—	224	12.05	20	-46	-22	37 (M), 21 (C)
L	Dorsolateral prefrontal cortex	9	200	11.09	-42	12	36	26 (C), 21 (C)
L	Premotor cortex	6	168	11.2	-26	-6	50	34 (C), 38 (M)
L	Superior parietal lobule	7	160	9.79	-22	-68	44	21 (C)
R	Cerebellum, posterior lobe, declive	—	152	9.69	16	-58	-16	11 (M), 21 (C)

Abbreviations: FDR, false discovery rate; Lat, laterality; BA, Brodmann area; ALE, activation likelihood estimation; x, y, z, stereotaxic coordinates in Talairach space; L, left hemisphere; R, right hemisphere; (C), cognitive skill trained; (M), motor skill trained.

Variability in reporting of behavioral data across studies precluded further investigation of the impact of performance gains (eg, effect size estimates) on patterns of functional brain change.

Training-Related Decreases in Brain Activity

The contrast of posttraining < pretraining revealed a number of brain areas associated with reduced activation following training (see Table 2 and Figure 1).

These included bilateral areas of the frontal lobe, including the dorsolateral PFC (Brodmann area [BA] 9/46), inferior frontal gyrus (BA 9), dorsal ACC (BA 6), and the right lateral frontal pole (BA 10). Significant decreases were also observed in the premotor cortex (BA 6) and superior parietal lobule (BA 7) bilaterally. Reduced activation was also recorded in the left dentate subregion of the anterior cerebellum, with clusters of reduced activation extending into the right anterior and posterior lobes. Posttraining decreases were also identified in the right anterior insula (BA 14) and left middle occipital gyrus (BA 19).

Training-Related Increases in Brain Activity

The posttraining > pretraining ALE contrast revealed a number of brain areas associated with increased activation following training (see Table 3 and Figure 1).

These included the left mPFC (BA 9), left posterior cingulate (BA 31), left inferior parietal lobule (angular gyrus; BA 39), and right postcentral gyrus (BA 40). Posttraining increases were also identified in both the lingual gyri (BA 18) and fusiform gyri (left: BA 19; right: BA 37), bilaterally, as well as the putamen, bilaterally, and right caudate and anterior cerebellum bilaterally.

Contributing Studies by Training Domain

To investigate whether the ALE clusters reflected domain-general training effects across cognitive and motor skills training interventions, we categorized each study as either cognitive ($n = 23$) or motor ($n = 15$) skills training (see Table 1) based. Studies were allocated based on the author's description, the nature of the training task, and outcome measures reported in each study. We then examined the distribution of studies contributing to each ALE cluster (Tables 2 and 3). Many of the ALE clusters had both cognitive and motor training studies contributing (9 of 18 clusters for training-related decreases in brain activity; 9 of 14 clusters for training-related increases in brain activity). For those clusters with 3 or more contributing studies, 5 of 6 clusters for training-related decreases in brain activity were of mixed domain (ie, motor and cognitive), and all clusters were mixed domain for training-related increases in brain activity. For those clusters with only 2 contributing studies,

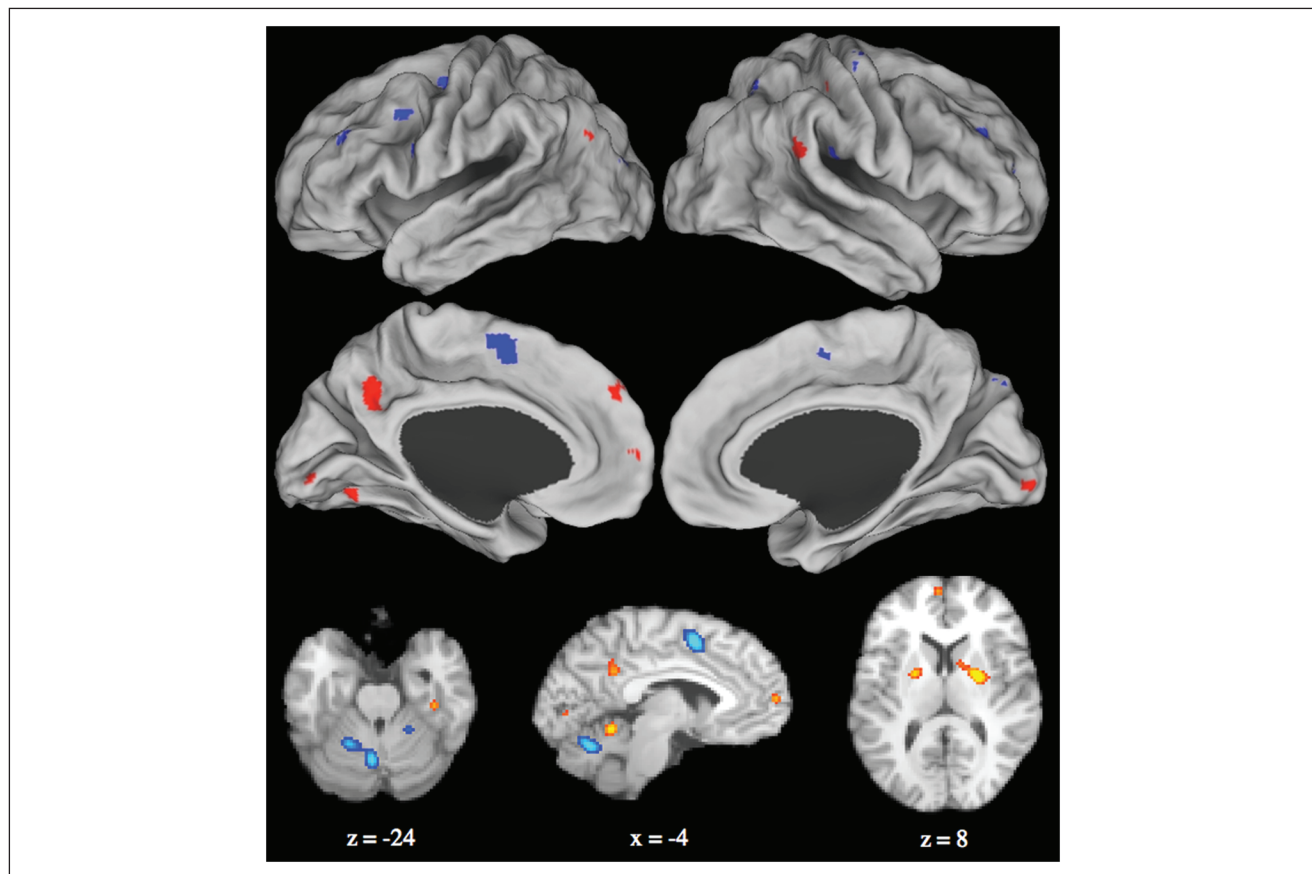


Figure 1. Combined activation likelihood estimation map showing significant activation clusters: red = posttraining > pretraining; blue = pretraining > posttraining. Surface maps of the activation likelihood clusters (false discovery rate $P < .05$) are shown on an inflated surface map in Caret (Van Essen, 2005, rows 1-2). Cerebellar and subcortical structures are presented in the volume in row 3.

Table 3. Brain Regions Showing Reliable Increases in Activity Across Studies Following Training ($P < .05$, FDR Corrected)

Lat	Region	BA	Volume (mm ³)	ALE (10-3)	x	y	z	Studies Contributing to Each Cluster
R	Putamen	—	1760	20.79	24	-4	4	15 (C), 3 (M), 27 (M), 2 (C), 36 (C), 20 (M), 24 (M)
R	Caudate	—		11.29	12	4	8	
L	Posterior cingulate cortex	31	664	13.65	-8	-52	34	11 (M), 32 (C), 24 (C), 20 (M)
L	Putamen	—	632	14.87	-20	-2	10	15 (C), 3 (M), 36 (C)
LR	Lingual gyrus	18	432	13.57	0	-84	-2	15 (C), 7 (C), 28 (M)
LR	Cerebellum, anterior lobe, culmen	—	424	15.89	-2	-52	-12	32 (C), 25 (C), 28 (M)
L	Medial prefrontal cortex	9	424	16.25	-10	48	34	15 (C), 21 (C), 20 (M)
R	Postcentral gyrus	40	352	14.22	40	-28	48	21 (C)
R	Inferior parietal lobule	40	344	13.65	56	-36	24	21 (C), 10 (M)
R	Lingual gyrus	18	272	13.04	46	-64	-16	36 (C), 38 (M)
L	Fusiform gyrus	19	240	12.94	-22	-64	-10	23 (C), 9 (C)
L	Angular gyrus	39	240	13.92	-46	-68	28	32 (C), 34 (C)
L	Anteromedial prefrontal cortex	10	176	12.88	-4	56	10	34 (C), 20 (M)
R	Lingual gyrus	18	160	11.29	8	-72	-10	23 (C), 9 (C)
R	Fusiform gyrus	37	152	12.7	38	-30	-24	25 (C)

Abbreviations: FDR, false discovery rate; Lat, laterality; BA, Brodmann area; ALE, activation likelihood estimation; x, y, z, stereotaxic coordinates in Talairach space; L, left hemisphere; R, right hemisphere; (C), cognitive skill trained; (M), motor skill trained.

4 of 11 clusters for analysis training-related decreases in brain activity and 3 of 6 for training-related increases in brain activity had contributing studies from both cognitive and motor domains.

Repeat Scanning and Practice Effects

We were unable to quantitatively parse the contribution of repeat scanning or practice effects to the pattern of brain changes reported here. This limitation reflects an ongoing challenge in the literature examining the functional neural basis of training, where few studies incorporate nontraining control groups. In our sample, 10 of the 38 included studies implemented controlled experimental designs for their neuroimaging analyses. Of these, 5 studies reported a significant group by session interaction,^{34,40–43} and 2 studies did not observe significant brain changes across the 2 sessions in their control group.^{44,45} Although not conclusive, a significant majority of the studies in our sample using a controlled group design demonstrated significant brain changes in their treatment group relative to untreated control groups. Thus, the pattern of functional brain changes emerging from our review is unlikely to be significantly attributable to repeat scanning or practice. However, limitations in the literature preclude further investigation of these effects on the ALE results.

Discussion

Using quantitative ALE meta-analytic methods, we reviewed findings from functional neuroimaging studies investigating the neural correlates of training in young adults. Our results demonstrated that training, irrespective of targeted domain, is associated with reduced activation in regions closely overlapping with the frontoparietal control and dorsal attention networks. Specific reductions were observed in dorsal ACC (BA6), dorsolateral and ventrolateral PFC (BA 9/46), anterior insula, and premotor (BA 6) and frontal polar cortices (BA 10). We also observed reductions from pretraining to posttraining in parietal (superior parietal lobule—BA 7) and cerebellar (anterior aspect) brain regions. Training-related decreases in the frontoparietal and dorsal attention networks suggest that training interventions reduce demands on externally focused attention, a finding consistent with a previous quantitative review of the training literature.⁹ Notably, these activation decreases were accompanied by increases in default network brain regions, areas typically suppressed during highly demanding tasks.⁴¹ Specific reductions were observed in medial aspects of the PFC (BA 9, 10) as well as the posterior cingulate cortex (BA 31), inferior parietal lobule (BA 40), and angular (BA 39) and postcentral (BA 40) gyri. Our review also demonstrated reliable patterns of increased activation in the striatum (caudate, putamen),

consistent with previous reports suggesting that training is associated with increased involvement of subcortical brain regions.^{3,4} These results implicate relative changes in large-scale functional brain networks as potential markers of training-related gains, irrespective of the training target.

Posttraining reductions in anterior, dorsal, and ventral aspects of the lateral PFC as well as the right dorsal ACC and the left anterior aspect of the inferior parietal lobule are in good agreement with previous reports demonstrating that both motor^{46,47} and cognitive^{20,34} skills training lead to reduced activity in frontoparietal control network brain regions. These areas highly overlap with those that comprise the frontoparietal control and dorsal attention networks. These sets of interconnected brain regions are known to be involved in controlled attention and goal-directed processing in response to shifting environmental contingencies.¹⁶ In addition, we observed bilateral reductions in the superior parietal lobule, a region that is reliably engaged during attention-demanding tasks.¹⁵ The distinct functional contributions of these attention-related regions to posttraining performance, however, remain less clear. For instance, the dorsal ACC is known to play a prominent role in performance monitoring by detecting error-prone states.⁴⁸ Neuroimaging studies have shown that activation of this region tracks error occurrence, increases with response conflict,⁴⁹ and positively correlates with task difficulty.⁵⁰ Thus, the dorsal ACC would be expected to be involved in the early stages of learning where effort, conflict monitoring, and flexibility are critical.⁵¹ Reduced activity posttraining may thus reflect lower demand for performance monitoring as skilled performance emerges.

Reduced recruitment of brain regions implicated in attention control reflects a shift from more controlled to automatic forms of task performance following training.^{3,4,9,10,30,52} Indeed, previous findings have revealed that those classified as “good” learners on a motor sequence learning task exhibited a quicker decrease in activation of prefrontal regions as compared with “poor” performers.²⁸ Activation decreases across key nodes of the frontoparietal control network may therefore hold predictive value in identifying those individuals who would take longer to reach more automated (ie, less controlled) levels of performance. Training-related automaticity may also decrease the need to suppress task-irrelevant information.² That is, reduced engagement of frontoparietal control network regions may attenuate suppression of the default network, allowing for greater task-independent processing.

Reliable training-related increases in brain activation were observed in core regions of the default network, including the posterior cingulate cortex (BA 31), medial PFC (BA9 and BA10), and left posterior inferior parietal lobule (BA 39). The default network has been observed to increase in activation under conditions of low attention demand^{12,53} as well as decrease in activity as task difficulty

increases.⁵⁴⁻⁵⁶ Higher levels of activity within the default network have been associated with greater task ease and mind wandering,⁵⁷ whereby participants are able to perform a task well while simultaneously recollecting past events or imagining personal future events, processes supported by the default network.⁵⁸ Greater activation of the default network and less demand for controlled attentional processing may free the brain to explore its dynamic repertoire of internal thoughts, memories, and future goals following training. Based on these data, we hypothesize that increased default network activity, combined with reduced frontoparietal control network activity, may provide a candidate neural marker of training-related performance gains.

Our findings provide evidence that relative shifts between large-scale brain network activity may reveal reliable functional brain markers that generalize across a wide range of cognitive and motor skills training interventions. However, the behavioral correlates of changes to the balance among distributed brain networks are just beginning to be understood. Although we were unable to directly evaluate the impact of functional brain changes on behavior in our data, we suggest that brain changes at the level of interacting functional networks may provide important insights into treatment efficacy in both training and neurorehabilitation contexts. Indeed, in 1 recent report, training-related changes in network flexibility—dynamic shifts in the allegiance of nodes to specific brain networks—was shown to be predictive of training-related gains in performance on a motor-learning task.²²

In addition to cortical brain changes, our analyses also revealed posttraining increases in the bilateral putamen and right caudate nucleus. This finding reflects the growing body of studies reporting increased striatal activity after both motor^{40,59,60} and cognitive^{34,61,62} skills training. Greater involvement of the basal ganglia after training is thought to reflect a shift in the balance of corticostriatal activity from untrained to trained task performance.⁴ In the context of working memory, this may reflect greater engagement of gating functions mediated by basal ganglia to facilitate context-specific and flexible updating of skill representations in the frontal cortex as learning occurs.⁶³ After training, such flexible updating is no longer necessary, enabling representations of the trained skill to be maintained by the basal ganglia.³⁴ The idea that the basal ganglia may serve as a “memory store” for well-trained performance is also supported by motor skills training studies showing that the basal ganglia remain active, even when trained performance is tested after a delay. Albouy et al⁶⁴ reported that bilateral activation of the putamen was associated with improved performance on an oculomotor sequence learning task over the course of training and was sustained following a 24-hour delay, consistent with a hypothesized role for this region in maintaining representations of trained skills.

The basal ganglia also play an important role in reinforcement learning because dopaminergic neurons in the striatum respond to stimuli that predict reward and adjust their firing rate according to the magnitude of the expected reward.⁶⁵⁻⁶⁷ Training may therefore serve to strengthen stimulus-response associations by promoting successful behaviors that are reinforced through reward signaling mediated by corticostriatal circuits. Indeed, recent animal findings demonstrated that blockage of the anterior fore-brain pathway, a cortical-basal ganglia circuit, during training of a complex motor skill disrupted gradual skill improvement that normally occurs with training.⁶⁸ Unblocking these channels posttraining reinstated learning. This suggests a crucial role for corticostriatal reward circuits in supporting and maintaining representations of trained skills. Indeed, it is now well understood that aspects of the frontoparietal control network, particularly regions of the lateral PFC, are highly functionally connected with the basal ganglia^{69,70} and that these connections are altered with training.³⁴ Although we are unable to address this directly here, the results of this meta-analysis raise the intriguing possibility that alterations in cortical-subcortical functional connectivity may serve to modulate the dynamic interactions among cortical brain networks. Investigating how these large-scale, distributed brain networks interact and how these interactions are modulated by training, aging, brain disease, or injury represent important areas of future inquiry.

Our meta-analysis also demonstrated that training was associated with a large cluster of reduced activity in the dentate subregion of the anterior cerebellum. This parallels previous findings showing reduced activity in the dentate nucleus after extensive practice on a motor sequence task.⁴⁶ We also observed a smaller cluster of increased activity in the anterior region of the cerebellum, consistent with hypothesized involvement of this region in highly trained motoric performance.⁷¹ However, activation increases in anterior cerebellar regions are often transient, potentially reflecting rapid learning and adaptation processes not fully captured in the extended training paradigms reviewed here. Moreover, both motor and cognitive studies contributed to these clusters. Training-induced functional cerebellar changes may reflect both the degree and speed with which automaticity is attained over the course of training, and this may vary across motor and cognitive tasks. Further work will be needed to determine how the composition of training tasks influence automaticity and how this is reflected in activation changes in cerebellar subregions.

Our findings that training is associated with changes in large-scale cortical and subcortical brain networks may have important implications for training and rehabilitation intervention design. In the context of neurorehabilitation, Chen and colleagues¹ recently identified a neural marker of goal-directed attention that was significantly altered by

neurorehabilitation training in a sample of patients with acquired brain injury. They observed functional changes in distributed brain regions purported to mediate goal-directed behavior that were associated with significant performance gains on behavioral measures of attention regulation. The authors also reported that baseline PFC activation, a purported mediator of attentional regulation, predicted post-training changes in this region, a potential marker of treatment readiness not accessible through behavioral data alone. Similarly, Strangman and colleagues⁷² observed that moderate baseline prefrontal activity was associated with greater treatment gains than either high or low baseline PFC response. Although much work remains, these data suggest that neural markers obtained at baseline may predict response to neurorehabilitation interventions, thus informing treatment planning and potential triaging of patients to appropriate training protocols. Moreover, changes in neural response from pretraining to posttraining may also provide informative outcome data regarding mechanisms of treatment efficacy that are not accessible through standard behavioral measures.

Markers of functional brain response can also be used to interpret negative training outcomes.⁶⁰ This later contribution of functional brain data to interpreting negative training outcomes was recently highlighted in a study by Dahlin and colleagues.³⁴ The authors reported that older adults failed to show transfer of training from one working memory task to another. Both tasks had been shown to recruit overlapping areas in the subcortical striatum, and this overlap was hypothesized to be important for mediating training transfer between working memory tasks in younger adults. Older adults' failure to engage these striatal brain regions posttraining was posited to underlie their inability to generalize training gains, suggesting a potential role for striatal brain regions in mediating training transfer among working memory tasks. Here functional brain data were used to identify a potentially important neural mechanism critical for training transfer in a specific cognitive domain. This mechanism could be targeted in future training and treatment protocols, again highlighting the importance of neural markers in treatment design and evaluation.

Our findings suggest that changes in the activation of large-scale functional brain networks may provide important neural markers of training-related performance gains irrespective of training domain or specific training task. Changes in distributed functional networks from pretraining to posttraining may thus inform the development of reliable, domain-general markers of treatment response in training and neurorehabilitation settings. Mapping the intrinsic neural architecture of the regional connections comprising the default, frontoparietal control and dorsal attention networks is under way.⁷³ Determining training-related changes in distributed network activation, in addition to interregional

coupling of activity, may represent a critical step toward developing functional neural markers to elucidate the mechanisms and evaluate the efficacy of neurorehabilitation interventions.

Appendix

Meta-analysis Studies

1. Arima T, Yanagi Y, Niddam DM, et al. Corticomotor plasticity induced by tongue-task training in humans: a longitudinal fMRI study. *Exp Brain Res*. 2011;212:199-212.
2. Dahlin E, Neely AS, Larsson A, Bäckman L, Nyberg L. Transfer of learning after updating training mediated by the striatum. *Science*. 2008;320:1510-1512.
3. Debaere F, Wenderoth N, Snaert S, Van Hecke P, Swinnen SP. Changes in brain activation during the acquisition of a new bimanual coordination task. *Neuropsychologia*. 2004;42:855-867.
4. Floyer-Lea A, Matthews PM. Distinguishable brain activation networks for short and long-term motor skill learning. *J Neurophys*. 2005;94:512-518.
5. Gaab N, Gaser C, Schlaug G. Improvement-related functional plasticity following pitch memory training. *Neuroimage*. 2006;31:255-263.
6. Golestani N, Zatorre RJ. Learning new sounds of speech: Reallocation of neural substrates. *Neuroimage* 2004;21:494-506.
7. Ilg R, Wohlschläger AM, Gaser C, et al. Gray matter increase induced by practice correlates with task specific activation: a combined functional and morphometric magnetic resonance imaging study. *J Neurosci*. 2008;28:4210-4215.
8. Jäncke L, Gaab N, Wüstenberg T, Scheich H, Heinze H-J. Short-term functional plasticity in the human auditory cortex: an fMRI study. *Cogn Brain Res*. 2001;12:479-485.
9. Jolles DD, Grol MJ, Van Buchem MA, Rombouts SA, Crone EA. Practice effects in the brain: changes in cerebral activation after working memory practice depend on task demands. *Neuroimage*. 2010;52:658-668.
10. Katiushcia S, Franco C, Federico D, Divide M, Sergio D, Giuliano G. Reorganization and enhanced functional connectivity of motor areas in repetitive ankle movements after training in locomotor attention. *Brain Res*. 2009;1297:124-134.
11. Kim DE, Shin M-S, Lee K-M, et al. Musical training induced functional reorganization of the adult brain: functional magnetic resonance imaging and transcranial magnetic stimulation study on amateur string players. *Hum Brain Mapp*. 2004; 23:188-199.
12. Kondo Y, Suzuki M, Mugikura S, et al. Changes in brain activation associated with use of a memory strategy: a functional MRI study. *Neuroimage*. 2005;24:1154-1163.
13. Kwon YJ, Lee JK, Shin DH, Jeong JS. Changes in brain activation induced by the training of hypothesis generation skills: an fMRI study. *Brain Cogn*. 2009;69:391-397.

14. Miotto EC, Savage CR, Evans JJ, et al. Bilateral activation of the prefrontal cortex after strategic semantic cognitive training. *Hum Brain Mapp.* 2006;27:288-295.
15. Newman-Norlund RD, Frey SH, Petitto L-A, Grafton ST. Anatomical substrates of visual and auditory miniature second-language learning. *J Cogn Neurosci.* 2006;18:1984-1997.
16. Nyberg L, Eriksson J, Larsson A, Marklund P. Learning by doing versus learning by thinking: an fMRI study of motor and mental training. *Neuropsychologia.* 2006;44:711-717.
17. Nyberg L, Sandblom J, Jones S, et al. Neural correlates of training-related memory improvement in adulthood and aging. *Proc Natl Acad Sci U S A.* 2003;100:13728-13733.
18. Olesen PJ, Westerberg H, Klingberg T. Increased prefrontal and parietal activity post-training of working memory. *Nat Neurosci.* 2004;7:75-79.
19. Parsons MW, Harrington DL, Rao SW. Distinct neural systems underlie learning visuomotor and spatial representations of motor skills. *Hum Brain Mapp.* 2005;24:229-247.
20. Penhune VB, Doyon J. Dynamic cortical and subcortical networks in learning and delayed recall of timed motor sequences. *J Neurosci.* 2002;22:1397-1406.
21. Petersson KM, Sandblom J, Gisselg rd J, Ingvar M. Learning related modulation of functional retrieval networks in man. *Scand J Psychol.* 2001;42:197-216.
22. Poldrack RA, Desmond JE, Glover GH, Gabrieli JDE. The neural basis of visual skill learning: an fMRI study of mirror reading. *Cereb Cortex.* 1998;8:1-10.
23. Poldrack RA, Gabrieli JDE. Characterizing the neural mechanisms of skill learning and repetition priming: evidence from mirror reading. *Brain.* 2001;124:67-82.
24. Puttemans V, Wenderoth N, Swinnen SP. Changes in brain activation during the acquisition of a multifrequency bimanual coordination task: from the cognitive stage to advance levels of automaticity. *J Neurosci.* 2005;25:4270-4278.
25. Raboyeau G, Marie N, Balduyck S, Gros H, D monet J-F, Cardebat D. Lexical learning of the English language: a PET study in healthy French subjects. *Neuroimage.* 2004;22:1808-1818.
26. Raboyeau G, Marcotte K, Adrover-Roig D, Ansaldo AI. Brain activation and lexical learning: the impact of learning phase and word type. *Neuroimage.* 2010;49:2850-2861.
27. R my F, Wenderoth N, Lipkens K, Swinnen SP. Acquisition of a new bimanual coordination pattern modulates the cerebral activations elicited by an intrinsic pattern: an fMRI study. *Cortex.* 2008;44:482-493.
28. Ronsse R, Puttemans V, Coxon JP, et al. Motor learning with augmented feedback: modality-dependent behavioural and neural consequences. *Cereb Cortex.* 2011;21:1283-1294.
29. Sacco K, Cauda F, Cerliani L, Mate D, Duca S, Geminiani GC. Motor imagery of walking following training in locomotor attention: the effect of "the tango lesson." *Neuroimage.* 2006;32:1441-1449.
30. Schiltz C, Bodart JM, Dubois S, et al. Neuronal mechanisms of perceptual learning: changes in human brain activity with training in orientation discrimination. *Neuroimage.* 1999; 9:46-62.
31. Schiltz C, Bodart J-M, Michel C, Crommelinck M. A PET study of human skill learning: changes in brain activity related to learning an orientation discrimination task. *Cortex.* 2001;37:243-265.
32. Schmidt-Wilcke T, Rosengarth K, Luerding R, Bogdahn U, Greenlee M. Distinct patterns of functional and structural neuroplasticity associated with learning Morse code. *Neuroimage.* 2010;51:1234-1241.
33. Takeuchi H, Taki Y, Hashizume H, et al. Effects of training processing speed on neural systems. *J Neurosci.* 2011;31:12139-12148.
34. Thomas AG, Marrett S, Saad ZS, Ruff DA, Martin A, Bandettini PA. Functional but not structural changes associated with learning: an exploration of longitudinal voxel- Based morphometry (VBM). *Neuroimage.* 2009;48:117-125.
35. Tracy J, Flanders A, Madi S, et al. Regional brain activation associated with different performance patterns during learning of a complex motor skill. *Cereb Cortex.* 2003;13:904-910.
36. Wong PC, Perrachione TK, Parrish TB. Neural characteristics of successful and less successful speech and word learning in adults. *Hum Brain Mapp.* 2007;28:995-1006.
37. Wu T, Kansaku K, Hallett M. How self-initiated memorized movements become automatic: a functional MRI study. *J Neurophys.* 2004;91:1690-1698.
38. Zhang H, Xu L, Wang S, et al. Behavioral improvements and brain functional alterations by motor imagery training. *Brain Res.* 2011;1407:38-46.

Acknowledgments

We thank Julia Spaniol and Lixia Yang for their helpful comments on earlier versions of this manuscript. We apologize to any authors whose work was mistakenly overlooked.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: GRT recognizes the Heart and Stroke Foundation of Canada, Centre for Stroke Recovery and the Faculty of Health, York University, ON, Canada, for their generous support.

References

1. Chen A J-W, Novakovic-Agopian T, Nycum TJ, et al. Training of goal-directed attention regulation enhances control over neural processing for individuals with brain injury. *Brain.* 2011;134:1541-1554.

2. Kelly C, Garavan H. Human functional neuroimaging of brain changes associated with practice. *Cereb Cortex*. 2005; 15:1089-1102.
3. Dahlin E, Bäckman L, Neely AS, Nyberg L. Training of the executive component of working memory: subcortical areas mediate transfer effects. *Restor Neurol Neurosci*. 2009;27: 405-419.
4. Doyon J, Bellec P, Amsel R, et al. Contributions of the basal ganglia and functionally related brain structures to motor learning. *Behav Brain Res*. 2009;199:61-75.
5. Kelly C, Foxe JJ, Garavan H. Patterns of normal human brain plasticity after practice and their implications for neurorehabilitation. *Arch Phys Med Rehabil*. 2006;87:S20-S29.
6. Klingberg T. Training and plasticity of working memory. *Trends Cogn Sci*. 2010;14:317-324.
7. Poldrack RA. Imaging brain plasticity: conceptual and methodological issues. A theoretical review. *Neuroimage*. 2000; 12:1-13.
8. Ungerleider LG, Doyon J, Karni A. Imaging brain plasticity during motor skill learning. *Neurobiol Learn Mem*. 2002; 78:553-564.
9. Chein JM, Schneider W. Neuroimaging studies of practice-related change: fMRI and meta-analytic evidence of a domain-general control network for learning. *Cogn Brain Res*. 2005;25:607-623.
10. Jansma JM, Ramsey NF, Slagter HA, Kahn RS. Functional anatomical correlates of controlled and automatic processing. *J Cogn Neurosci*. 2001;13:730-743.
11. Peterson SE, van Mier H, Fiez JA, Raichle ME. The effects of practice on the functional anatomy of task performance. *Proc Natl Acad Sci U S A*. 1998;95:853-860.
12. Buckner RL, Andrews-Hanna JR, Schacter DL. The brain's default network: anatomy, function, and relevance to disease. *Ann N Y Acad Sci*. 2008;1124:1-38.
13. Mazoyer B, Houdé O, Joliot M, Mellet E, Tzourio-Mazoyer N. Regional cerebral blood flow increases during wakeful rest following cognitive training. *Brain Res Bull*. 2009;80: 133-138.
14. Kim Y-H, Yoo W-K, Ko M-H, Park C-h, Kim ST, Na DL. Plasticity of attentional networks after brain injury and cognitive rehabilitation. *Neurorehabil Neural Repair*. 2009;23: 468-477.
15. Fox MD, Snyder AZ, Vincent JL, Corbetta M, Van Essen DC, Raichle ME. The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proc Natl Acad Sci U S A*. 2005;102:9673-9678.
16. Vincent JL, Kahn I, Snyder AZ, Raichle ME, Buckner RL. Evidence for a frontoparietal control system revealed by intrinsic functional connectivity. *J Neurophys*. 2008;100:3328-3342.
17. Spreng RN, Stevens WD, Chamberlain J, Gilmore AW, Schacter DL. Default network activity, coupled with the frontoparietal control network, supports goal-directed cognition. *Neuroimage*. 2010;31:303-317.
18. Niendam TA, Laird AR, Ray KL, Dean YM, Glahn DC, Carter CS. Meta-analytic evidence for a superordinate cognitive control network subserving diverse executive functions. *Cogn Affect Behav Neurosci*. 2012;12:241-268.
19. Corbetta M, Shulman GL. Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci*. 2002; 3:215-229.
20. Erickson KI, Colcombe SJ, Wadhwani R, et al. Training-induced functional activation changes in dual-task processing: an fMRI study. *Cereb Cortex*. 2007;17:192-204.
21. Petersson KM, Sandblom J, Gisselgård J, Ingvar M. Learning related modulation of functional retrieval networks in man. *Scand J Psychol*. 2001;42:197-216.
22. Bassett DS, Wymbs NF, Porter MA, Mucha PJ, Carlson JM, Grafton ST. Dynamic reconfiguration of human brain network during learning. *Proc Natl Acad Sci U S A*. 2011;108: 7641-7646.
23. 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;30:2907-2926.
24. Landau SM, Schumacher EH, Garavan H, Druzgal TJ, D'Esposito M. A functional MRI study of the influence of practice on component processes of working memory. *Neuroimage*. 2004;22:211-221.
25. Landau SM, Garavan H, Schumacher EH, D'Esposito M. Regional specificity and practice: dynamic changes in object and spatial working memory. *Brain Res*. 2007;1180:78-89.
26. Toni I, Krams M, Turner R, Passingham RE. The time course of changes during motor sequence learning: a whole-brain fMRI study. *Neuroimage*. 1998;8:50-61.
27. Tracy J, Faro SS, Mohammed F, Pinus A, Christensen H, Burkland D. A comparison of "early" and "late" stage brain activation during brief practice of a simple motor task. *Cogn Brain Res*. 2001;10:303-316.
28. Sakai K, Hikosaka O, Miyauchi S, Takino R, Sasaki Y, Putz B. Transition of brain activation from frontal to parietal areas in visuomotor sequence learning. *J Neurosci*. 1998;18: 1827-1840.
29. Wiser AK, Andreasen N, O'Leary DS, et al. Novel vs. well-learned memory for faces: A positron emission tomography study. *J Cogn Neurosci*. 2000;12:255-266.
30. Hempel A, Giesel FL, Garcia Caraballo NM, et al. Plasticity of cortical activation related to working memory during training. *Am J Psychiatry*. 2004;161:745-747.
31. Karni A, Meyer G, Jezard P, Adams MM, Turner R, Ungerleider LG. Functional MRI evidence for adult motor cortex plasticity during motor skill learning. *Nature*. 1995;377: 155-158.
32. Xiong J, Ma L, Wang B, et al. Long-term motor training induced changes in regional cerebral blood flow in both task and resting states. *Neuroimage*. 2009;45:75-82.

33. Callan DE, Tajima K, Callan AM, Kubo R, Masaki S, Akahane-Yamada R. Learning-induced neural plasticity associated with improved identification performance after training of a difficult second-language phonetic contrast. *Neuroimage*. 2003;19:113-124.
34. Dahlin E, Neely AS, Larsson A, Bäckman L, Nyberg L. Transfer of learning after updating training mediated by the striatum. *Science*. 2008;320:1510-1512.
35. Nyberg L, Eriksson J, Larsson A, Marklund P. Learning by doing versus learning by thinking: an fMRI study of motor and mental training. *Neuropsychologia*. 2006;44:711-717.
36. Turkeltaub PE, Eden GF, Jones KM, Zeffiro TA. Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. *Neuroimage*. 2002;16:765-780.
37. Talairach J, Tournoux P. *Co-planar Stereotaxic Atlas of the Human Brain*. New York, NY: Thieme; 1998.
38. Lancaster JL, Tordesillas-Gutierrez D, Martinez M, et al. Bias between MNI and Talairach coordinates analyzed using the ICBM-152 brain template. *Human Brain Mapp*. 2007;28:1194-1205.
39. Van Essen DC. A population-average: landmark- and surface-based (PALS) atlas of human cerebral cortex. *Neuroimage*. 2005;28:635-662.
40. Debaere F, Wenderoth N, Sunaert S, Van Hecke P, Swinnen SP. Changes in brain activation during the acquisition of a new bimanual coordination task. *Neuropsychologia*. 2004;42:855-867.
41. Jolles DD, Grol MJ, Van Buchem MA, Rombouts SA, Crone EA. Practice effects in the brain: changes in cerebral activation after working memory practice depend on task demands. *Neuroimage*. 2010;52:658-668.
42. Schmidt-Wilcke T, Rosengarth K, Luerding R, Bogdahn U, Greenlee M. Distinct patterns of functional and structural neuroplasticity associated with learning Morse code. *Neuroimage*. 2010;51:1234-1241.
43. Takeuchi H, Taki Y, Hashizume H, et al. Effects of training processing speed on neural systems. *J Neurosci*. 2011;31:12139-12148.
44. Kwon YJ, Lee JK, Shin DH, Jeong JS. Changes in brain activation induced by the training of hypothesis generation skills: an fMRI study. *Brain Cogn*. 2009;69:391-397.
45. Sacco K, Cauda F, Cerliani L, Mate D, Duca S, Geminiani GC. Motor imagery of walking following training in locomotor attention: the effect of "the tango lesson." *Neuroimage*. 2006;32:1441-1449.
46. Léhericy S, Benali H, van deMoortele PF, et al. Distinct basal ganglia territories are engaged in early and advanced motor sequence learning. *Proc Natl Acad Sci U S A*. 2005;102:12566-12571.
47. Poldrack RA, Sabb F, Foerke K, et al. The neural correlates of motor skill automaticity. *J Neurosci*. 2005;25:5356-5364.
48. Carter CS, Macdonald AM, Botvinick MM, et al. Parsing executive processes: strategic vs. evaluative functions of the anterior cingulate cortex. *Proc Natl Acad Sci U S A*. 2000;97:1944-1948.
49. Carter CS, Braver TS, Barch DM, Botvinick MM, Noll D, Cohen JD. Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science*. 1998;280:747-749.
50. Paus T, Koski L, Caramanos Z, Westbury C. Regional differences in the effects of task difficulty and motor output on blood flow response in the human anterior cingulate cortex: a review of 107 PET activation studies. *Neuroreport*. 1998;9:R37-R47.
51. Bush G, Luu P, Posner MI. Cognitive and emotional influences in the anterior cingulate cortex. *Trends Cogn Sci*. 2000;4:215-222.
52. Doyon J, Penhune V, Ungerleider LG. Distinct contribution of the corticostriatal and cortico-cerebellar systems to motor skill learning. *Neuropsychologia*. 2003;41:252-262.
53. Gould RL, Brown RG, Owen AM, Bullmore ET, Howard RJ. Task-induced deactivations during successful paired associated learning: an effect of age but not Alzheimer's disease. *Neuroimage*. 2006;31:818-831.
54. McKiernan KA, Kaufman JN, Kucera-Thompson J, Binder JR. A parametric manipulation of factors affecting task-induced deactivation in functional neuroimaging. *J Cogn Neurosci*. 2003;15:394-408.
55. Mayer JS, Roebroeck A, Maurer K, Linden DE. Specialization in the default mode: task-induced brain deactivations dissociate between visual working memory and attention. *Hum Brain Mapp*. 2010;31:126-139.
56. Gusnard DA, Raichle ME. Searching for a baseline: functional imaging and the resting human brain. *Nat Rev Neurosci*. 2004;2:685-694.
57. Mason MF, Norton MI, Van Horn JD, Wegner DM, Grafton ST, Macrae CN. Wandering minds: the default network and stimulus-independent thought. *Science*. 2007;315:393-395.
58. Spreng RN, Mar RA, Kim ASN. The common neural basis of autobiographical memory, prospection, navigation, theory of mind and the default mode: a quantitative meta-analysis. *J Cogn Neurosci*. 2009;21:489-510.
59. Floyer-Lea A, Matthews PM. Distinguishable brain activation networks for short and long-term motor skill learning. *J Neurophys*. 2005;94:512-518.
60. Penhune VB, Doyon J. Dynamic cortical and subcortical networks in learning and delayed recall of timed motor sequences. *J Neurosci*. 2002;22:1397-1406.
61. Newman-Norlund RD, Frey SH, Petitto L-A, Grafton ST. Anatomical substrates of visual and auditory miniature second-language learning. *J Cogn Neurosci*. 2006;18:1984-1997.
62. Wong PC, Perrachione TK, Parrish TB. Neural characteristics of successful and less successful speech and word learning in adults. *Hum Brain Mapp*. 2007;28:995-1006.
63. Frank MJ, Loughry B, O'Reilly RC. Interactions between frontal cortex and basal ganglia in working memory: a computational model. *Cogn Affect Behav Neurosci*. 2001;1:137-160.
64. Albouy G, Ruby P, Phillips C, Luxen A, Peigneux P, Maquet P. Implicit oculomotor sequence learning in humans: time course of offline processing. *Brain Res*. 2006;1090:163-171.

65. Galvan A, Hare TA, Davidson M, Spicer J, Glover G, Casey BJ. The role of the ventral frontostriatal circuitry in reward-based learning in humans. *J Neurosci*. 2005;25:8650-8656.
66. Seger CA, Spiering BJ. A critical review of habit learning and the basal ganglia. *Front Syst Neurosci*. 2011;5:66.
67. Yin HH, Ostlund SB, Balleine BW. Reward-guided learning beyond dopamine in the nucleus accumbens: the integrative functions of cortico-basal ganglia networks. *Eur J Neurosci*. 2008;28:1437-1448.
68. Charlesworth JD, Warren TL, Brainard MS. Covert skill learning in a cortical-basal ganglia circuit. *Nature*. 2012;486:251-255.
69. Barnes KA, Cohen AL, Power JD, et al. Identifying basal ganglia divisions in individuals using resting-state functional connectivity MRI. *Front Syst Neurosci*. 2010;4:18.
70. Di Martino A, Scheres A, Margulies DS, et al. Functional connectivity of human striatum: a resting state FMRI study. *Cerebral Cortex*. 2008;18:2735-2747.
71. Puttemans V, Wenderoth N, Swinnen SP. Changes in brain activation during the acquisition of a multifrequency bimanual coordination task: from the cognitive stage to advance levels of automaticity. *J Neurosci*. 2005;25:4270-4278.
72. Strangman GE, O'Neil-Pirozzi TM, Goldstein R, et al. Prediction of memory rehabilitation outcomes in traumatic brain injury by using functional magnetic resonance imaging. *Arch Phys Med Rehabil*. 2008;89:974-981.
73. Spreng RN, Sepulcre J, Turner GR, Stevens WD, Schacter DL. Intrinsic architecture underlying the relations among the default, dorsal attention, and frontoparietal control networks of the human brain. *J Cogn Neurosci*. In press.