Motor Imagery: A Backdoor to the Motor System After Stroke?

Nikhil Sharma, Valerie M. Pomeroy and Jean-Claude Baron

The online version of this article, along with updated information and services, is
located on the World Wide Web at:

http://stroke.ahajournals.org/cgi/content/full/37/7/1941

Motor Imagery
A Backdoor to the Motor System After Stroke?

Nikhil Sharma, MB, ChB, MRCP(UK); Valerie M. Pomeroy, PhD;
Jean-Claude Baron, MD, FRCP, FmedSci

Background and Purpose—Understanding brain plasticity after stroke is important in developing rehabilitation strategies. Active movement therapies show considerable promise but depend on motor performance, excluding many otherwise eligible patients. Motor imagery is widely used in sport to improve performance, which raises the possibility of applying it both as a rehabilitation method and to access the motor network independently of recovery. Specifically, whether the primary motor cortex (M1), considered a prime target of poststroke rehabilitation, is involved in motor imagery is unresolved.

Summary of Review—We review methodological considerations when applying motor imagery to healthy subjects and in patients with stroke, which may disrupt the motor imagery network. We then review firstly the motor imagery training literature focusing on upper-limb recovery, and secondly the functional imaging literature in healthy subjects and in patients with stroke.

Conclusions—The review highlights the difficulty in addressing cognitive screening and compliance in motor imagery studies, particularly with regards to patients with stroke. Despite this, the literature suggests the encouraging effect of motor imagery training on motor recovery after stroke. Based on the available literature in healthy volunteers, robust activation of the nonprimary motor structures, but only weak and inconsistent activation of M1, occurs during motor imagery. In patients with stroke, the cortical activation patterns are essentially unexplored as is the underlying mechanism of motor imagery training. Provided appropriate methodology is implemented, motor imagery may provide a valuable tool to access the motor network and improve outcome after stroke. (***Stroke***. 2006;37:1941-1952.)

Key Words: magnetic resonance imaging, functional ∎ recovery of function ∎ rehabilitation ∎ stroke
∎ tomography, emission computed

Motor impairment after stroke is a major cause of permanent disability. Recovery of the hand is crucial in order to perform activities of daily living but is often variable and incomplete.[1] Neuroscience-based rehabilitation is gaining strength as a way to improve outcome, even in situations where the deficit appears to be permanent.[2] Understanding the effect of rehabilitative techniques on brain plasticity is potentially important in providing a neural substrate to underpin rehabilitation and hence in developing novel rehabilitation strategies.

Active movement training (AMT) such as constraint-induced therapy (CIT) benefits from translational research; following a primary motor cortex (M1) infarct in primates, AMT can prevent loss of the peri-infarct hand territory and can even force expansion into adjacent areas.[3] In chronic stroke patients CIT may be able to overcome "learned nonuse", resulting in cortical hand expansion and functional gains at 6 months.[2] When applied directly to humans, consistent relationships have emerged between motor recovery and cortical activation patterns after stroke, such that predominant ipsilesional activation, ie, positive Laterality Index, is associated with better recovery (see reviews by Ward and Cohen,[4] Calautti and Baron[5]). Moreover AMT can result in both cortical reorganization and improved motor performance. Specifically in the chronic stage of stroke, CIT-like procedures can increase ipsilesional premotor and somatosensory cortex activation,[6] whereas AMT can result in increases in ipsilesional M1 activation with a positive Laterality index shift.[7] The idea is therefore emerging that "forcing" the use of the idle motor network, particularly M1, promotes long-term recovery, provided M1 is present and not isolated from the anterior horn cell.

Nevertheless, AMT has limitations; rodent models suggest CIT should be restricted during the early phase of stroke because it may result in infarct expansion,[8] although this has not been encountered clinically.[9] Difficulties implementing CIT in the clinical setting have resulted in a modified CIT protocol.[10] However, poor motor performance still excludes almost 4 of 5 otherwise eligible subacute stroke patients from CIT.[11] Attempts to bridge the period of poor motor performance by combining

different AMTs, such as electromyography-triggered neuromuscular stimulation and modified CIT,[12,13] have produced unconvincing results with some severely affected subjects verbalizing frustration.

Alternative strategies such as passive mobilization can be used in persons with hemiplegia to access the motor system although it produces mainly proprioceptive input to motor pathways.[14] Yet, in healthy subjects passive mobilization neither improves performance nor induces the cortical plasticity shown with active movement, supporting a key role for voluntary drive in motor learning and neuro-rehabilitation.[15]

In principle a therapy based on attempted movement is conceivable because it combines both M1 activation[16] and voluntary drive. The authors are unaware of any published trials that use attempted movement as a rehabilitation invention; this perhaps reflects the practical difficulties in avoiding patient frustration and fatigue.[12] Moreover, in subjects with hemiplegia, attempted movement is likely to be complicated by proximal or undesirable movement, and furthermore there would be no way to assess compliance (see below). Overall, the clinical uses of AMT in stroke are limited by their dependence on a degree of motor performance.

Motor imagery represents an intriguing new "backdoor" approach to accessing the motor system and rehabilitation at all stages of stroke recovery.[17] Unlike active and passive motor therapies, motor imagery, in principle, is not dependent on residual function but still incorporates voluntary drive. Importantly, in the primate, M1 is directly involved in motor imagery as suggested by direct cellular recordings.[18] In patients with stroke, motor imagery may therefore provide a substitute for executed movement as a means to activate the motor network.

Additional parallels between motor imagery and executed movement are worth mentioning; there is close temporal coupling between motor imagery and executed movement, ie, the time taken to mentally perform an action closely mirrors the executed movement.[19] During imagined movement, the reduction in accuracy with increasing speed (ie, Fitt Law) is maintained[20] and the asymmetry between dominant and nondominant hand is also preserved.[21] Motor imagery produces similar autonomic changes as executed movement, with significant increase in heart and respiratory rates.[22,23,24] Nevertheless, these principles can be disrupted by structural lesions in specific brain areas,[25] the implications of which will be discussed later.

In athletes, a structured program of motor imagery movement, motor imagery training, can lead to an improvement in performance. The effects are independent of subclinical muscle activation.[26] Perhaps unsurprisingly, motor imagery training produces less practical improvement compared with physical training.[27] Although widely used in conjunction with physical training, motor imagery training can independently improve motor performance and produce similar cortical plastic changes,[28] providing a useful alternative when physical training is not possible.

As will be discussed, a few early studies suggest that motor imagery training may improve functional recovery after stroke.[29–33] However, how effective it is and in what setting it is best used remains unclear and will form the second section of this review. But in order to effectively target the correct patient population it is imperative to understand how motor imagery training may work, and hence how motor imagery allows access to the motor network. It is widely assumed that motor imagery activates similar pathways as executed movement,[34] but as will be seen there are some important differences. Particular attention will be given to whether motor imagery activates M1 because this would imply greatest efficiency, although as will be discussed effects on nonprimary motor areas may also provide gains.

This systematic review of the functional imaging and motor imagery training literature will focus on hand function, because of the lateralized and large cortical representation as well as the obvious key importance of the hand in activities of daily living, and will consist of 4 sections: the first will briefly discuss general cognitive considerations, particularly when investigating motor imagery in the context of structural lesions and relevant methods of assessment; the second will review studies investigating the effectiveness of motor imagery training at restoring upper-limb motor function after stroke; the third will address the cortical network activated during motor imagery in healthy subjects and the potential implications for patient selection. In the fourth section the motor imagery functional imaging studies in patients with stroke will be reviewed. Finally, the results will be discussed and summarized, concluding with suggestions for future research.

Cognitive Considerations

Motor imagery can be defined as a dynamic state during which the representation of a specific motor action is internally reactivated within working memory without any overt motor output, and that is governed by the principles of central motor control.[19,20,35] Operationally, this can be considered as occurring from the 1st person perspective.[36] The interested reader is referred to dedicated reviews on the cognitive neuroscience theories of motor imagery.[36,37]

Motor Imagery in Stroke

Motor imagery is an integral part of the wider motor system that can be represented by internal models or programs, which develop over time and are consistently changing.[38] In chronic disease states temporal coupling is often preserved; in Parkinson disease the asymmetrical bradykinesia is mirrored during motor imagery,[39] as is the performance in the chronic fatigue syndrome.[40] However, in patients with stroke it is important to consider both the ability to perform motor imagery accurately and temporal coupling because, depending on the site and extent of the stroke, either or both may be affected.

Because the parietal lobe is involved in the preservation and generation of a kinaesthetic model,[41] it is perhaps not surprising that parietal damage can reduce motor imagery accuracy.[42,43] By excluding subjects with parietal or premotor lesions, Johnson[44] used a prehensile task to suggest that both subacute and chronic hemiplegic patients[45] may still perform motor imagery. Moreover, the authors even suggest that subjects with chronic stroke may be more accurate during motor imagery with the affected limb, a "hemiplegic advantage".

Late disruption of M1 (hand area) by transcranial magnetic stimulation (TMS) can also reduce motor imagery accuracy and increases response time during the mental rotation of

hands but not feet; the authors suggest that M1 is not only involved in motor imagery but is required.[46] Conversely, others have reported that M1 is not necessary to perform motor imagery,[25] whereas direct stimulation of M1 via an implanted electrode array may not disrupt motor imagery accuracy but increase response time.[47]

Temporal uncoupling may occur after either parietal[25] or frontal lobe damage[44] but can be preserved after cerebellar stroke.[48] In partially recovered patients, Malouin et al[49] speculated that stroke could result in temporal uncoupling of the nonaffected limb while being preserved in the affected limb. However, the authors acknowledge that this unexpected finding could be explained by the extensive strokes included in the study causing either cortical–cortical disruption of the motor imagery network or a deficit in working memory, which in itself may reduce the effectiveness of motor imagery training.[50] However, Sabate et al[51] reported that temporal coupling can be preserved after stroke.

Despite the limited samples and the wide variety of lesion location in these studies, overall, the ability to perform motor imagery may be preserved after stroke, but it appears that both accuracy and temporal coupling can be disrupted. We have referred to this as chaotic motor imagery.

Chaotic motor imagery can be defined as an inability to perform motor imagery accurately or if having preserved accuracy, demonstration of temporal uncoupling. Further characterization of motor imagery performance in subjects unable to perform accurately or with temporal uncoupling is likely to produce incongruent results. Chaotic motor imagery may be limb-specific, affecting distal but not proximal movement[25] probably attributable to differences in cortical organization. Although we primarily use the term "chaotic motor imagery" here to designate inability to perform motor imagery in people with central nervous system damage, it is possible that it also applies to a small percentage of the normal population.

Motor Imagery: Assessment of Ability, Performance and Compliance

It follows from the definition of motor imagery that because of its concealed nature, a subject may surreptitiously use alternative cognitive strategies that, if not screened for, could confound investigations and produce conflicting results. Applied to the normal population these alternative strategies can be distilled into 4 components: the inability to perform motor imagery or inaccuracy; a simple failure to comply; the concealed use of alternative strategies such as counting or visual imagery; and a failure to suppress movement. In addition, when applied to the study of patients with stroke, chaotic motor imagery should be considered.

In order to select appropriate subjects for clinical studies, particularly functional imaging and motor imagery training, a dichotomic approach to motor imagery, able versus unable, is imperative; however, it should be noted that motor imagery is a complex cognitive process.[37,52] As such, important information which further characterizes the quality and vividness of the motor imagery effected by the enrolled subjects performed should be obtained.[22,53]

Inability to Perform Motor Imagery

When cognitive screening for the ability to perform motor imagery accurately is applied to a normal population, a small fraction of subjects will fail the assessment. Historically, questionnaires (eg, Mental Imagery Questionnaire (MIQ)[54]) were used which were aimed primarily at athletes, subjectively selecting those who were skilled at motor imagery. The questionnaire requires subjects to perform complex tasks physically and then using motor imagery, after which subjects rate their performance on both a kinaesthetic and visual scale. Because of the difficulties in performing the tasks, a modified MIQ has been produced which comprises of simpler gestures,[55] though it still does not provide objective evidence of motor imagery ability.

An interesting alternative is the Controllability of Motor Imagery Scale[56]: subjects follow a series of instructions each specifying a single mental movement of a limb; at the end the subject must assume the position produced by the combination of movement. Those unable to do so are excluded, providing objective evidence of motor imagery ability. Although the use of alternative strategies such as visual imagery is not addressed, it remains a more useful assessment than the MIQ.

Perhaps the most appropriate method to assess motor imagery accuracy is to use a prehensile task, similar to Johnson[44,45] because this provides objective evidence and intrinsically activates the motor imagery network.[57]

Simple Failure to Comply

Unlike executed movement paradigms during which compliance can be checked by observation of the task, motor imagery is concealed and requires more complex monitoring. Hanakawa[58] used visually presented numbers to "guide" subjects through a prelearned finger-tapping sequence. In this procedure, subjects are instructed which finger to begin and then presented a number; the subject then moves the corresponding steps through the sequence, and at end of block is asked to confirm the position. Although this method does provide evidence of compliance, it encourages the use of alternative techniques, particularly counting.

We have used a variant of this method; the motor imagery task is paced and unexpectantly stops and the subject has to confirm their position.[59] Although this technique would be pragmatically difficult to include into a motor imagery training program, it is of particular interest in functional imaging studies when it can be incorporated into the paradigm, with those who fail to correctly confirm being excluded. Regardless of these details, the task must be of sufficient complexity to contain a number of possible positions so a correct response is unlikely to be attributable to chance.

A similar method is the application of mental chronometry, ie, (re)action times for instance; the number of foot taps in various time blocks can be compared with the number of imagined taps.[50,60,61] This method is particularly useful during motor imagery training,[28] providing an objective assessment of compliance; however, in the way it has been used so far it is unable to exclude a noncompliant individual.

Nonetheless, it remains that all of these tasks can easily be solved by the use of alternative strategies such as counting, visual imagery or 3rd person imagery.

Concealed Use of Alternative Strategies

Because the aim of motor imagery is to activate the motor networks, it is crucial that subjects perform the mental task from the 1st person perspective, in contrast to 3rd person perspective or visual imagery.[36] Likewise, they should also be instructed not to count, as also by doing so a subject could fool an exclusion criteria based on confirmation of position. This has not been addressed in the literature but a form of objective assessment is clearly needed.

Failure to Suppress Movement

Several methods can be used to monitor overt or covert movement during motor imagery. The electromyogram (EMG) has been used during training before the functional imaging sessions[62,63] to ensure subjects do not move. This presents practical challenges during motor imagery training and functional MRI (fMRI), although it is possible in the latter[58] and during positron-emission tomography (PET) studies. Close inspection of the subject is the simplest way to highlight overt movement, though once again this is difficult in the MRI bore and small amplitude movements may be missed. Alternatively, a dynamometer,[64] an accelerometer[65] or goniometer[66] could be used in the fMRI session but not easily during motor imagery training. Specifically for the fMRI sessions, video observation may present an alternative method. We have successfully used fiber-optic MR-friendly gloves.[59]

Chaotic Motor Imagery

The identification of subjects performing chaotic motor imagery is not addressed by any published assessments, yet this is possibly a very important confound in both the interpretation of previous studies[50,51] and the application of motor imagery training and motor imagery to patients with stroke. Crucially, the potential screening tools discussed above would not be suitable for subjects performing chaotic motor imagery. Moreover, including subjects who perform chaotic motor imagery into a motor imagery training program may dilute any positive affects.

Furthermore, a lack of more general cognitive ability (dysphasia, dementia, neglect or inattention) would make an assessment of motor imagery ability very difficult or impossible.

For these reasons at this stage, theoretically a subject whose stroke is subcortical and does not involve M1 or the parietal lobe are likely to benefit the most from early motor imagery training. However, it is possible that many other factors may influence motor imagery training, such as gender, handedness, affected hemisphere, dysphasia, precise lesion location and time elapsed since stroke.

Review of the Literature

Motor Imagery Training Effectiveness

We will review studies investigating the effectiveness of motor imagery training at restoring motor function after stroke.

Inclusion Criteria

A systematic literature search using the electronic database on PubMed was performed. Only studies that focus exclusively on motor imagery of the upper-limb function and rehabilitation after stroke will be considered. Although other articles have been published[67–75] only 5 fulfilled the criteria.[29,30–33]

Clinical Data

Details of the number and characteristics of subjects included in the 5 primary studies are given in Table 1. Age and gender ratio are similar across studies but there are large differences in the time since stroke.

Lesion location and affected hemisphere is poorly reported across all the studies, as is any clinical classification or description of the stroke. Motor function is not always described in sufficient detail; of note is that all the studies excluded subjects with hemiplegia. General cognitive assessment was performed in 4 studies, 3[29,30,33] using the Mini Mental State Examination. It is likely that with such a wide range of cognitive ability combined with a lack of topographic data, a portion of subjects will have been performing chaotic motor imagery.

TABLE 1. Upper-Limb Motor Imagery Training Studies: Demographics

Study	Subject No. and Gender	Mean Age, y	Mean TSS, mo	Stroke Classification/ Location	Affected Hemisphere L:R	Motor Function	Cognitive Function
Page (2001)[29]	13 (10 M)	64.6	6.5	N/A	4:9	FMA=29 ARAT 24.7	Inclusion Criteria MMSE>20
Crosbie (2004)[30]	10 (6 M)	63.9	1.3	7×PACS, 1×LACS 1×TACS 1×uncertain	N/A	Mean MI 30	Mean MMSE 27 (16–30)
Dijkerman (2004)[31]	20 (14 M)	64	24	N/A	11:9	GS 68% Barthel 95.5	N/A
Liu (2004)[32]	49 (22 M)	71.9	13.9	MCA territory	N/A	FIM motor score=42	FIM cognitive score=30.4
Page (2005)[33]	11 (9 M)	63.2	23.4	N/A	N/A	AOU 1 MAL 1.1 QOM 0.56 ARAT=33.1	Modified MMSE>70

MMSE indicates Mini Mental State Examination; TSS, time since stroke; GS, grip strength affected/grip strength non-affected; AOU, Amount of use scale; QOM, Quality of Movement scale; PACS/LACS/TACS, Bamford Clinical Classification Stroke[122]; FIM, Functional Independence Measure; ARAT, Action Research Arm Test; MI, Motricity Index.

TABLE 2.   Upper-Limb Motor Imagery Training Studies: Protocol Details.

Study	Design	Background Rehabilitation	Specific Motor Imagery Instructions	Frequency of intervention and Setting	Motor Imagery Intervention		Control Intervention		Outcome measures
					Task	Duration	Task	Duration	
Page (2001)[29]	Randomized 2 groups Motor Imagery (n=8) Control (n=5)	Therapy given 3 × per wk in 1-h blocks for 6 wk	External Visual images	3 time per wk twice at home for 6 wk OPD	After Therapy 10 min tape UL functional tasks	10 min	After therapy 10-min tape stroke information	10 min	FMA Upper limb ARAT
Crosbie (2004)[30]	Replicated single-case	Conventional rehabilitation	Visualize the task	Daily for 2 wk In Patient	R&G Task PP 1 attempt Motor Imagery 2×10 reps	Not controlled Subject practices independently	Nil	N/A	Motricity Index (upper limb)
Dijkerman (2004)[31]	Pseudorandomization 3 groups Motor Imagery (n=10), VI (n=5) and NI (n=5)	R&G Task	1st person	Daily for 4 wk Patient's Home	Motor Imagery Gp R&G 1×PP 3×Motor Imagery	N/A	VI Group* visual pictures NI Group*	N/A	Trained and Untrained task (TTC & errors) HPT GS
Liu (2004)[32]	Randomized 2 groups Motor Imagery (n=26), FR (n=20)	1-h Conventional Rehabilitation	Imagine his/her performance	Daily For 3 wk In Patient	Motor Imagery Gp 3 sets of 5 daily tasks	1 h	Functional Rehabilitation Group 3 sets of 5 daily tasks	1 h	Trained & Untrained tasks FMA
Page (2005)[33]	Randomized controlled single blinded Motor Imagery (n=6) Control (n=5)	30 minutes therapy sessions 2 days a wk for 6 wk	Internal Polysensory images	Twice a wk For 6 wk OPD	After Therapy 30 min Motor Imagery tape UL tasks	30 min	After therapy 30-min relaxation tape	30 min	MAL ARAT

See TABLE 1 for other abbreviations. R&G indicates reach & grasp; N/A, not reported or not applicable; UL, upper limb; MAL, Motor Activity Log; FMA, Fugel-Meyer Assessment; TTC, time to complete; OPD, out-patient department; HPT, 10 Hole Peg test; reps, repetitions; PP, physical practice; VI, visual imagery; NI, no imagery.
    *Groups were combined for analysis.

Study Design, Interventions and Outcome Measures

The details of design of the 5 studies are outlined in Table 2. Three studies[29,32,33] were randomized controlled trials although sample size was not based on a power calculation. Where applicable, groups were reasonably balanced, with no significant differences in motor performance. Three studies[29,32,33] used a blinded assessor to undertake the outcome measures.

All studies provided a control intervention except 1[30] whose replicated case design removed the need. Both the control intervention and motor imagery training were provided in addition to a background rehabilitation therapy that in 2 studies[31,33] was related to the motor imagery training. Only 2 studies[31,33] specifically instructed subjects to perform motor imagery; the remaining were either vague or encouraged visual imagery.

Both the control intervention and motor imagery training were balanced for frequency and duration. Across the studies the control intervention varied markedly, as did the motor imagery training; of note 1 study[32] used a motor imagery training program based on the functional retraining program used as a control intervention, thus limiting inclusion to stroke patients with a degree of movement.

Outcome measures varied between studies limiting direct comparison, although all measured motor function of the paretic upper limb. In addition 2 studies[31,32] used the trained task (task used in motor imagery) and an untrained task to assess outcome.

Subject Performance

Only 1 study[29] assessed motor imagery ability using the MIQ; however, this was not used in their subsequent study.[33] None of the studies assessed the use of alternative strategies, subtle movement or monitored compliance, which may be particularly relevant for instructions delivered via prerecorded tape.

Findings

The heterogeneity in subject characteristics, interventions and outcome measures across the 5 studies precludes any general conclusion, but overall all studies found that motor imagery training had encouraging effects on motor function compared with the control condition. One study[32] found a significant advantage for the motor imagery training group for both untrained and trained tasks, maintained at 1 month, whereas another study[31] found a significant advantage only for the trained task. In addition, 1 study[29] demonstrated an improved outcome in the motor imagery training group (no probability value given) on the Fugl-Meyer and Action Research Arm Test scores 1 week after end of training, and another[30] showed a significant change (no probability value given) in Motricity Index in 8 of 9 subjects during the intervention. Further, still another study[33] confirmed a significant increase in the Action Research Arm Test immediately after training in the motor imagery training group. In addition to showing that motor imagery had positive effects on motor function, these studies also suggest that the effects might generalize beyond the tasks being trained. With only 1 study[32]

TABLE 3. Motor Imagery Functional Imaging Studies in Healthy Subjects: Methodological Details*

Author	Objective of Study	Subject No. Gender and Handedness	Age Mean (Range)	Method	Activation Task (rate of external pacing)
Binkofski (2000)[92]	Broca's region & imagery of motion	6 (6 M, 6 RH)	N/A (25–40)	fMRI	†Index finger performing double circle (0.5Hz)
Gerardin (2000)[62]	Neural networks Motor Imagery and executed movement	8 (5 M, 8 RH)	26.6 (21–35)	fMRI	**Flex/Ext of fingers (0.5 Hz)
Boecker (2001)[93]	Effect of Sequence Structure	6 (3 M, 6 RH)	39	PET	Finger Tapping Sequence (1 Hz)
Naito (2002)[63]	Effect of Sensory feedback on Motor Imagery	10 (10 M, 10 RH)	N/A (20–25)	PET	Wrist Flex/Ext (Not paced)
Lacourse (2005)[94]	Comparing novel and skilled movement	54 (19 M, # 5.28)	24.5	fMRI	Finger tapping Sequence (selfpaced 4 Hz)

PET indicates positron-emission tomography; RH, right-handed.

*All of these studies used a box car design and rest as a contrast; †arm was imagined to be outstretched during task; **auditory stimuli continued during rest; #mean score on Handedness Scale (range 0–7). 7 completely right-handed.

following-up subjects after 1 month after the training period, it is unclear, however, whether motor imagery training is able to produce long-term gains.

Functional Imaging Studies

Healthy Subjects

A systematic search on PubMed was performed. For the purpose of this review, to explore the neural mechanism of motor imagery and allow an appropriate frame of reference, only studies that contrasted motor imagery of a hand action with rest, as opposed to another more or less complex cognitive task,[76–84] will be included in this review (also see Discussion section). Furthermore, to allow meaningful comparison only articles with published stereotactic coordinates based on whole-brain voxel-based analysis of motor imagery contrasted with rest will be analyzed in detail. Although numerous studies have been published[28,34,52,60,61,85–91] only 5[92,62,63,93,94] fulfilled these criteria. However, 6 otherwise relevant Region of Interest (ROI)–based studies[58,66,95–97] will be also commented on.

Main Studies

General Features. Demographics are given in Table 3. The objective of the studies varied; in only one study[62] was it the primary aim to investigate the motor imagery network. Of note 1 study[94] included subjects who were not completely right-handed; as will be seen, this is of particular relevance when considering cortical activation patterns.

Functional Imaging Paradigm. The activation task and pacing varied markedly across the studies; of note 1 study[92] used a motor imagery task that required the subject to imagine their arm outstretch while performing the finger task. Only 1 study[62] explicitly states that the auditory stimuli were continued during rest.

Subject Performance. Table 4 documents the methods each study used to tackle the difficult cognitive challenges. Overall, the methods used were sparse. Instructions to subjects were limited; only 1 study[92] was specific and only 1[93] asked subjects not to perform visual imagery or count. All the studies except 1[93] attempted to assess motor imagery ability; however, this particular study was unique in that they monitored compliance during the imaging paradigm. This was achieved by asking subjects to confirm their position after the finger-tapping sequence during both the training and the positron-emission tomography session. Interestingly, the block duration was fixed (50 seconds) but the tapping sequence varied in length ensuring a different end position, yet whether the subject was informed of this is unclear. The remaining studies had no confirmation of performance. No study assessed alternative strategies. All studies, bar 1,[94] monitored for subtle movement in either the task training, imaging paradigm or both.

Data Analysis. All the studies used versions of the Statistical Parametric Mapping (SPM) software, either SPM 96[62,92] or SPM 99.[63,93,94] Two studies[62,94] used random effect analysis, with the remaining using fixed effects analysis. Statistical

TABLE 4. Functional Imaging Studies: Cognitive Considerations

Study	Specific Motor Imagery Instructions	Motor Imagery Ability	Failure to Comply Training	Failure to Comply fMRI/PET	Alternative Strategies	Suppress Movement Training	Suppress Movement fMRI/PET
Binkofski (2000)[92]	Image somatosensory sensation of movement	MRT-A	N/A	N/A	N/A	N/A	EMG
Gerardin (2000)[62]	N/A	MIQ	N/A	N/A	N/A	EMG	N/A
Boecker (2001)[93]	Not to count	N/A	N/A	Confirmation of position	N/A	N/A	EMG and Video
Naito (2002)[63]	N/A	CMI	N/A	N/A	N/A	EMG	EMG
Lacourse (2005)[94]	N/A	MIQ	N/A	N/A	N/A	N/A	N/A

Specific instruction, ie NOT to perform visual imagery or 3rd person imagery.

MRT indicates mental rotation task[123]; EMG, electromyography; Obs, observation; N/A, not addressed; CMI, controllability of motor imagery.[56]

TABLE 5. Functional Imaging Studies: Activation Patterns During the Motor Imagery Task vs Rest, Using Voxel-Based Whole-Brain Analysis

Study	M1		SMA		Pre-SMA		Ba6		GPo		Ba 44/45/46		Ba 9,10,11		Sup.P		Ant.Cing		Inf.P		Cb	
	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I
Binkofski (2000)[92]	−	−	+	−	−	+	+	+	−	−	−	−	−	−	−	−	+	−	+	−	−	−
Gerardin (2000)[62]	−	−	−	−	−	−	+	+	+	+	+	+	−	+	+	+	−	−	+	−	−	−
Boecker (2001)[93]	−	−	−	−	−	−	+	+	+	−	−	−	−	+	−	−	−	−	+	−	−	+
Naito E (2002)[63]	−	−	+	−	−	−	+	−	−	−	−	−	−	−	−	−	−	−	+	−	−	+
Lacourse (2005)[94]	+	+	−	−	+	+	−	−	−	−	+	−	−	+	+	−	−	−	+	+	−	+

M1 indicates primary motor cortex; SMA, supplementary motor cortex; Ba, brodman area; Sup.P, superior parietal lobe; Inf.P, inferior parietal lobe; Gpo, post central gyrus; CB, cerebellar; Ant.Cing, anterior cingulate.

thresholds varied; 2 studies[63,92] used $P<0.01$ (corrected), 2[62,94] $P<0.001$ (corrected) and 1[93] $P<0.001$ (uncorrected).

Activation Patterns. When needed, the published activation coordinates were transformed into Talairach space using Mni2tal[98] and then checked manually against the Talairach atlas. Table 5 summarizes cortical activation patterns in M1, the secondary motor structures and motor-related areas. Only 1 study,[94] documents M1 activation during motor imagery, which was bilateral and localized to the hand area; however, the activation was less than during executed movement. The use of random effect analysis on only 8 subjects, as performed in 1 study,[62] is conservative and may have contributed to the failure to demonstrate M1 activation, particularly as they report that 50% of the subjects showed M1 activation on individual analysis (precise location not reported). Dorsal premotor was activated in all studies bar 1,[94] whereas 1 study[93] reported ventral premotor activation. Two studies[62,93] reported S1 activation and 3 (pre) supplementary motor cortex activation.[63,92,94] Three studies[62,93,94] demonstrated dorsolateral prefrontal cortex activation. The contralateral inferior parietal lobule was consistently activated as was the ipsilateral cerebellum (with 2 exceptions[62,92]).

ROI Studies

General Features. The 6 relevant ROI-based studies are detailed in Table 6. The objective of the studies varied; 3 studies[58,96,99] focused primarily on aspects of the motor imagery network. The studies are similar with regards to subject demographics, except the inclusion of left-handed subjects by 2 studies.[66,96] Across the studies, motor imagery ability was not assessed and 2 studies[96,99] did not explicitly instruct subjects to perform motor imagery. During the training phase, different methods were used to detect overt movement: observation,[95,97] goniometer,[66] and EMG.[99] In this particular study[99] the subjects continued training until they subjectively scored >4 on a kinaesthetic scale with a silent EMG.

TABLE 6. ROI-Based Functional Imaging Studies*

Author	Objective of Study	Subject No Gender and Handedness	Activation (Paced)	ROI Used	Statistical Methods	PcG Activation During Motor Imagery
Lotze (1999)[99]	Cortical activation patterns particularly M1 and 2nd Motor Structures	10 (5 M, 10 RH)	Fisting (1 Hz)	Anatomical	Voxel based $P<0.01$ (uncorrected)	Bilateral M1
Hanakawa (2003)[58]	Cortical activation patterns Motor Imagery	10 (7 M, 10 RH)	Finger tapping (Non paced)	Functional ROI	Signal based in suprathreshold voxels $P<0.001$	No M1 activation
Rodriguez (2004)[66]	Role of M1 in different conditions	10 (7 M, 8 RH)	Finger tapping (phasic/tonic/ Motor Imagery) (1.5 Hz)	Anatomical	Signal based $P<0.05$	Contra-lateral M1
Solodkin (2004)[96]	Network Modelling Motor Imagery	9 (18 in study) (9 M, 14 RH)	Finger tapping (2 Hz)	Anatomical	Signal based $P<0.05$	Contra-lateral M1
Niyazov (2005)[97]	Compare executed movement and Motor Imagery fMRI and TMS	6 (3 M, 6 RH)	finger thumb Opposition Self paced (1 Hz)	Anatomical	Voxel Based $P<0.01$ (corrected)	Contra-lateral PcG (PMd)
Hanakawa (2005)[95]	Ipsilateral precentral motor areas	8 (5 M, 8 RH)	†Finger tapping	Anatomical	Voxel Based $P<0.001$ (uncorrected)	Ipsilateral PcG (PMd) only

Abbreviations: See previous tables. PMd indicates dorsal premotor; PcG, precentral gyrus.

*All of these studies used a box car design unless stated and rest as a contrast; † event-related design.

Design. All studies used fMRI and either auditory or visual pacing. Of note, 1 study[58] used MRI-compatible EMG to detect subtle movement, and moreover objectively assessed compliance. Subjects learned the simple finger tapping sequence and at the beginning of each block were presented with a visual number which corresponded to the start position, after which they confirmed (using a button box) their position.

ROIs. All studies report prior hypotheses to justify the ROI analysis. There is a wide variation among studies in the ROIs used. One study[58] used functional ROIs, 2 studies[96,99] created ROIs from anatomical landmarks; as a result the anterior border of M1 was defined as the precentral sulcus. This will have included premotor areas,[100] which may be of relevance. The statistical thresholds and methods varied across studies and were generally liberal with 3 studies using signal based analysis.[58,66,96]

Results. The results are shown in Table 6. Two studies[66,96] reported contralateral M1 activation and 1 suggested bilateral activation,[99] Although 1 study[97] found activation of the contralateral precentral gyrus, it was anterior to the M1 hand area. Likewise, 1 study[95] suggests that motor imagery failed to activate contralateral M1, activating ipsilateral precentral gyrus (dorsal premotor) instead. This is consistent with their earlier study[58] that failed to report activation in M1, although they reported activation in 1 of the 10 subjects studied. Overall, the findings are in keeping with the previously presented literature suggesting robust premotor activation but weak or fleeting activation of M1 during motor imagery. Consistent with this, in the 3 studies that reported M1 activation during motor imagery, when the activation was compared with executed movement it was found to be much reduced[96,99] and in 1 instance, similar,[66] but in this study subjects we not monitored adequately for subtle movement during the imaging session.

Stroke Patients
A detailed systematic search on PubMed was performed. The search revealed only 1 study in stroke.[101] Lehéricy et al[101] used fMRI and motor imagery to examine the role of prefrontal, premotor and motor cortex in secondary dystonia. Although the study does not assess the relationship between motor imagery and hand motor recovery, it does raise some methodological considerations relevant to the review. The cortical activation patterns will not be described in detail.

The study compared 6 patients with adult-onset subcortical stroke and unilateral dystonia to 7 control subjects. Both controls and patients were screened using the MIQ. No further details of current functional level were given; parietal lobe dysfunction was suggested but not described in detail. The same paradigm as Gerardin et al[62] was used (see above). Subjects were observed not to move during training and there was no monitoring within the paradigm. Overall, the authors suggest an over-activation of the premotor and parietal areas during motor imagery of the dystonic hand compared with controls, in whom they report less sensorimotor cortex and more prefrontal activation during motor imagery than executed movement, but no further details are reported.

Discussion
Motor Imagery Training
The findings of the 5 studies reviewed suggest that motor imagery training might have an encouraging effect on motor function after stroke. However, interpretation of these results is limited by small sample sizes and heterogeneity in subject characteristics, motor imagery interventions and outcome measures used. In addition it is likely that some subjects may have been performing chaotic motor imagery as a result of the lesions involving the motor imagery network, yet despite this they still managed to achieve a positive effect on functional performance. This does raise an interesting paradox: motor imagery training, which is less effective than physical practice in controls,[27] may produce greater functional gains than executed movement in patients with stroke who can move, as claimed by Liu et al.[32] This observation being isolated, however, it should be considered with caution. Furthermore, a possible explanation was alluded to by Crosbie et al[30]: subjects often continue motor imagery training unsupervised, increasing the frequency of intervention. Alternatively, it is conceivable that patients performing chaotic motor imagery are more sensitive to and have the most to gain from training. Clearly more research is needed in this area.

Although motor imagery training is theoretically independent of motor recovery, in the studies reviewed the control intervention required motor performance. In doing so, they excluded subjects with severe hemiparesis, who may have a different response to motor imagery training. For instance, 1 intriguing paradigm could be to use motor imagery at the stage of complete hand paresis so as to activate the motor network as a substitute to CIT, and to switch to modified CIT as soon as sufficient hand movement has returned.

Furthermore, the optimal period to start motor imagery training is unclear. Unlike AMT, motor imagery could potentially be started early after stroke when the brain may be most "receptive" to intervention, although it is becoming increasingly clear that active motor training may be effective even in the chronic stage of stroke. Nonetheless, whether motor imagery training is capable of producing long-term gains is unknown.

In summary, motor imagery training is a promising intervention to improve motor function after stroke, but adequately powered clinical trials are needed in groups of well-characterized, stroke subjects. Furthermore, adequate screening and monitoring tools should be used to ensure that subjects included in these trials are able to and do perform motor imagery. Finally, the most appropriate target population, ie, those with severe hemiparesis, have not been studied as yet.

Functional Imaging
The findings from the 5 main studies detailed here highlighted robust and consistent activation of the secondary motor network and ipsilateral cerebellum during motor imagery, but only weak or inconsistent M1 activation.

To what extent these results are affected by methodological pitfalls is unclear. None of the studies reviewed complied with all the quality controls discussed above (see also implications for future studies below). Across the studies, subject screening and monitoring during both the training and imaging paradigm varied markedly in its purpose, with no study adequately assessing all facets of noncompliance. Hanakawa et al[58] was the closest to optimal by including monitoring of performance during scanning, yet even with the additional statistical powering

of ROI analysis found no M1 activation whatsoever in 9 of their 10 subjects. In contrast, Lacourse et al[94] used whole-brain analysis and documented strong bilateral M1 activation; however, some of their subjects were left-handed. Moreover, attributable to the lack of appropriate screening/monitoring, the validity of the results is uncertain.

Although the use of rest (with cues on) as a baseline condition provides an appropriate contrast and eases comparison between paradigms, it can be difficult to control.[102] Nonetheless, motor imagery studies that use cognitive baseline conditions rather than rest, which are difficult to place in context, are also undecided about the role of M1. Using visual imagery as a baseline, Porro et al[81,82] and Kuhtz-Buschbeck et al[76] report M1 activation, although significantly less than during executed movement; conversely, Dechent et al[78] used the same paradigm but failed to show M1 activation, although suggested fleeting M1 activation on the initiation of motor imagery. Nonetheless, by contrasting body parts specific activation, Ehresson et al[88] have suggested that motor imagery engages somatotopically organized areas of the M1, as did also Stippich et al.[87] Alternative methods of accessing the motor imagery network such as Luria hand rotation task[57] activate secondary motor structures but not M1.

The repeated failure to consistently activate M1 in functional imaging studies when other investigative methods, such as magnetoencephalography (MEG),[103,104] electroencephalogram (EEG),[105,106] and TMS,[107–110] are supportive of its involvement is puzzling. The higher spatial resolution of fMRI may be a contributing factor. However, it is plausible that during motor imagery, M1 has a different role beside executive, and so its activation is less sustained than during actual movement, producing a much-reduced signal. Importantly, in the primate, M1 is involved in spatial processing during motor imagery.[18] In addition, M1 can participate in the processing of both serial order information[111,112] and task-related spatial information,[113] whereas in humans it can be modulated by attention[114] and has the capacity to store short-term procedural information,[115] implying motor imagery may involve generation of motor representations without movement.[92]

Yet, despite differences in both subject selection and baseline tasks, the secondary motor structures, normally involved in motor learning, preparation, programming and memorizing,[36] have consistently shown activation. Therefore, an alternative explanation for the weak and inconsistent M1 activation during motor imagery may be that the premotor areas inhibit an otherwise executive M1. In primates, premotor areas can modulate M1 in an inhibitory manner as well as excitatory.[116] TMS studies in humans suggest that premotor-M1 interactions can also be inhibitory.[117,118] Furthermore, connectivity analysis of fMRI data sets supports an inhibitory effect of supplementary motor cortex and superior parietal lobe on M1 during motor imagery.[96] Although inhibition by secondary motor areas at the level of the anterior horn cell has been considered,[36] this would be expected to be associated with high or even excessive M1 activation.

Because it is widely believed that effective training and rehabilitation methods after stroke should involve M1, does the apparently weak and inconsistent activation of M1 during motor imagery make it a doomed rehabilitative approach? Not necessarily so, for 3 distinct reasons. Firstly, this finding needs to be confirmed in methodologically flawless fMRI studies. Secondly, even a weak activation might be sufficient to prevent learned nonuse and "prime" the motor representations enough to result in minimal active movement, bridging the gap across to modified CIT.[119] Thirdly, it remains possible that any effects of motor imagery are mediated by the premotor areas bypassing M1 via direct corticospinal projections, or improving preparation and programming rather than execution.[28] Further speculation about the role of M1 and the secondary motor areas in healthy volunteers is difficult until the issues of subject selection and noncompliance have been dealt with.

The study of secondary dystonia does not clarify the involvement of M1; nonetheless, it highlights some of the difficulties in applying motor imagery to patients with stroke: (1) patients had parietal dysfunction and may have been performing chaotic motor imagery even though they still scored well on the MIQ; (2) the potential difficulties in interpreting cortical activation patterns when subject compliance cannot be objectively confirmed; and (3) dystonia after adult onset stroke is a very unusual condition whose relevance to stroke in general is uncertain.

An interesting parallel are motor imagery studies in patients with complete spinal cord injury (SCI), where the lesion resembles subcortical stroke to a greater extent. Functional imaging[120,121] studies in SCI patients have reported marked M1 activation during motor imagery of the feet. Alkadhi et al[120] surprisingly reported a similar M1 cluster size in SCI patients as during executed movement in controls, who, notably, failed to activate M1 during motor imagery. This provides further support that the premotor areas may be inhibiting an otherwise executive M1 during motor imagery. Interestingly, healthy volunteers were screened with the MIQ, but SCI subjects were unable to perform the movements required by the MIQ, highlighting the need for alternative methods of assessment. It is possible, however, that motor imagery performed by SCI subjects differs in some fundamental aspects from that performed by healthy subjects.

Implications for Study Design

Subject Selection
Based on the above review, subjects, particularly those with stroke, should have an objective assessment of their capacity to perform motor imagery and exclude chaotic motor imagery before inclusion into either motor imagery training or functional imaging studies. They should also be given clear instructions; these should include specifying 1st person motor imagery and advice against the use of alternative strategies such as counting or visual imagery. Attempts should be made to identify noncompliant subjects.

Motor Imagery Training
Because motor imagery is, in principle, independent of motor performance, it would seem prudent that the control intervention for future motor imagery training studies does not require motor performance. This will further characterize the effects of motor imagery training, as will monitoring for uncontrolled motor imagery training use. Pragmatically, monitoring

for noncompliance during motor imagery training is challenging; however, the use of mental chronometry[28] is likely to be an effective means. Finally, further research should compare the effects of intervention in groups of low and high performers, to test the "bridging" hypothesis.

Functional Imaging Paradigm Design

Motor imagery may prove to be a consistent activation task that can be used across the full range of recovery and is largely independent of motor performance. The activation task should be simple and quick enough to be completed by patients with stroke while allowing objective evidence of compliance. To allow meaningful interpretation, particularly in subjects with stroke, the baseline condition should be rest (with cues).

Conclusions

The literature reviewed suggests that in healthy subjects motor imagery activates the motor network, providing a plausible mechanism for motor imagery training in athletes. No useful information is available as yet in patients with stroke, and the underlying mechanism of motor imagery training–induced improved performance suggested by the literature remains unexplained. However, if the same relationship as SCI patients is maintained in stroke, this may suggest that patients with chronic hemiplegia would involve M1 to a greater degree during motor imagery, providing a potential target group for motor imagery training.

Sources of Funding

Disclosure

None.

References

1. Duncan PW GL, Matchar D, Divine GW, Feussner J. Measurement of motor recovery after stroke. Outcome assessment and sample size requirements. *Stroke*. 1992;23:1084–1089.
2. Liepert J, Bauder H, Miltner WHR, Taub E, Weiller C. Treatment-induced cortical reorganization after stroke in humans. *Stroke*. 2000;31:1210–1216.
3. Nudo RJ WB, SiFuentes F, Milliken GW. Neural substrates for the effects of rehabilitative training on motor recovery after ischemic infarct. *Science*. 1996;272:1791–1794.
4. Ward NS CL. Mechanisms underlying recovery of motor function after stroke. *Arch Neurol*. 2004;61:1844–1848.
5. Calautti C, Baron J-C. Functional neuroimaging studies of motor recovery after stroke in adults: A review. *Stroke*. 2003;34:1553–1566.
6. Johansen-Berg H, Dawes H, Guy C, Smith SM, Wade DT, Matthews PM. Correlation between motor improvements and altered fMRI activity after rehabilitative therapy. *Brain*. 2002;125:2731–2742.
7. Carey JR, Kimberley TJ, Lewis SM, Auerbach EJ, Dorsey L, Rundquist P, Ugurbil K. Analysis of fMRI and finger tracking training in subjects with chronic stroke. *Brain*. 2002;125:773–788.
8. DeBow SB MJ, Kolb B, Colbourne F. Immediate constraint-induced movement therapy causes local hyperthermia that exacerbates cerebral cortical injury in rats. *Can J Physiol Pharmacol*. 2004;82:231–237.
9. Dromerick AW, Edwards DF, Hahn M. Does the application of constraint-induced movement therapy during acute rehabilitation reduce arm impairment after ischemic stroke? *Stroke*. 2000;31:2984–2988.
10. Page SJ, Sisto S, Johnston MV, Levine P, Hughes M Modified constraint-induced therapy in subacute stroke: A case report. *Arch Phys Med Rehabil*. 2002;83:286–290.
11. Grotta JC, Noser EA, Ro T, Boake C, Levin H, Aronowski J, Schallert T. Constraint-induced movement therapy. *Stroke*. 2004;35:2699–2701.
12. Fritz SL CY, Malcolm MP, Patterson TS, Light KE. Feasibility of electromyography-triggered neuromuscular stimulation as an adjunct to constraint-induced movement therapy. *Phys Ther*. 2005;85:428–442.
13. Page SJ, Levine P. Back from the brink: Electromyography-triggered stimulation combined with modified constraint-induced movement therapy in chronic stroke. *Arch Phys Med Rehabil*. 2006;87:27–31.
14. Nelles G, Spiekermann G, Jueptner M, Leonhardt G, Muller S, Gerhard H, Diener HC. Reorganization of sensory and motor systems in hemiplegic stroke patients: A positron-emission tomography study. *Stroke*. 1999;30:1510–1516.
15. Lotze M, Braun C, Birbaumer N, Anders S, Cohen LG. Motor learning elicited by voluntary drive. *Brain*. 2003;126:866–872.
16. Cramer SC, Lastra L, Lacourse MG, Cohen MJ. Brain motor system function after chronic, complete spinal cord injury. *Brain*. 2005;128:2941–2950.
17. Jackson PL, Lafleur MF, Malouin F, Richards C, Doyon J. Potential role of mental practice using motor imagery in neurologic rehabilitation. *Arch Phys Med Rehabil*. 2001;82:1133–1141.
18. Georgopoulos AP LJ, Petrides M, Schwartz AB, Massey JT. Mental rotation of the neuronal population vector. *Science*. 1989;243:234–236.
19. Decety J, Jeannerod M, Prablanc C. The timing of mentally represented actions. *Behav Brain Res*. 1989;34:35–42.
20. Decety J, Jeannerod M. Mentally simulated movements in virtual reality: Does Fitts's law hold in motor imagery? *Behav Brain Res*. 1995;72:127–134.
21. Maruff P, Wilson PH, De Fazio J, Cerritelli B, Hedt A, Currie J. Asymmetries between dominant and non-dominant hands in real and imagined motor task performance. *Neuropsychologia*. 1999;37:379–384.
22. Roure R, Collet C, Deschaumes-Molinaro C, Delhomme G, Dittmar A, Vernet-Maury E. Imagery quality estimated by autonomic response is correlated to sporting performance enhancement. *Physiol Behav*. 1999;66:63–72.
23. Jeannerod M, Frak V. Mental imaging of motor activity in humans. *Curr Opin Neurobiol*. 1999;9:735–739.
24. Kazuo Oishi TKaTM. Autonomic response specificity during motor imagery. *Journal of Physiological Anthropology and Applied Human Science*. 2000;19:255–261.
25. Sirigu A, Duhamel JR, Cohen L, Pillon B, Dubois B, Agid Y. The mental representation of hand movements after parietal cortex damage. *Science*. 1996;273:1564–1568.
26. Zijdewind I, Toering ST, Bessem B, Van Der Laan O, Diercks RL. Effects of imagery motor training on torque production of ankle plantar flexor muscles. *Muscle Nerve*. 2003;28:168–173.
27. Pascual-Leone A, Nguyet D, Cohen LG, Brasil-Neto JP, Cammarota A, Hallett M. Modulation of muscle responses evoked by transcranial magnetic stimulation during the acquisition of new fine motor skills. *J Neurophysiol*. 1995;74:1037–1045.
28. Jackson PL, Lafleur MF, Malouin F, Richards CL, Doyon J. Functional cerebral reorganization following motor sequence learning through mental practice with motor imagery. *Neuroimage*. 2003;20:1171–1180.
29. Page SJ, Levine P, Sisto S, Johnston MV. A randomized efficacy and feasibility study of imagery in acute stroke. *Clin Rehabil*. 2001;15:233–240.
30. Crosbie JH MS, Gilmore DH, Wiggam MI. The adjunctive role of mental practice in the rehabilitation of the upper limb after hemiplegic stroke: A pilot study. *Clin Rehabil*. 2004;18:60–68.
31. Dijkerman HC LM, Johnston M, MacWalter RS. Does motor imagery training improve hand function in chronic stroke patients? A pilot study. *Clin Rehabil*. 2004;18:538–549.
32. Liu KP, Chan CC, Lee TM, Hui-Chan CW. Mental imagery for promoting relearning for people after stroke: A randomized controlled trial. *Arch Phys Med Rehabil*. 2004;85:1403–1408.
33. Page SJ, Levine P, Leonard AC. Effects of mental practice on affected limb use and function in chronic stroke. *Arch Phys Med Rehabil*. 2005;86:399–402.
34. Grezes JDJ. Functional anatomy of execution, mental simulation, observation, and verb generation of actions: A meta-analysis. *Hum Brain Mapp*. 2001;12:1–19.

35. Decety J, Grezes J. Neural mechanisms subserving the perception of human actions. *Trends in Cognitive Sciences*. 1999;3:172–178.

36. Jeannerod M. Mental imagery in the motor context. *Neuropsychologia*. 1995;33:1419–1432.

37. Berthoz A. The role of inhibition in the hierarchical gating of executed and imagined movements. *Brain Res Cogn Brain Res*. 1996;3:101–113.

38. Wolpert DM GZ. Computational principles of movement neuroscience. *Nat Neurosci*. 2000;3:Suppl:1212–1217.

39. Dominey P, Decety J, Broussolle E, Chazot G, Jeannerod M. Motor imagery of a lateralized sequential task is asymmetrically slowed in hemi-Parkinson's patients. *Neuropsychologia*. 1995;33:727–741.

40. de Lange FP, Kalkman JS, Bleijenberg G, Hagoort P, vd Werf SP, van der Meer JWM, Toni I. Neural correlates of the chronic fatigue syndrome–an fMRI study. *Brain*. 2004;127:1948–1957.

41. Sirigu A, Daprati E, Pradat-Diehl P, Franck N, Jeannerod M. Perception of self-generated movement following left parietal lesion. *Brain*. 1999;122(Pt 10):1867–1874.

42. Tomasino B, Toraldo A, Rumiati RI. Dissociation between the mental rotation of visual images and motor images in unilateral brain-damaged patients. *Brain and Cognition*. 2003;51:368–371.

43. Tomasino B, Rumiati RI, Umilta CA. Selective deficit of motor imagery as tapped by a left-right decision of visually presented hands. *Brain Cogn*. 2003;53:376–380.

44. Johnson SH. Imagining the impossible: Intact motor representations in hemiplegics. *Neuroreport*. 2000;11:729–732.

45. Johnson SH, Sprehn G, Saykin AJ. Intact motor imagery in chronic upper limb hemiplegics: Evidence for activity-independent action representations. *J Cogn Neurosci*. 2002;14:841–852.

46. Ganis G, Keenan JP, Kosslyn SM, Pascual-Leone A. Transcranial magnetic stimulation of primary motor cortex affects mental rotation. *Cereb Cortex*. 2000;10:175–180.

47. Tomasino BBR, Mondani M, Skrap M, Rumiati RI. Mental rotation in a patient with an implanted electrode grid in the motor cortex. *Neuroreport*. 2005;16:1795–1800.

48. Gonzalez BRM, Ramirez C, Sabate M. Disturbance of motor imagery after cerebellar stroke. *Behav Neurosci*. 2005;119:622–626.

49. Malouin FRC, Desrosiers J, Doyon J. Bilateral slowing of mentally simulated actions after stroke. *Neuroreport*. 2004;15:1349–1353.

50. Malouin F, Belleville S, Richards CL, Desrosiers J, Doyon J. Working memory and mental practice outcomes after stroke. *Arch Phys Med Rehabil*. 2004;85:177–183.

51. Sabate M, Gonzalez B, Rodriguez M. Brain lateralization of motor imagery: Motor planning asymmetry as a cause of movement lateralization. *Neuropsychologia*. 2004;42:1041–1049.

52. Jeannerod M, Decety J. Mental motor imagery: A window into the representational stages of action. *Curr Opin Neurobiol*. 1995;5:727–732.

53. Guillot A, Collet C. Contribution from neurophysiological and psychological methods to the study of motor imagery. *Brain Research Reviews*. 2005;50:387–397.

54. Hall CR, Pongrac J, and Buckholz E. The measurement of imagery ability. *Human Movement Science*. 1985;4:107–118.

55. Hall CMK. Measuring movement imagery abilities: A revision of the movement imagery questionnaire. *Journal of Mental Imagery*. 1997;21:143–154.

56. Naito E. Controllability of motor imagery and transformation of visual imagery. *Percept Mot Skills*. 1994;78:479–487.

57. Parsons LM, Fox PT, Downs JH, Glass T, Hirsch TB, Martin CC, Jerabek PA, Lancaster JL. Use of implicit motor imagery for visual shape discrimination as revealed by PET. *Nature*. 1995;375:54–58.

58. Hanakawa T, Immisch I, Toma K, Dimyan MA, Van Gelderen P, Hallett M. Functional properties of brain areas associated with motor execution and imagery. *J Neurophysiol*. 2003;89:989–1002.

59. Sharma NSL, Jones PS, Day DJ, Carpenter TA, Warburton EA, Baron JC. Is the primary motor cortex (M1) involved during mental motor imagery (MMI) in stroke patients: A functional magnetic resonance imaging (fMRI) study. *Cerebralvascular Disease*. 2006;21(suppl 4):2.

60. Lafleur MF, Jackson PL, Malouin F, Richards CL, Evans AC, Doyon J. Motor learning produces parallel dynamic functional changes during the execution and imagination of sequential foot movements. *NeuroImage*. 2002;16:142–157.

61. Malouin F, Richards CL, Jackson PL, Dumas F, Doyon J. Brain activations during motor imagery of locomotor-related tasks: A PET study. *Hum Brain Mapp*. 2003;19:47–62.

62. Gerardin E, Sirigu A, Lehericy S, Poline JB, Gaymard B, Marsault C, Agid Y, Le Bihan D. Partially overlapping neural networks for real and imagined hand movements. *Cereb Cortex*. 2000;10:1093–1104.

63. Naito E, Kochiyama T, Kitada R, Nakamura S, Matsumura M, Yonekura Y, Sadato N. Internally simulated movement sensations during motor imagery activate cortical motor areas and the cerebellum. *J Neurosci*. 2002;22:3683–3691.

64. Cramer SC, Nelles G, Schaechter JD, Kaplan JD, Finklestein SP. Computerized measurement of motor performance after stroke. *Stroke*. 1997;28:2162–2168.

65. Calautti C. JP, Persaud N, Guincestre JY, Naccarato M, Warburton EA, Baron JC. Quantification of finger tapping rate regularity after stroke with tri-axial accelerometry. *Brain Res Bull*. 2006;70:1–7.

66. Rodriguez M, Muniz R, Gonzalez B, Sabate M. Hand movement distribution in the motor cortex: The influence of a concurrent task and motor imagery. *NeuroImage*. 2004;22:1480–1491.

67. Dickstein RDA, Marcovitz E. Motor imagery for gait rehabilitation in post-stroke hemiparesis. *Phys Ther*. 2004;84:1167–1177.

68. Gaggioli AMF, Walker R, Meneghini A, Alcaniz M, Lozano JA, Montesa J, Gil JA, Riva G. Training with computer-supported motor imagery in post-stroke rehabilitation. *Cyberpsychol Behav*. 2004;7:327–332.

69. Jackson PL, Doyon J, Richards CL, Malouin F. The efficacy of combined physical and mental practice in the learning of a foot-sequence task after stroke: A case report. *Neurorehabil Neural Repair*. 2004;18:106–111.

70. Liu KP CC, Lee TM, Hui-Chan CW. Mental imagery for relearning of people after brain injury. *Brain Inj*. 2004;18:1163–1172.

71. Malouin F, Richards CL, Doyon J, Desrosiers J, Belleville S. Training mobility tasks after stroke with combined mental and physical practice: A feasibility study. *Neurorehabil Neural Repair*. 2004;18:66–75.

72. Page SJ, Levine P, Sisto SA, Johnston MV. Mental practice combined with physical practice for upper-limb motor deficit in subacute stroke. *Phys Ther*. 2001;81:1455–1462.

73. Stevens JA, Stoykov MEP. Using motor imagery in the rehabilitation of hemiparesis. *Arch Phys Med Rehabil*. 2003;84:1090–1092.

74. Yoo E, Park E, Chung B. Mental practice effect on line-tracing accuracy in persons with hemiparetic stroke: A preliminary study. *Arch Phys Med Rehabil*. 2001;82:1213–1218.

75. Weiss THE, Rost R, Beyer L, Merten F, Nichelmann C, Zippel C. Mental practice of motor skills used in poststroke rehabilitation has own effects on central nervous activation. *Int J Neurosci*. 1994;78:157–166.

76. Kuhtz-Buschbeck JP, Mahnkopf C, Holzknecht C, Siebner H, Ulmer S, Jansen O. Effector-independent representations of simple and complex imagined finger movements: A combined fMRI and TMS study. *Eur J Neurosci*. 2003;18:3375–3387.

77. Decety J, Perani D, Jeannerod M, Bettinardi V, Tadary B, Woods R, Mazziotta JC, Fazio F. Mapping motor representations with positron emission tomography. *Nature*. 1994;371:600–602.

78. Dechent P, Merboldt K-D, Frahm J. Is the human primary motor cortex involved in motor imagery? *Cognitive Brain Research*. 2004;19:138–144.

79. Grafton ST AM, Fadiga L, Rizzolatti G. Localization of grasp representations in humans by positron emission tomography. 2. Observation compared with imagination. *Exp Brain Res*. 1996;112:103–111.

80. Krams M, Rushworth MFS, Deiber M-P, Frackowiak RSJ, Passingham RE. The preparation, execution and suppression of copied movements in the human brain. *Exp Brain Res*. 1998;120:386–398.

81. Porro CA, Francescato MP, Cettolo V, Diamond ME, Baraldi P, Zuiani C, Bazzocchi M, di Prampero PE. Primary motor and sensory cortex activation during motor performance and motor imagery: A functional magnetic resonance imaging study. *J Neurosci*. 1996;16:7688–7698.

82. Porro CA, Cettolo V, Francescato MP, Baraldi P. Ipsilateral involvement of primary motor cortex during motor imagery. *Eur J Neurosci*. 2000;12:3059–3063.

83. Stephan KM, Fink GR, Passingham RE, Silbersweig D, Ceballos-Baumann AO, Frith CD, Frackowiak RS. Functional anatomy of the mental representation of upper extremity movements in healthy subjects. *J Neurophysiol*. 1995;73:373–386.

84. Vingerhoets G, de Lange FP, Vandemaele P, Deblaere K, Achten E. Motor imagery in mental rotation: An fMRI study. *NeuroImage*. 2002;17:1623–1633.

85. Johnson SH, Rotte M, Grafton ST, Hinrichs H, Gazzaniga MS, Heinze HJ. Selective activation of a parietofrontal circuit during implicitly imagined prehension. *Neuroimage*. 2002;17:1693–1704.

86. Luft AR, Skalej M, Stefanou A, Klose U, Voigt K. Comparing motion- and imagery-related activation in the human cerebellum: A functional MRI study. *Hum Brain Mapp*. 1998;6:105–113.

87. Stippich C, Ochmann H, Sartor K. Somatotopic mapping of the human primary sensorimotor cortex during motor imagery and motor execution by functional magnetic resonance imaging. *Neuroscience Letters*. 2002; 331:50–54.

88. Ehrsson HH, Geyer S, Naito E. Imagery of voluntary movement of fingers, toes, and tongue activates corresponding body-part–specific motor representations. *J Neurophysiol*. 2003;90:3304–3316.

89. Nair DG, Purcott KL, Fuchs A, Steinberg F, Kelso JAS. Cortical and cerebellar activity of the human brain during imagined and executed unimanual and bimanual action sequences: A functional MRI study. *Cognitive Brain Research*. 2003;15:250–260.

90. Roth M, Decety J, Raybaudi M, Massarelli R, Delon-Martin C, Segebarth C, Morand S, Gemignani A, Decorps M, Jeannerod M. Possible involvement of primary motor cortex in mentally simulated movement: A functional magnetic resonance imaging study. *Neuroreport*. 1996;7: 1280–1284.

91. Jahn K, Deutschlander A, Stephan T, Strupp M, Wiesmann M, Brandt T. Brain activation patterns during imagined stance and locomotion in functional magnetic resonance imaging. *NeuroImage*. 2004;22: 1722–1731.

92. Binkofski FAK, Stephan KM, Posse S, Schormann T, Freund H, Zilles K, Seitz RJ. Broca's region subserves imagery of motion: A combined cytoarchitectonic and fMRI study. *Human Brain Mapping*. 2000;11: 273–285.

93. Boecker H, Ceballos-Baumann AO, Bartenstein P, Dagher A, Forster K, Haslinger B, Brooks DJ, Schwaiger M, Conrad B. A h215o positron emission tomography study on mental imagery of movement sequences–the effect of modulating sequence length and direction. *NeuroImage*. 2002;17:999–1009.

94. Lacourse MG, Orr ELR, Cramer SC, Cohen MJ. Brain activation during execution and motor imagery of novel and skilled sequential hand movements. *NeuroImage*. 2005;27:505–519.

95. Hanakawa T, Parikh S, Bruno MK, Hallett M. Finger and face representations in the ipsilateral precentral motor areas in humans. *J Neurophysiol*. 2005;93:2950–2958.

96. Solodkin A, Hlustik P, Chen EE, Small SL. Fine modulation in network activation during motor execution and motor imagery. *Cereb Cortex*. 2004;14:1246–1255.

97. Niyazov DM, Butler AJ, Kadah YM, Epstein CM, Hu XP. Functional magnetic resonance imaging and transcranial magnetic stimulation: Effects of motor imagery, movement and coil orientation. *Clinical Neurophysiology*. 2005;116:1601–1610.

98. Chau W, McIntosh AR. The Talairach coordinate of a point in the MNI space: How to interpret it. *NeuroImage*. 2005;25:408–416.

99. Lotze M, Montoya P, Erb M, Hulsmann E, Flor H, Klose U, Birbaumer N, Grodd W. Activation of cortical and cerebellar motor areas during executed and imagined hand movements: An fMRI study. *J Cogn Neurosci*. 1999;11:491–501.

100. Johansen-Berg H, Rushworth MFS, Bogdanovic MD, Kischka U, Wimalaratna S, Matthews PM. The role of ipsilateral premotor cortex in hand movement after stroke. *PNAS*. 2002;99:14518–14523.

101. Lehericy SCG, Gerardin E, Poline JB, Meunier S, Van de Moortele PF, Le Bihan D, Vidailhet M. Motor execution and imagination networks in post-stroke dystonia. *Neuroreport*. 2004;15:1887–1890.

102. Gonzalez-Hernandez JA, Cespedes-Garcia Y, Campbell K, Scherbaum WA, Bosch-Bayard J, Figueredo-Rodriguez P. A pre-task resting condition neither 'baseline' nor 'zero'. *Neurosci Lett*. 2005;391:43–47.

103. Schnitzler A, Salenius S, Salmelin R, Jousmaki V, Hari R. Involvement of primary motor cortex in motor imagery: A neuromagnetic study. *NeuroImage*. 1997;6:201–208.

104. Kawamichi H, Kikuchi Y, Endo H, Takeda T, Yoshizawa S. Temporal structure of implicit motor imagery in visual hand-shape discrimination as revealed by MEG. *Neuroreport*. 1998;9:1127–1132.

105. Caldara R, Deiber M-P, Andrey C, Michel CM, Thut G, Hauert C-A. Actual and mental motor preparation and execution: A spatiotemporal ERP study. *Exp Brain Res*. 2004;159:389–399.

106. Pfurtscheller G, Neuper C, Ramoser H, Muller-Gerking J. Visually guided motor imagery activates sensorimotor areas in humans. *Neurosci Lett*. 1999;269:153–156.

107. Fadiga L, Buccino G, Craighero L, Fogassi L, Gallese V, Pavesi G. Corticospinal excitability is specifically modulated by motor imagery: A magnetic stimulation study. *Neuropsychologia*. 1998;37:147–158.

108. Hashimoto R, Rothwell JC. Dynamic changes in corticospinal excitability during motor imagery. *Exp Brain Res*. 1999;125:75–81.

109. Vargas CD, Olivier E, Craighero L, Fadiga L, Duhamel JR, Sirigu A. The influence of hand posture on corticospinal excitability during motor imagery: A transcranial magnetic stimulation study. *Cereb Cortex*. 2004;14:1200–1206.

110. Cicinelli P, Marconi B, Zaccagnini M, Pasqualetti P, Filippi MM, Rossini PM. Imagery-induced cortical excitability changes in stroke: A transcranial magnetic stimulation study. *Cereb Cortex*. 2006;16:247–253.

111. Carpenter AF, Georgopoulos AP, Pellizzer G. Motor cortical encoding of serial order in a context-recall task. *Science*. 1999;283:1752–1757.

112. Pellizzer GSP, Georgopoulos AP. Motor cortical activity in a context-recall task. *Science*. 1995;269:702–705.

113. Shen L, Alexander GE. Neural correlates of a spatial sensory-to-motor transformation in primary motor cortex. *J Neurophysiol*. 1997;77: 1171–1194.

114. Binkofski F, Fink GR, Geyer S, Buccino G, Gruber O, Shah NJ, Taylor JG, Seitz RJ, Zilles K, Freund H-J. Neural activity in human primary motor cortex areas 4a and 4p is modulated differentially by attention to action. *J Neurophysiol*. 2002;88:514–519.

115. Classen J, Liepert J, Wise SP, Hallett M, Cohen LG. Rapid plasticity of human cortical movement representation induced by practice. *J Neurophysiol*. 1998;79:1117–1123.

116. Tokuno H, Nambu A. Organization of nonprimary motor cortical inputs on pyramidal and nonpyramidal tract neurons of primary motor cortex: An electrophysiological study in the macaque monkey. *Cereb Cortex*. 2000;10:58–68.

117. Civardi C, Cantello R, Asselman P, Rothwell JC. Transcranial magnetic stimulation can be used to test connections to primary motor areas from frontal and medial cortex in humans. *NeuroImage*. 2001;14:1444–1453.

118. Munchau A, Bloem BR, Irlbacher K, Trimble MR, Rothwell JC. Functional connectivity of human premotor and motor cortex explored with repetitive transcranial magnetic stimulation. *J Neurosci*. 2002;22: 554–561.

119. Pomeroy VM, Clark CA, Miller JSG, Baron J-C, Markus HS, Tallis RC. The potential for utilizing the "Mirror neurone system" to enhance recovery of the severely affected upper limb early after stroke: A review and hypothesis. *Neurorehabil Neural Repair*. 2005;19:4–13.

120. Alkadhi H, Brugger P, Boendermaker SH, Crelier G, Curt A, Hepp-Reymond M-C, Kollias SS. What disconnection tells about motor imagery: Evidence from paraplegic patients. *Cereb Cortex*. 2005;15: 131–140.

121. Sabbah P, de Schonen S, Leveque C, Gay S, Pfefer F, Nioche C, Sarrazin J-L, Barouti H, Tadie M, Cordoliani Y-S. Sensorimotor cortical activity in patients with complete spinal cord injury: A functional magnetic resonance imaging study. *J Neurotrauma*. 2002;19:53–60.

122. Bamford JSP, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet*. 1991;337:1521–1526.

123. Peters M, Laeng B, Latham K, Jackson M, Zaiyouna R, Richardson C. A redrawn vandenberg and kuse mental rotations test - different versions and factors that affect performance. *Brain and Cognition*. 1995;28: 39–58.