Mental Practice through motor imagery in gait rehabilitation following acquired brain injury

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Preface

The last two decades imaging technology (e.g. functional magnetic resonance imaging; fMRI) has profoundly changed our insights into rehabilitation and rehabilitation techniques.

Research has shown that repeatedly practising a functional task does not only change motor performance of our patients but actually guides neural plasticity. Frequent repetition of functionally relevant tasks has been proven to influence cortical reorganization and to prevent maladaptive non-use.

Motor learning brings about a permanent change in an individual’s motor performance as a result of practice and shows the capacity of the adult brain to adapt and change!

Furthermore, fMRI research has demonstrated that execution of a certain action and imaging and observation of this action activate overlapping brain regions. This functional equivalence opens various opportunities for the development of new rehabilitation strategies.

Mental practice is a training method whereby repetitive imagination of a movement is required but no actual movement takes place. Mental practice through motor imagery has long been recognized by sport performers and coaches as a valuable technique to promote the learning of motor skills. During the last decade several investigators have shown that mental practice using motor imagery can also be applied in people with neurological disorders to promote motor recovery. Most of this research however focused on upper limb rehabilitation after stroke. Moreover, most studies focused on teaching a single skill which is rarely relevant to the level of activity and participation of the individual. Applying mental practice in gait rehabilitation would offer the opportunity to teach skills that are rated as very important by most patients. Additionally, practicing daily functional skills such as climbing a stair or walking in different challenging environments could potentially enhance the participation level of the patients post-stroke.

Furthermore, once the Mental Practice technique is acquired, it can be practiced by the patient in the home environment without the continuous assistance of a therapist, thus enhancing the patients’ self-efficacy.

Working in the gait lab with Frank Plasschaert, Malcolm Forward and Kim Jones, it seemed a great opportunity to apply our knowledge about hemiplegic gait and to investigate the results of this intriguing new rehabilitation technique in gait rehabilitation after stroke.

Guided by the neuropsychological insights of Prof Dr Guy Vingerhoets, we further investigated motor imagery ability after acquired brain injury and tried to link brain lesions to poor motor imagery performance.

Chapter 1

General introduction

1.1 Motor Imagery

1.1.1 Definition

Mental imagery refers to the remarkable capacity to represent and manipulate perceptual information in the mind in the absence of an immediate related sensory input. Perceptual information is generated within the working memory, giving rise to the experience of ‘seeing with the mind’s eye, ‘hearing with the mind’s ear’ or ‘sense the movement of the body through one’s mind’.[1]

Mental imagery has been studied for centuries since the time of Plato but has fallen in and out of fashion because it was difficult to study due to its inherently internal nature. However, the emergence of cognitive neuroscience and the possibilities of new neuro-imaging techniques have boosted imagery research for the last three decades.

Mental imagery can involve all the senses but this thesis will focus on motor imagery (MI), the mental simulation of a given motor action in the absence of its actual execution [2,3].

MI can be defined as the cognitive process of imagining a movement of a body (-part) without actually moving that body (-part) [4]. It involves the generation of a complete motor plan that is blocked at some level from operating on the body. MI represents an image generation within the working memory that further can be transformed, maintained and inspected [5].

MI enables one to practice movements without needing to physically perform them. For this reason, MI has proven to be valuable in a variety of circumstances such as athlete's or musician training, training of surgical skills and rehabilitation after stroke [6].

The ‘simulation’ hypothesis states that overt movement and MI (covert movement) are essentially based on the same neural mechanisms. This implies that MI may be seen as an off-line activation of the motor system in the brain [5]. Moreover several behavioral studies have shown that imagined actions follow the same constraints as their corresponding executed actions and thus conform to Fitts’ law that describes the inverse and logarithmic relationship between the difficulty of a movement and the speed with which it can be performed [3,7].

MI is closely related to cognitive movement strategies such as the preparation for and anticipation of a motor action and is thus widely used to study the cognitive aspects of neural control of motor actions in both healthy people and clinical populations [8-10].

Different varieties of motor imagery have been described according to three related image characteristics: image modality, image agency and image perspective [11,12]. Several **imagery modalities** can be distinguished. Visual imagery implies self-visualization of a movement, whereas kinesthetic imagery requires a person to ‘feel’ the movement by asking them to focus on vivid kinesthetic sensations related to that movement. Imagery can further be categorized from the **image perspective** as either external or internal. The internal perspective involves a person’s engagement from the *first person perspective*, i.e. one can feel or see one’s own body (-part) move with respect to one’s body. The external perspective involves imaging oneself from *the third person* perspective, i.e. one can see how a body (-part) would move as if looking from a distance at oneself. *External imagery* can involve the self or another individual as the **imagery agent**. One can imagine the person or the environment or both. It has been demonstrated that different brain areas are involved during motor imagery depending on the image perspective and image modality used. Kinesthetic imagery elicits a brain activation that is most similar to neural activation during actual execution and is therefore promoted for use in MI practice [13,14].

Motor imagery can further be elicited **implicitly** or **explicitly**, the main difference being the degree of awareness of motor simulation that the participant has when performing the tasks [15]. *Explicit imagery* tasks require participants to mentally execute a movement and imply that the individual consciously performs a mental simulation of a motor task. Here imagery involves a voluntary active imagination. On the other hand *implicit imagery* tasks require the participant to make a judgment about handedness of a limb for example (Hand Laterality Task) or to answer which kind of grip he would prefer to grasp a dowel/wooden bar in a particular orientation (Grip Selection Task). Here motor imagery is used covertly without awareness of the mental simulation. Implicit motor imagery tasks allow us to quantify motor imagery performance, by counting the number of correct answers over the total number of presented stimuli or by evaluating the (differences in) duration between motor-related decisions. These behavioral data are used to measure motor imagery accuracy [16,17].
Motor imagery ability can vary widely between individuals. Moreover, researchers have successfully demonstrated a relationship between imagery ability and motor performance [18]. High imagers were shown to learn a set of simple movements in the least number of trails and with more accuracy than low imagers. Therefore it is well-advised to assess an

individual’s MI ability before implementing mental practice. However, the internal cognitive process of MI is inherently difficult to measure objectively.
How do we know if people are able to imagine movements vividly and accurately? The following paragraph provides an overview of the different methods used to measure motor imagery ability.

1.1.2 Motor Imagery Ability

Questionnaires, mental chronometry paradigms, and tasks based on mental rotation paradigms are most often used to measure the different domains of imagery, more specifically MI vividness, temporal organization, and MI accuracy. Individual performance on these different measures may vary and different tasks seem to address different components of MI ability. Therefore MI ability should best be measured using a combination of these different MI tasks [19].

Questionnaires such as the Motor Imagery Questionnaire (MIQ) measure MI vividness, more specifically the clarity/sharpness of images and intensity of sensations during MI [20]. Subjects have to indicate the ease with which they are able to imagine certain movements. The MIQ incorporates two subscales, the visual and kinesthetic subscale, designed to measure the visual and kinesthetic components of movement imagery. MI questionnaires are shown to be reliable and valid tools to screen for MI vividness [21]. The scores remain a subjective reflection of the MI capacity of the individual and this subjectivity of the information given by the subject remains an important disadvantage of this MI measure [17]. However, a study by Lorey [22], examining brain activation patterns during the imaging of movements, has shown a close relationship between the MI vividness scores and the level of brain activation
The Motor Imagery Questionnaire-Revised, Second edition (MIQ-RS) is a questionnaire developed by Gregg and co-workers [23] to measure motor imagery vividness in people with restricted mobility. Both the MIQ-RS and the Kinesthetic and Visual Imagery Questionnaire (KVIQ) developed by Malouin, were specifically designed to assess MI ability in stroke populations [24,25]. All of the tasks they comprise, are safe and not physically demanding. Moreover the functional tasks included on the MIQ-RS are a valid representation of an individual’s daily activities [24].

Second, ***mental chronometry tasks*** give information about the temporal coupling between real and simulated movements and the ability to preserve the temporal organization of the imagined movement [26]. Chronometry studies have shown that there is a close temporal correlation between actual and imagined movements. Decety and his colleagues showed, in several experiments, that the time it takes to physically perform a given task is nearly identical to the time taken to mentally imagine the same task [27]. Executed and imagined writing of the same letters of the alphabet, or executed and imagined walking of the same distance show the same durations. Fitt's law, that states that more difficult movements take more time to produce than do easier ones, also applies to imagined movements [3]. Imagined walking times increase with increasing movement distance and difficulty. For example, Bakker reported that imagined walking along a narrow path required more voluntary control than walking along a broad path, with imagined movement times increasing with increasing path length and decreasing path width [28]. The ability to preserve the strong relationship between imagined and actual movement times is a reliable marker for MI accuracy [16,26]. Personnier showed that older adults systematically overestimate the duration of imagined movements, indicating a decline in motor imagery ability and motor planning in the aging brain [29].

Malouin and co-workers developed two different chronometric tests to measure temporal organization of motor imagery in neurologic conditions [30]. The Time-dependent motor imagery (TDMI) screening test measures the number of imagined movements over 3 periods of time. It is expected that the number of movements will increase with an increasing time period. The TDMI test only involves imagined movements and provides a first indication that patients understand the instructions and are able to simulate movements. The temporal congruence test compares real and imagined movement times and the imagined movement time/ executed movement time ratio provides a quantitative measure of the temporal organization of motor imagery. Temporal congruence implies that factors influencing executed movement times yield parallel changes on imagery movement times. However mental chronometry is influenced by several factors, such as duration and complexity of the task, the type of MI (kinesthetic or visual) and task instructions [31]. It has been shown that real-virtual temporal congruency increases with task complexity. Whereas simple motor tasks that can be partially automated, give rise to low temporal congruence, complex movements that need conscious supervision are characterized by high temporal correspondence [32]. Real and imagined movement durations can be highly correlated, but with a persistent overestimation or underestimation due to task specificities. This absence of isochrony is not necessarily due to a lack of MI ability. Task duration should ideally range from 5 to 25 sec to avoid a negative impact on isochrony [26,33].

A third method for measuring motor imagery ability is based on ***mental rotation paradigms*** and measures mental rotation times. In (Hand) Laterality Judgement tasks, pictures of hands (or other body parts) are presented in different orientations and participants have to make a laterality judgement, i.e. decide whether a left or right hand is presented, as fast and as accurately as possible. Parsons showed that the time required to make a handedness judgement about a visually presented hand is proportional to the time required to actually move the hand from its current position into the stimulus orientation [7]. Moreover response times of rotation of bodily parts are dependent on biomechanical constraints. The mental rotation time of biomechanically difficult rotations is slower than the response time for biomechanically easy rotations [34].

In Prospective Action Judgement tasks the participants are asked to make judgements about a grip selection. The time needed to make a prospective grip selection increases with the level of awkwardness that the selected grip causes. These results suggest that participants are engaged in implicit MI during these mental rotation tasks [19].

Finally, several studies have shown that ***vegetative responses*** (e.g. heart rate, respiratory rhythms, oxygen consumption) during mental practice vary to the same extent as the imagined effort [17]. Three different physiological categories can be recorded: the electro-dermal category (skin resistance), the thermo-vascular category (skin temperature, skin blood flow) and the cardio-respiratory category (heart rate and respiratory frequency). This autonomic neuron system monitoring seems to be complementary to the aforementioned psychometric tests [17]. The observed increase in heart rate and respiration frequency is thought to be regulated in the brain and seems to suggest that the brain prepares the body as if the movement is going to be executed [35].

Many researchers have investigated brain activity that occurs when one is imagining a movement and its relationship with brain activity provoked by real movement. Neuroimaging findings have shown that similar areas of the brain are activated when both imagining and physically performing a movement. This motor imagery related brain activity will be highlighted in the next paragraph.

1.1.3 Motor Imagery and neuroimaging

Research suggests that MI shares cortical circuitry with movement preparation and movement execution [36]. Imagined and actual motor activity are so called ‘functionally equivalent’, a term which refers to the similarity between both actions. Indeed, the time to mentally perform an action is similar to the time needed to actually perform the action. The vegetative responses associated with mentally performed actions are closely related to the vegetative responses that accompany real action. Furthermore, evidence from different imaging techniques reveals that both, real and imagined action, partially activate the same neural circuitry [16,36]. Especially first person and kinesthetic MI seem to show functional equivalence with actual motor execution [37]. Although a reduced brain activity intensity by 30 to 50 % is recorded during MI compared with brain activity during actual motor execution, MI expertise has been shown to lead to a more focused recruitment of the involved brain region and higher activation intensity [16,38].

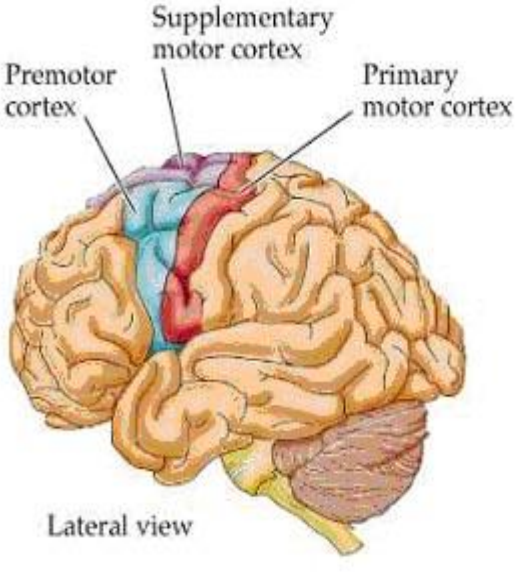
In an activation likelihood estimation (ALE) meta-analysis, Hetu was able to compile a map of structures involved in MI brain activation. The meta-analysis reveals the existence of a large fronto-parietal network, which is activated during MI, in addition to relevant subcortical and cerebellar regions [39]. The parts of the neural system that are most frequently reported to be involved in motor imagery include the pre-motor cortex, the dorsolateral prefrontal cortex, the inferior frontal cortex, the posterior parietal cortex, the cerebellum, and the basal ganglia [16,39,40]. The posterior supplementary motor area (SMA) and the premotor cortex seem to be highly important areas for movement imagery, as they are consistently reported to be active in all MI protocols [5,36,41]. The SMA region is involved in the preparation of movements and thus is closely related to MI.

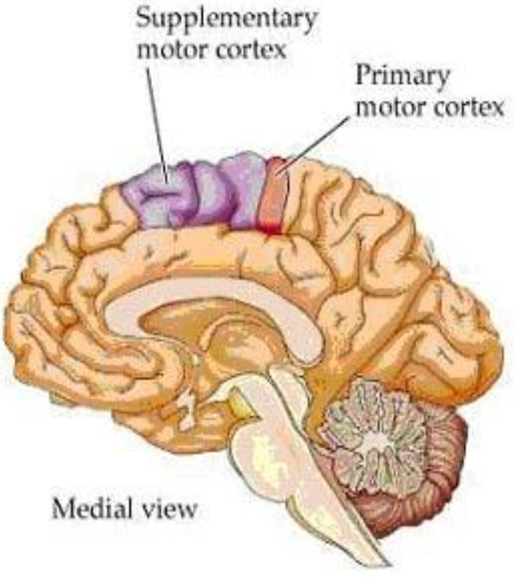
Brain activity during MI also seems to present in a somatopic pattern. Bakker showed that motor imagery of gait resulted in activation of the bilateral dorsal premotor cortex, the superior parietal lobule, the right rostral cingulate zone and the left putamen. Neural activity related to gait was adjacent but distinct from regions involved in motor imagery of hand movements [42].

Several authors have also demonstrated left hemisphere dominance for motor planning and motor imagery in humans, particularly when complex sequential movements are involved [43-46].

Recently Sharma and Baron performed a multi-variate fMRI analysis and reported that imagined and executed movements do indeed share a broad neural network [47]. An important area that was shown to be shared is the primary motor cortex M1. The activation of the primary motor cortex during motor imagery is considered to be controversial [48]. Imagery is normally assumed to be performed in the absence of overt movement, and M1 primarily represents the executional part of the motor system. So no activity is to be expected in this motor area during the imagination of movements. However several studies reveal significant M1 activation, although smaller compared with that in execution [9]. MI activation of the M1 region seems to be intensity dependent and motor neurons activated during imagery are probably located more anteriorly to those active during execution [35].

It can be concluded that MI and motor execution share many neural substrates but that these are not completely overlapping. The shared networks are activated in a hierarchical manner with MI leading to less intensive neural activity than executed movement. Furthermore, most functional brain imaging studies show an anterior-posterior extension toward additional prefrontal and posterior parietal regions during MI as compared to motor execution [49]. Therefore complete functional equivalence between MI and actual motor execution cannot be assumed [12].





1.1.4 Motor Imagery ability after acquired brain injury

Although not completely overlapping, MI and motor execution share many neural networks. What happens when these neural pathways are damaged due to an acquired brain injury? A patient's brain damage may prevent successful MI performance. Are patients with a brain lesion caused by a TBI or by cerebrovascular disease still able to imagine movements and hence become candidates for mental practice through MI?

TBI survivors frequently have persistent cognitive impairments, involving attention, memory and impulse control. Connectivity between key-parts of the neural network can be compromised by the injury, resulting in cognitive and motor decline. The spatially remote nature of the motor network structures makes this network especially vulnerable to white matter lesions. Lotze and co-workers [50] showed a correlation between clinical impairment and a diminished fMRI signal in the contra-lateral primary sensorimotor cortex and bilateral supplementary motor cortex (SMA). This reduced SMA activation after TBI could equally impair the planning of a motor action. Moreover many TBI patients present with prefrontal lesions. A reduced input from the prefrontal region potentially leads to a reorganization of the motor preparatory network and reduced motor imagery ability [51].

Overall, the neural process controlling MI seems to be following the same reorganization that is apparent in active movement [36].

A review by Di Rienzo investigated MI ability in different neurologic populations.

This investigator concluded that overall cerebral activity in stroke patients seems to reflect structural and functional neuroplasticity [16].

Although the ability to perform MI seems to be at least partially preserved after stroke, MI vividness, accuracy, and temporal coupling can be hampered. Sharma refers to this disturbed accuracy and/or temporal uncoupling as ‘chaotic’ post-stroke MI [52,53].

However, using the Kinesthetic and Visual Imagery Questionnaire (KVIQ), Malouin and co-workers found that persons after stroke- without severe communication and perceptual problems- presented similar levels of MI vividness compared to age-matched healthy controls. Persons with stroke however displayed higher imagery scores when imaging movements on the unaffected side [54].

These investigators further demonstrated that the temporal coupling between real and imagined movements was impaired after stroke. Imagined movement times/ executed movement times ratios were quite variable across subjects in their stroke cohort in contrast to the healthy controls. These findings were confirmed by Sirigu, who also demonstrated that patients with posterior parietal lesions were deficient in imagining the temporal aspects of movements. Patients with left parietal lesions exhibited partial or complete bilateral impairment of MI [55]. Overall four types of temporal coupling patterns have been described after stroke: preserved temporal coupling, similar to that in healthy persons, preserved temporal coupling reflecting the motor deficit, temporal uncoupling restricted to the impaired limb and finally temporal uncoupling irrespective of the clinical deficit [16]. Liepert reported that stroke patients with somatosensory deficits were more impaired when performing mental chronometry tasks than patients with a pure motor deficit and raised the question of whether these patients might still be suitable for MI training [31].

Using implicit MI tasks Johnson and co-workers found that the ability to construct action representations was largely unaffected in patients with chronic hemiparesis and independent from actual motor recovery if no parietal cortex or premotor areas were involved [56]. In a study by Li on the other hand, patients with putamen and cortical (frontotemporal/frontoparietal) lesions showed impaired limb-specific first-person movement imagery [57].

In stroke patients, the activation of the neural MI network seems to reflect the neuroplasticity related to both motor deficit and motor recovery. Functional equivalence is preserved after stroke with MI recruiting the same reorganized network as that of physical practice [16]. Several authors have demonstrated a preservation of similar brain activation patterns between MI and action execution in stroke patients, mirroring this neuroplasticity [36,58,59]. Dodakian found that in individuals with hemiparesis after stroke, MI associated with movement engaged additional brain regions compared to that of movement alone. More specifically, the dorsal prefrontal cortex and inferior parietal lobule were activated during movement combined with MI [60]. Confalonieri reported preserved shared brain activations during MI and motor execution in stroke patients, involving a distributed frontoparietal network and subcortical structures. Moreover patients with higher kinesthetic MI ability exhibited lower cortical activation compared to patients with a lower kinesthetic subscore [61].

In conclusion it appears therefore that results concerning MI ability in stroke patients are equivocal and possibly dependent on different lesion size and localization. The difference in the time since stroke when MI is assessed, can further influence MI ability outcome. de Vries showed that implicit MI ability improved significantly between 3 and 6 weeks after stroke [62]. Moreover this author demonstrated that implicit and explicit MI was differently affected in stroke patients. The patients in their study cohort scored below controls for both aspects of the MIQ-RS while accuracy scores of an implicit MI task did not significantly differ from the control group [63].

1.2 Mental Practice

1.2.1 Definition

The former paragraphs have addressed the different aspects of MI ability. When MI is used as a training method it is referred to as mental practice (MP), a training technique based on a repetitive motor imaging of different movements and daily tasks.

MI refers to the process of imagining a movement once or a few times, whereas the term ‘mental practice’ encompasses the training method that can use various cognitive rehearsal techniques, including MI [64]. MP using MI is a training method that uses cognitive rehearsal of an action or task to improve performance of that action or task without actually physically performing it [21,65]. The movement is not actually produced but is rehearsed in the individual’s imagination. The main philosophy that supports the use of MP is that the same neural motor network is activated when imaging motor actions as when actually performing them. The use of MP in sports, in particular repeated MI from the first person perspective, has been considered for many years to promote the learning of skilled movements [6,66]. MP can improve the execution of movements in individual athletes and help in the acquisition of new skilled behaviours [6,20]. Combining MP and physical practice (PP) has been proven to be more efficient, or at least equal to, physical execution.

Moreover the number of physical repetitions needed to acquire a new skill, can substantially be reduced when MP is performed prior to PP, reflecting a priming effect of motor imagery on the subsequent physical training [67].

Although PP is superior to MP alone, MP can augment PP and can be used in situations where PP is not (yet) possible. The effect of MP has been demonstrated to enhance speed, muscle force, and movement execution [64]. In addition MP appears to enhance the self-efficacy of the individual that uses this technique. In this way MP seems to have a two-fold function, including a cognitive (learning) and motivational (emotional) function [68].

However, results of MP in the literature remain equivocal and the technique is seldom well described. To be effective, mental practice needs to meet certain conditions and these will be addressed in the next paragraph.

1.2.2 Mental Practice and training strategies

Before mental practice can be administered in and outside therapy, the technique should first **be taught** to optimize the patients' MI ability and it should be closely monitored by the therapist. Familiarization is a key element at the start of MI training. Wondrush and co-workers developed a Motor Imagery Introduction Program (MIIP), which consists of 3 standardized introductory sessions [69]. The program includes MI theory and MI practice. At the end of the program patients should be fully familiar with the important aspects of MI training (what, who, when, where and how).

Before starting mental practice the therapist should establish whether the patient has a **correct representation** of the task to improve. Using task analysis, several parts of the movement or task can be identified and analyzed. The patient can then be asked to describe the movement sequence of the given task so that the therapist can then assess if the patient has a good grasp of the sequence and timing of the actions needed to perform the task successfully. When a patient has difficulties with a part of the movement (problem identification), he or she can practice this part mentally before embedding it into the entire movement later [68,70].

Linking physical activities and mentally performed movements appears essential for the effective implementation of MP [71]. Combining MP and overt movements in one training protocol supplies subjects with the appropriate kinesthetic information. It has been shown that the kinesthetic representation of a movement must exist before MP can be effective [4]. Although stroke patients may exhibit abnormal movement post stroke, prior to the onset of the stroke they would have developed intact normal neural pathways for movement and they will have retained this historic kinesthetic knowledge, i.e. the ability to appreciate a movement which has been practiced unknowingly over many years prior to the occurrence of the stroke.

Globally 3 types of mental practice strategies are described in the literature [67]. The first two procedures include the combination of MP and PP, the third only applies MP without any form of physical training. Because MP is considered to be an adjunct of PP, priming physical performance, people are expected to gain more benefit from a combined MP/PP therapy. When PP and MP are combined, the latter can be embedded in therapy in the same training session or delivered in a separate session. When MP is offered in a separate session, it can be provided using an audio recording or guided by an individual therapist [72]. When mental repetitions are alternated with PP the number of repetitions of the latter can be diminished considerably, yet result in the same training effect [67].

MP can further be facilitated by a wide range of different **sensory input modalities**, including visual, auditory, tactile and kinesthetic cueing. When administering MP, the therapist should make the image as vivid as possible by using these different sensory cues. Videos or pictures can be used in MP programs to provide visual information about normal movement phases and to help patients identify their own movement problems [73]. Heremans investigated imagery quality during externally cued and non-externally cued MI. Results showed that visual-movement related cues improved the spatial accuracy of MI and that auditory cues enhanced temporal accuracy of MI, both in patients and in healthy subjects [74,75]. Kim compared the effect of visual and kinesthetic imagery and studied the clinical feasibility to incorporate auditory step rhythm into the training. This investigator found walking performance of stroke patients to be more enhanced by the kinesthetic imagery mode, especially when an auditory step rhythm was added [76].

Toussaint confirmed this superiority of kinesthetic imagery over visual imagery. However when visual information was presented before MI - while performing the physical practice task- visual imagery also promoted motor learning. Overall, the efficiency of the imagery modality depended on the sensory information presented in the phase of PP [13].

Practicing **individually meaningful tasks** with specific self-identified goals has proven to be most effective for all rehabilitation interventions. The patients must be able to choose the meaningful activities that they want to improve using imagery techniques [68]. Moreover for both real and imagery exercises, interventions should always be administered at the appropriate level of impairment or function [77].

As the imagery technique is to be used outside regular rehabilitation therapy and preferably in the patients’ own environment, it is important that MP is taught correctly and **incorporated in daily familiar activities.** A study by Guillot showed that context motor imagery, including influences of the appropriate environment, gave higher and longer autonomic neuron system responses than MI presented in a neutral environment [17].

Relaxation has been shown to promote optimal conditions for concentration and prepare the patient to image more effectively [77]. Therefore relaxation exercises should be provided before starting the MP session. MP is generally applied with the client lying down and with the eyes closed [71,77]. When practicing locomotor tasks, a sitting position could be preferable, placing the patient in the same starting position as that used during physical practice [78].

Further, **duration of MP sessions** are recommended to be shorter than physical practice sessions. Mental fatigue might occur rapidly during mental training and thus MP should be applied in limited successive trials [16,71]. For individuals with stroke, optimal training times of 15 minutes are reported. When MP is embedded in physical practice, proportions ranging from 1 physical performance over 5 mental repetitions to 1 physical performance over 10 mental repetitions are advocated [67].

Finally, it is important to **monitor for compliance**. Therapists need to check patient adherence to the MI therapy and control for first person imagery quality by asking them regularly what they ‘see’ or ‘feel’ [67].

1.2.3 Mental Practice in neurological rehabilitation

In recent years MP has been proven to be a therapeutically relevant technique to promote motor recovery following neurologic disorders such as stroke, Parkinson’s disease and cerebral palsy [79-84].

Motor learning theories suggest that active participation, intensive practice and meaningful goals are the cornerstones of learning [85]. MP practice meets these requirements and can thus be theoretically considered as a beneficial additional rehabilitation tool. It is a non-invasive, inexpensive rehabilitation method that enables patients to practice frequently and safely, engaging in repetitive, task-specific training, even at an early stage of neurorehabilitation. The fact that MP can be performed by the patient without the presence of a therapist can increase training opportunities substantially.

Giving autonomy to the patient in their rehabilitation process is an important aspect of client-centred care. Unguided imagery can not only increase therapy intensity but also give the patient a feeling of empowerment and improve self-confidence.

Recovery of motor function after stroke is accompanied by a redistribution of activity within the neural network and reinforcement of the spared area adjacent to the brain lesion. This neuroplasticity ability of the brain to reorganize is an important component of recovery after brain injury. MP is proposed as an efficient neurological rehabilitation technique in light of a ‘therapy guided’ neuroplasticity after brain damage. MP has been shown not only to improve the affected function, but also to influence cortical reorganization in response to training [86]. MP offers patients a strategy to facilitate cortical brain reorganization. When the neurological condition of the patient does not allow the patient to produce movements, mental practice can potentially keep the motor program active, thus preventing learned non-use and facilitating the future execution of movements. When recovery progresses, patients can use mental practice in addition to PP to learn new skills. In this stage MP can be used to multiply the number of repetitions of a movement at the cerebral level.

During the last decade numerous clinical studies using MP in neurological rehabilitation have been published. MI rehabilitation has successfully been applied in stroke patients with acute, chronic, mild and severe hemiparesis [87-89]. However some recent trials have shown that not all patients may benefit from MP [90,91]. In a multi-centre, prospective study by Timmermans et al [90] patients with an upper limb paresis after stroke were included. The patients in the experimental group received a video-instructed MP program while patients in the control group followed a neurodevelopmental therapy-based program, as well as their usual therapy. All patients improved on their Fugl-Meyer test and Wolf motor function test but a significant improvement on the Frenchay arm test was found only in the experimental group. However the authors concluded that the use of MP in addition to therapy as usual in patients with subacute stroke had no additional effect over neurodevelopmental therapy in addition to therapy as usual.

Ietswaart and co-workers [91] investigated the effect of 4 weeks of MP without any specific related physical practice in a large cohort of stroke patients. Their results showed that MP did not enhance motor recovery in stroke patients early post-stroke. These results suggest that the benefit of MP is essentially due to its priming role in combined physical and mental practice. In their review Barclay-Goddard and co-workers state that MP in combination with other treatment appears more effective in improving upper extremity function post-stroke than the other treatment alone [65]. For individuals with hemiparesis, promising findings were reported for enhancing reaching as well as for isolated movements of the hand and fingers

[79,83]. Crajé found positive effects of MP on relatively simple hand function tasks after a relatively short intervention of 3 weeks. She states that for more complex hand function tasks a longer training period would be necessary [92].

MP-related improvement of activities of daily living was also reported. Liu and co-workers used MP to relearn functional activities in their patients. The experimental protocol focused on task analysis, then problem identification and finally task performance. Significant gains were achieved in household and community tasks [70].

The effects of MP to promote the learning of motor skills of the lower extremities have not been as well investigated and such studies have included merely patients in a chronic phase after stroke [93-95]. Dickstein and colleagues successfully developed a home-based MP training program for gait rehabilitation after stroke. Moreover, these authors reported excellent adherence of all participants to the MP program [94,95]. Malouin reported that when MP was combined with a minimal amount of PP in a cohort of stroke patients, an increase of loading on the affected leg was retained at follow-up [78]. Recently, a few studies have reported a positive effect of motor imagery training on balance and gait performance following stroke [73,96]. Hwang and co-workers found an increased walking velocity and improved kinematic parameters in their experimental group [73].

Although these studies suggest that MP can lead to improvement in gait and other tasks involving coordinated lower limb movements, randomized clinical trials with larger samples are necessary to confirm and generalize these findings.

1.3 Mental Practice in gait rehabilitation post-stroke

1.3.1 Stroke and recovery of walking capacity

Stroke is defined as a sudden loss of brain function, caused by the interruption of blood flow to the brain (ischemic stroke) or the rupture of blood vessels in the brain (hemorrhagic stroke). Sacco and co-workers [97] recently proposed an updated definition of stroke defining it as an episode of acute neurological dysfunction presumed to be caused by ischemia or hemorrhage, persisting ≥ 24 hours or until death. Ischemic stroke is defined as an episode of neurological dysfunction caused by focal cerebral infarction.

Cerebral vascular disease is a leading cause of disability and handicap throughout the world.

In most European countries the national incidences vary between 100 and 500 per 100000 inhabitants [98]. In Belgium the incidence is estimated at 200 per 100.000 annually [99]. Following stroke, patients may develop a hemiplegia with a profound effect upon their walking ability. Initial walking function is impaired in two out of three patients with acute stroke [100]. Kollen found that only 62 % of patients after a first time stroke regained independent gait after six months. Independent gait was classified as FAC (functional ambulation categories) > or = 4. Approximately 50 % to 80 % of patients who survive a stroke will eventually be able to ambulate independently [101].

Regaining walking ability is of great importance to stroke patients and it is also a prime factor in determining whether a patient will eventually go home or into a nursing home. Thus retraining of gait toward independent community ambulation is a major goal for all rehabilitation programs. Although the optimal treatment is currently unknown, recent evidence highlights the importance of intensive, repetitive practice of the walking task itself, applied in conditions that emulate the natural environment of the individual [102].

1.3.2 Gait rehabilitation after stroke

The upper motor neuron syndrome post-stroke induces muscle weakness, exaggerated reflex activity, spasticity, impaired selective motor control and proprioceptive problems that can result in an asymmetrical hemiplegic gait [103]. Impaired balance can further attribute to gait disturbances, especially in a challenging outdoor environment.

Although many patients regain their walking ability, hemiplegic gait is often characterized by a reduced walking speed and altered kinetic and kinematic gait profiles, leading to an inefficient gait and limited walking activity in the home and community [104]. Mechanisms of hemiplegic gait disturbance differ individually and the combination of gait deviations can vary. Thus adaptation of gait training to an individual patient’s gait pattern appears important. Although clinical observation can contribute to gait evaluation, three-dimensional gait analysis seems to be the most accurate technique to guide individualized gait rehabilitation [105,106].

Gait velocity is a valid, reliable and sensitive parameter to detect changes in gait capacity [107]. Gait velocity of patients with mild to moderate stroke has been found to correlate significantly with motor recovery of the affected lower limb as measured by Brunnstrom’s stages or by the Lower-extremity Fugl-Meyer assessment motor subscale [108]. The average walking velocity of people with hemiparesis post-stroke is lower than that of persons without impairments with values ranging from 0.23 to 0.73 m/s depending on the severity of the hemiparesis [109]. Moreover, Perry found that walking speed is a predictor of community walking: a walking speed of <0.4 m/s implies household walking, 0.4-0.8 m/s implies limited community walking and >0.8 m/s implies unlimited community walking [110].

A substantial number of studies have investigated the effects of various interventions on walking ability in individuals post-stroke. Overall locomotor rehabilitation has been found to have a beneficial effect on motor function, balance and gait velocity. Therapy appears to be most effective when the therapist applies **a mixture of different treatments** from the wide range of treatments available [111]. Conventional stroke rehabilitation includes physical therapy with neurodevelopmental techniques, balance and task-oriented training, preferably incorporated into real-life activities. However as pointed out by several reviews, outcome studies have shown equivocal results and **did not confirm the superiority of any particular type of approach**. A review by Langhorne reported that interventions promising improvement in gait included fitness training, training- both cardiorespiratory and a mixture cardiorespiratory and strength training-, high-intensity training and repetitive task training [102]. Each of these training strategies probably addresses different gait problems in post-stroke patients with impaired mobility. Van de Port investigated the effectiveness of training programs on walking competency after stroke and found that gait-oriented training whilst targeting improved strength and fitness, proved to be the most successful method of improving gait speed and endurance [112].

The specificity, amount, and intensity of walking practice are thought to be critical variables for successful gait rehabilitation [104]. Especially **higher intensity** of practice seems to be a crucial factor for effective therapy. Veerbeek reports a necessity of at least 45 minutes of exercise on each weekday [113].

Repetition is an important principle of motor learning that relies on the phenomenon of neuroplasticity and long term potentiation, the molecular mechanism by which neuronal synapses encode new information [113,114]. Therefore r**epetitive** task-specific practice might be the most effective rehabilitation principle when trying to promote motor recovery after stroke [108]. A slight variation between repetitions seems to be most beneficial for effective learning.

Due to **task-specificity** and the lack of transfer to unpractised tasks, exercises should be as close to functional tasks as possible to enhance daily life performance.

It can be concluded that intensity, repetition and task-specificity are key elements for effective gait training, considering their importance in guiding brain plasticity.

1.3.3. Mental Practice and gait rehabilitation

Dickstein and colleagues [82] were the first to develop an MI training program for gait rehabilitation post-stroke. The effects of this training program were first described in a few case reports. Later Dunsky et al [95] investigated the effect of a home-based MP program in a group of 17 people in a chronic phase post-stroke. At 6 weeks post-intervention, the main gait velocity increased by 40%. The gain of 15 cm/s corresponded to a moderate treatment effect. MI training consisted of MP without any PP in this study. The study findings further indicated that the increase in gait velocity was mainly the result of an increase in stride length. Despite the addition of a 30 minutes treadmill training Cho et al [96] reported the same speed gains in their MP group. These researchers included patients in a chronic post-stroke phase: 15 patients received MI training and gait training, 13 controls received only gait training. The subjects were assessed with a Timed up-and-go test, a 10-m walk test and a Fugl-Meyer assessment scale. There were significant differences between both groups at follow-up with respect to all parameters tested. Hwang and colleagues [73] included 13 hemiparetic subjects and 11 controls who were at least 6 months post-stroke in a four-week intervention. They also reported a larger increase in gait velocity in their experimental group than in the control group but the small speed gain of 7 cm/s was close to the standard error of the measure which is 5 cm/s [115]. The changes in affected and less affected limbs stride length were also significantly greater in their experimental group

In all studies, gait training through motor imagery was delivered in a separate session. MP was guided by a therapist in an individual one to one session or delivered by a videotape [73, 96]. Moreover, in the study by Deutsch and co-workers telerehabilitation was used to deliver MP in the patients’ home [93].

Hwang and co-workers [73] used two videotapes, one showing a normal young adult ambulating along a 10-m walkway, the second videotape showed the patient before training and after two weeks of training. The MP protocol consisted of 5 stages: progressive relaxation, external imagery, problem identification, internal imagery and mental rehearsal.

In a study by Kim and co-workers [76] the effect of visual, kinesthetic, visual with auditory step rhythm, and kinesthetic with auditory step rhythm locomotor imagery training on walking performance was compared, using a randomized cross-over design. A total of 15 patients in a chronic phase post-stroke were recruited. Study results revealed that kinesthetic MI training may result in a greater benefit on walking performance than visual MI training and that these effects are further enhanced with the incorporation of an auditory step rhythm. Overall, muscle activity improved in the hamstrings, tibialis anterior, gastrocnemius and quadriceps. Walking ability was further assessed by the timed up-and-go test which also improved after kinesthetic MI training with an auditory step rhythm cue.

This improvement of loading patterns when standing up and sitting down after MP was already shown by Malouin and co-workers [78]. The gains in loading in their study were obtained after a single 30-min training session, consisting of a 1PP:5MP training ratio.

In a half-cross-over randomized study Dickstein and co-workers [94] integrated motor and motivational imagery to enhance walking ability in community-dwelling subjects who were between 6 months and 2 years post-stroke. Both interventions were administered in the patients' home. Both kinesthetic and visual imagery of the walking activities were integrated in MP. Motivational imagery consisted of motivational imagery-promoting arousal (e.g. ’you feel energetic and determined’), motivational imagery-promoting problem-solving specific to the task (e.g. ’a cat is passing, you bypass a cat and continue to walk’) and motivational imagery-reward (e.g.’you succeeded to lift the phone on time, you are pleased with your achievement’). Mean walking speed increased with 16cm/s in the experimental group. However, there was no effect on community ambulation and fall-related self-efficacy.

When MP is used in gait rehabilitation post stroke, the treating physiotherapist can train both analytical (e.g. hip extension, knee flexion, ankle dorsiflexion) and functional movements (e.g. balance, climbing a stair, walking in the community), related to gait. Thus, it seems important to provide the patient with the necessary visual and kinesthetic information about the given movement. Gait analysis data (graphs, video) can further guide the patient and the therapist with important information about gait pattern progress and individual gait problems. Although currently data are still sparse and study cohorts mostly small, we can conclude that most studies about mental practice in gait rehabilitation after stroke suggest a clinical meaningful change for gait speed, exceeding 4 cm/s [115]. These findings warrant further research. Especially the effect of mental practice in a sub-acute rehabilitation phase poststroke needs further elaboration. The few studies that were carried out in a subacute phase after stroke, all targeted upper limb activities.

1.4 Aims of the thesis

During the last decade MP through MI has emerged as a new promising non-invasive, inexpensive rehabilitation technique to improve outcome on upper and lower limb function after stroke that can be effective even years after stroke. MP use is based on the premise that imagery is associated with neural activity in the brain similar but not identical to that occurring during overt movement, so-called ‘functional equivalence’.

Several sources of evidence suggest that experience influences change in the motor cortex after stroke and that anatomic enlargement of cortical motor maps may be correlated with functional recovery. Thus MP, being a repetitive task-related therapy, may add to cortical reorganization and ‘therapy guided’ neuroplasticity. MP with MI, incorporated in physical therapy, may provide an opportunity to involve a high-intensity, repetitive training regimen to improve locomotor skills, especially in people with severe disability that are unable to practice actual gait training.

However before using MP in a neurologic population, it is important to evaluate the MI ability of the participants to determine whether they are still able to perform MI. Unrelated to cerebral damage there are individual differences in MI ability. Moreover, because the MI related brain regions partially overlap with brain regions involved in overt motor performance- including the parietal cortex, the cerebellum, the basal ganglia and the premotor cortex-, any structural damage to these brain regions could affect both motor performance and MI ability. Additionally patients’ MI ability might change over the intervention period, due to a training effect.

Therefore the purpose of this thesis was to explore a number of these aforementioned issues associated with MI and MP, particularly addressing the following questions:

H1

MI ability has been investigated in several neurologic populations, including patients suffering from stroke, Parkinson disease, cerebral palsy and multiple sclerosis. To our knowledge, MI ability has not been investigated in patients with a traumatic brain injury, although this patient group constitutes an important part of the neurorehabilitation population.

We hypothesize that, due to the frequent presence of frontal and prefrontal brain lesions and disruption of the fronto-parietal network, MI ability is likely to be hampered in patients with a traumatic brain injury.

Three domains of Motor Imagery will be assessed: MI vividness, temporal organization and MI accuracy. Validated MI questionnaires will be used to measure MI vividness, temporal congruence tests will reveal the temporal organization of MI and mental rotation tasks will be used to assess MI accuracy.

H2

If MI is a skill, then like any skill, it can be trained and improved through regular practice. Training of MI may be important to optimize MP and to improve imagery skills in patients with so-called ‘chaotic’ MI.

We hypothesize that MI ability can be trained by MP such that a higher level of performance is attained.

Therefore patients will receive MP training for 6 weeks and psychometric tests, measuring MI vividness, temporal congruence and MI accuracy, will be applied before and after training to assess the training effect.

H3

MP has been shown to enhance motor performance in patients in a chronic phase post-stroke. Therefore, we hypothesize that MP through MI can be applied to enhance walking performance in patients after stroke. Moreover, we hypothesize that a gait rehabilitation program based on MP can be administered in a sub-acute rehabilitation phase in this patient group.

In a randomized controlled trial patients in a sub-acute phase after stroke will be allocated to one of two treatment protocols: MP added to a standard rehabilitation regimen versus muscle relaxation added to standard rehabilitation. Gait velocity (near transfer outcome measure) and motor recovery (far transfer outcome measure) of both groups of patients will be compared at baseline and after 6 weeks of rehabilitation practice.

H4

Neuroimagery findings have shown similar cerebral networks associated with imagination and execution of a movement. A large fronto-parietal network is involved when we imagine ourselves moving. Thus, a patient's brain damage in this area may prevent successful MI performance. We hypothesize that MI ability after stroke is related to specific brain lesion localizations, more specifically brain lesions involving the MI network.

Localization of cognitive processes through lesion analysis continues to reveal new information about brain-behaviour relationships in patient populations. Voxel-based lesion-symptom mapping will be used to analyze the relationship between brain tissue damage and MI ability on a voxel-by-voxel basis in our stroke cohort.

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Chapter 2

Motor imagery ability in patients with traumatic brain injury

Motor Imagery Ability in patients with traumatic brain injury.
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ABSTRACT

Motor imagery ability in patients with traumatic brain injury.

Objective: To assess motor imagery (MI) ability in patients with a moderate to severe traumatic brain injury (TBI).

Design: Prospective, behavioral study with matched controls

Setting: University hospital rehabilitation unit.

Participants: Patients with traumatic brain injury (mean coma duration 18 days) undergoing rehabilitation (n=20) and healthy controls (n=17) matched for age and education level.

Interventions: not applicable

Main Outcome Measures: The vividness of MI was assessed using a revised version of the movement imagery questionnaire (MIQ-RS); the temporal features assessed using the time dependent motor imagery (TDMI) test, the temporal congruence test and a walking trajectory imagery test and the accuracy of MI using a mental rotation test.

Results: The MIQ-RS revealed a decrease of MI vividness in the TBI group. An increasing number of stepping movements was observed with increasing time periods in both groups during the TDMI. The TBI group performed a significantly smaller number of imagery movements in the same movement time. The temporal congruence test revealed a significant correlation between imagery and actual stepping time in both groups. The walking trajectory test revealed an increase of the imagery and actual walking time with increasing path length in both groups but the ratio of imaginary walking over actual walking time was significantly greater than one in the TBI group. Results of the hand mental rotation test indicated significant effects of rotation angles on imagery movement times in both groups but rotation time was significantly slower in the TBI group.

Conclusions: Our patients with TBI demonstrated a relatively preserved MI ability indicating that MI could be used to aid rehabilitation and subsequent functional recovery.

Introduction

Motor imagery is the imagining of an action without its actual execution. It is a process during which the representation of an action is internally reproduced within the working memory without any overt output[1]. Mental practice can be described as a cognitive process in which movements are repeatedly mentally simulated without any overt body movement[2]. There is evidence that mental practice as an additional therapy has effects on motor recovery after damage to the central nervous system. Since mental practice based on motor imagery is not dependent on residual motor function, it can be used in neurological rehabilitation to train the more cognitive aspects of motor tasks and thus improve physical recovery[2-8]. However, before starting mental practice, it is imperative to assess whether the patient is still able to engage in motor imagery[9]. Unrelated to cerebral damage, there are individual differences in motor imagery ability. Hall et al[10] classified subjects as high or low imagers based on their Movement Imagery Questionnaire (MIQ) scores. They demonstrated that individual differences in motor imagery ability can influence motor task performance, with high imagers reproducing movements more accurately than low imagers[11]. Moreover, since motor imagery and motor execution are believed to share the same underlying neural network, any structural damage to the brain could affect both motor performance and motor imagery[9]. Motor imagery ability has already been assessed in several clinical populations. Individuals with motor impairments due to brain lesions caused by stroke, cerebral palsy or Parkinson’s disease, seem to show only partially preserved motor imagery capacities[12-17]. Therefore, patients with impaired motor imagery ability should be identified before starting any imagery therapy.

We will assess motor imagery ability in patients with a moderate to severe head injury using MI questionnaires, mental chronometry paradigms and mental rotation tasks[18]. Motor imagery questionnaires measure the vividness of motor imagery[19]. Subjects are asked to indicate the ease with which they are able to imagine a certain movement. Several studies indicate that ratings from imagery questionnaires provide a good indication of the ability to generate vivid images of movements[10,19-22]. The Movement Imagery Questionnaire-revised (MIQ-R) is a self-report questionnaire, developed and validated by Hall et al, in order to assess visual and kinesthetic modalities of movement imagery[10]. A revised version, the MIQ-RS, was developed and validated by Gregg et al[20] to measure the visual and kinesthetic components of motor imagery ability. The MIQ-RS is composed of 2 subscales of 7 relatively simple movements, for use in people with limited mobility, for example bending forward or pulling a door handle. Mental chronometry paradigms measure the temporal coupling between actual and imagery movements. The normal match is on a ratio of 1:1; that is, several investigators have demonstrated that it takes a similar amount of time to imagine and execute an action[23-25]. The match between imagined and actual movement times indicates a reliable use of motor imagery. Malouin et al developed, validated and confirmed the reproducibility of the temporal congruence test and the time dependent motor imagery (TDMI) screening test for measuring the temporal behaviour of motor imagery in healthy subjects and persons poststroke[16,25]. Because temporal characteristics of motor imagery should be screened for the task to be trained, we also introduced a walking trajectory test to quantify imagery of gait. This test, which was developed and validated by Bakker et al., demonstrated a high temporal congruence between actual and imagined walking in a healthy population[23].Finally,mental rotation tasks, measure implicit motor imagery ability and accuracy and the test used in our study was developed by Parsons[26]. The mental rotation time is the time it takes for the subject to mentally rotate a picture and this depends on the angular disparity of the picture with reference to its upright position. Moreover, using bodily stimuli, the mental rotation time follows the biomechanical constraints, in that biomechanically more difficult orientations result in slower reaction times[22]. In our study, we used a hand mental rotation test that was a two-dimensional variant of Parsons' hand laterality test, with imagery movement times measured without subjects making a left-right judgment[26].

To our knowledge, motor imagery ability in persons with a moderate to severe traumatic brain injury (TBI) has not been investigated. Therefore, this study was primarily designed to examine motor imagery ability in patients with a moderate to severe TBI, using a mental imagery questionnaire, mental chronometry paradigms and a mental rotation task. If motor imagery ability is at least partially preserved in these patients, then this cohort could potentially benefit from mental practice. This non-invasive, inexpensive method of repetitive, task-specific practice has been shown to increase task performance and to contribute to relearning of motor function and activities of daily living in patients with an acquired brain injury[8,27].

Methods

Study design and participants

Twenty patients receiving rehabilitation after a moderate to severe traumatic brain lesion[28] and 17 healthy controls matched for age and level of education volunteered and were recruited to take part in this study (from a total of 21 patients and 27 possible controls that were approached). All patients sustained their TBI between April 2008 and December 2009. The patients with TBI were recruited via the University Hospital and from hospitals from East- and West-Flanders to the Centre for Locomotor and Neurological Rehabilitation, Ghent University Hospital. Controls were recruited from family and friends of patients that were included in the study. Inclusion criteria consisted of a normal level of consciousness with no post traumatic amnesia. Those patients who were not fully conscious and/or exhibited signs of post traumatic amnesia were excluded from taking part. All subjects gave their informed consent and the protocol was approved by the Ghent University Hospital Ethics Committee where the study took place. For subject characteristics please refer to Tables 1 and 2.

Table 1 Participants' Characteristics

	TBI group (n = 20)	Control group (n = 17)
Sex (men: women)	16:4	13:4
Age (years)	31.2 ±12.3	32.1 ± 14.2
Education (years)	13.6 ±1.9	13.6 ± 2.4
Time since injury (months)	15.9 ± 9.5 (3-33)*	NA
Coma duration (days)	18.8 ±13.3 (2-49)*	NA
PTA duration (weeks)	6.3 ± 2.9 (2-12)*	NA
Hemiplegic side		
None	11	NA
Right	4	NA
Left	5	NA

*Mean±Standard Deviation (range)

Table 2 Description of Brain Injury Localization

TBI patient	Lesion localization	Imaging source
1	DAI	MRI
2	bifrontal contusion– DAI	MRI
3	bifrontal contusion– right temporal contusion – DAI	MRI
4	right frontal – temporo-occipital contusion	MRI
5	bifrontal – bitemporal contusion	MRI
6	bifrontal – right cerebellar contusion	MRI
7	left temporal contusion– DAI	MRI
8	right temporal contusion– DAI	MRI
9	left temporoparietal contusion	CT
10	right temporal contusion	MRI
11	right frontal contusion	CT
12	frontotemporal contusion– cerebellar contusion	CT
13	right frontoparietotemporal contusion – DAI	MRI
14	brainstem contusion	CT
15	DAI	MRI
16	right frontoparietotemporal contusion	CT
17	bifrontal contusion – DAI	MRI
18	right frontal contusion – DAI	MRI
19	Bifrontal-bitemporal contusion	CT
20	bitemporal contusion– DAI	MRI

* TBI : traumatic brain injury ; † DAI : diffuse axonal injury

Measures

The Movement Imagery Questionnaire-Revised second version. (MIQ-RS) [10,20]. The MIQ-RS is a self-report questionnaire aimed to assess imagery ability in individuals with movement limitations. The instrument consists of 2 sub-scales (kinesthetic and visual) each represented by 7 items. Completion of each item required 4 steps. First, the starting position of the movement was described by the examiner and then the subject was asked to assume it.

Second, the movement was described and then the subject was asked to perform it. Third, the subject was asked to reassume the starting position and then imagine producing the movement (no actual movement was made). Finally, the subject was instructed to rate the ease/difficulty with which he/she imagined the movement on a 7-point scale, where 1 = very difficult and 7 = very easy to picture (the visual sub-scale) and feel (the kinesthetic sub-scale).

Time Dependent Motor Imagery screening test (TDMI)[16,25]. The TDMI test is a chronometric screening test used to evaluate whether a person is able to mentally simulate movement. The subjects were seated in a chair and were instructed to imagine stepping movements over varying time periods. The stepping movement consisted of placing one foot forward on a board and then placing it back on the floor. First, the examiner demonstrated the movement and then the subjects were instructed to actually perform the movement physically twice. During the imagery task, the subjects were asked to close their eyes and to count each time they imagined touching the board. Each subject completed three trials. Each trial terminated after a varying time period of 15, 25 and 45 seconds. The examiner recorded the number of imagined movements in these three time periods.

Temporal congruence stepping test.[16,25] The temporal congruence test compares real and imagined movement times. Based on the temporal coupling between real and imagined movements, it is expected that movement times for both conditions will be similar. For this test, the subjects were seated in a chair and were instructed to first imagine and then to physically perform five stepping movements, placing the foot on a board in front of them. During the imagery task, the subjects had their eyes closed. The examiner recorded the duration of the two stepping series.

Walking trajectory test. [23] This test aims to quantify imagery of gait and demonstrates a tight behavioral relationship between imagined and actual gait. Mental imagery of gait was shown to be sensitive to the same temporal and spatial constraints as those in actual walking. The subjects were seated in a chair in front of a computer screen that displayed photographs of three walking trajectories. The walking trajectories were of varying lengths of 2, 5 and 10 m. The start of the walking trajectory was marked with a blue line; the end with a cone. There were two experimental sessions, an imagery session and an actual walking session. Each imagery session started with the presentation of a photograph of a walking trajectory. The subjects were then asked to close their eyes and to imagine walking along the path. The examiner recorded the duration of each trial. Subsequently, the subjects performed the actual walking trial. The actual walking session was always performed after the imagery session to minimize the amount of tacit knowledge about the time it actually takes to walk along the trajectory.

Hand mental rotation test [26]. The subjects were seated on a chair, facing a computer screen that displayed photographs of left and right hands. The hands were presented in varying two-dimensional orientations of 30°, 60°, 90° and 120°. Stimuli were presented in a random order. The subjects were instructed to imagine moving their hands from the upright position, palm down, to the position of the stimulus hand and to press the enter button as they completed their imagined action, thus recording the time taken for them to imagine the action.

Statistical analysis

Statistical analyses were performed with SPSS Statistics 17.0 software. Data are expressed as mean ± SD. Independent samples *t*-tests were used to investigate between-group differences after confirming homogeneity of variances (Levene's test). For nominal scale data, Pearson's Chi-square tests were used. Repeated measures analyses of variance were used for the analysis of the repeated TDMI, with imagery/actual walking measurements as within-subject variables, and Group (trauma patients, healthy controls) as between-subjects variables. Pearson correlations were calculated to evaluate the strength of the association between variables of at least interval scale. In all cases, significant differences were accepted at the level $p \leq 0.05$.

Results

We report the results from 20 subjects with TBI and 17 healthy volunteers (CTL group). These are summarised in Table 3.

The total MIQ-RS score and both kinesthetic and visual sub-scores were significantly higher (always $P<.05$) in the CTL group than in the TBI group, with a mean total score of 82 (SD 10) and 72 (SD 13), respectively. Further analysis showed a significantly higher score for MIQ-RS visual (T_{18}=-2, 92, P<.01) and MIQ-RS total (T_{18}=-2, 48, P=.024) in patients with frontal brain damage (11/20, see table 2). The MIQ-RS total score was not significantly correlated with the results of the mental chronometry tests (Temporal Congruence Test: r=0.06, P=0.73; Walking Trajectory Test: r=0.06, P=.72).

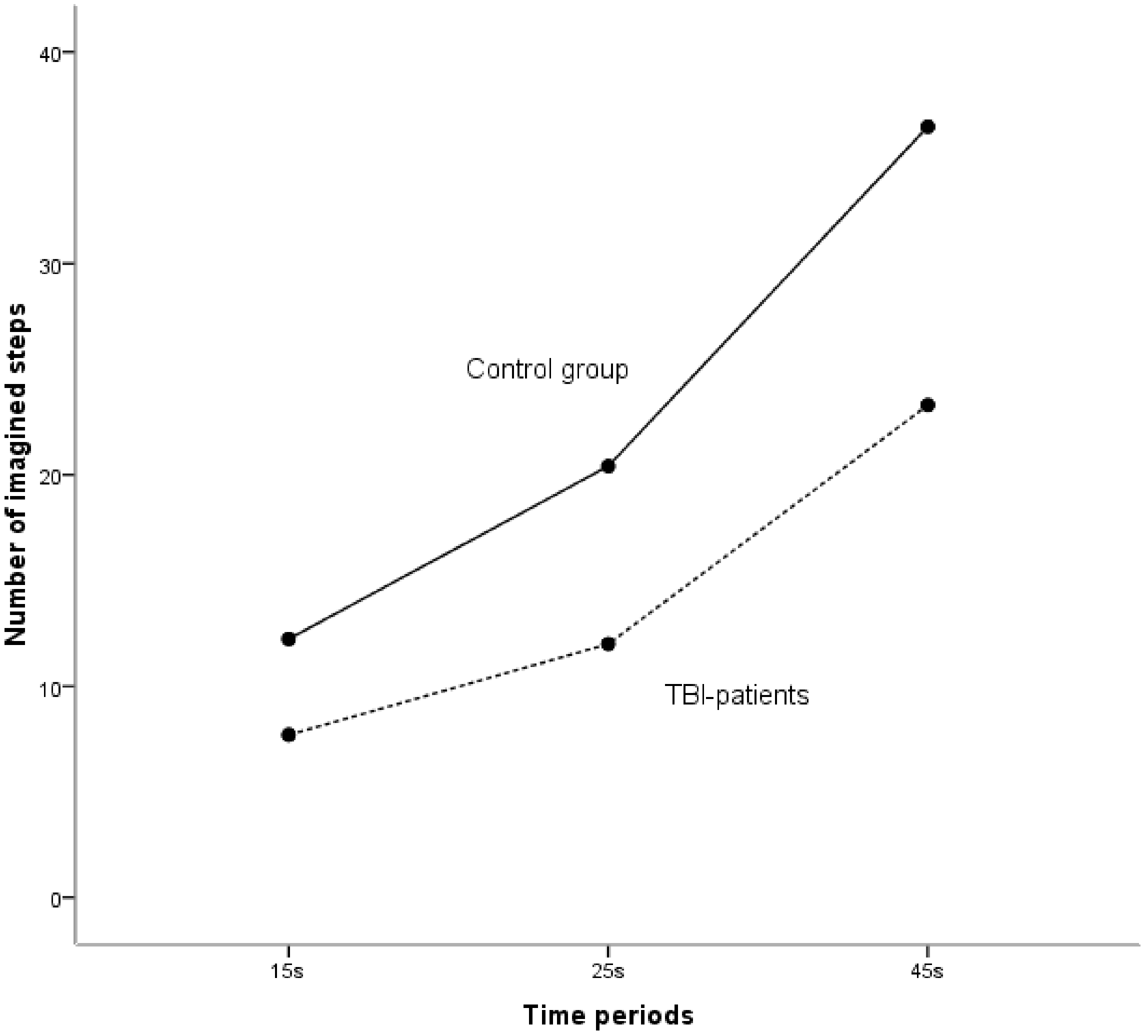
Table 3. Performance of TBI-patients and healthy controls: Mean (lower bound – upper bound 95% confidence interval).

	TBI-patients	Healthy controls
MIQ-RS		
Kinesthetic scale	37.3 (34.7 - 39.9)	42.0 (39.1 – 44.9)
Visual scale	35.3 (32.0 - 38.6)	40.9 (37.3 – 44.5)
Total scale	72.6 (67.1 - 78.1)	82.9 (76.9 – 88.9)
TDMI (number of steps)		
15s	7.7 (5.8 – 9.6)	12.2 (10.2 – 14.2)
25s	12.0 (9.4 -14.6)	20.0 (17.6 – 23.3)
45s	23.3 (18.5 – 28.1)	36.5 (31.2 – 41.7)
Temporal Congruence Stepping Test (s)		
Imagined stepping	12.9 (10.6 – 15.3)	6.9 (4.3 – 9.4)
Actual stepping	12.5 (10.1 – 14.8)	6.8 (4.2 – 9.4)
Walking Trajectories Test (s)		
Imagined walking (sum*)	30.5 (24.8 – 36.2)	16.3 (10.1 – 2.5)
Actual walking (sum*)	18.4 (15.2 – 21.6)	14.3 (10.8 – 17.8)
Hand Mental Rotation Test (ms)		
30°	2518 (1957 – 3079)	1566 (957 – 2174)
60°	2821 (2224 – 3418)	1755 1107 – 2403)
90°	2951 (2328 – 3575)	1978 (1302 – 2654)
120°	3376 (2685 – 4068)	2141 (1391 – 2891)

*Sum of walking times for each of 2, 5 and 10 m walks

The TDMI test revealed a statistically significant correlation between the number of imagined stepping movements and the duration of time periods in both groups ($F_{1,35}$= 153, P<.001). The TBI group, however performed significantly less imagined stepping movements than the control group ($F_{1,35}$=15, 5, P<.001) in the same movement time. There was also a significant TDMI x group interaction (p<.001), with the TBI group exhibiting a reduced increase in imagined stepping movements over increasing time periods (Fig 1).The temporal congruence stepping test scores revealed a statistically significant correlation between imagery stepping time and actual stepping time in both groups (TBI group, r=0,82, P< .001 and CTL group, r=0,80, P<.001).

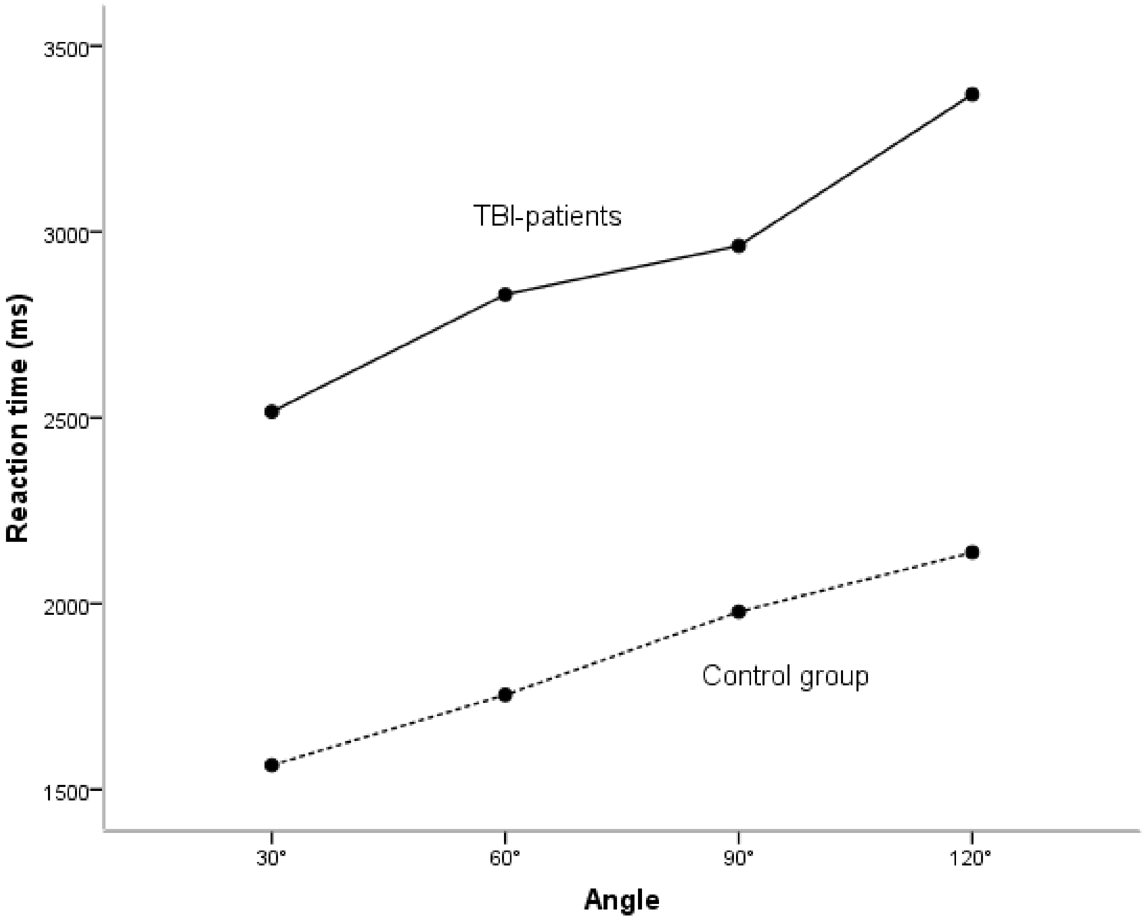
Figure 1. Performance of traumatic brain injury patients and control subjects on the Time Dependent Motor Imagery Test



The results of the walking trajectory test indicated that imagery and actual walking time increased significantly with increasing path length in both groups ($F_{2,34}$=81.75, P <.001).A strong relationship was found between imagery and actual walking times in both groups (10m, r =0,65, P<.001), but the sum of actual walking time/ sum of imagery walking time ratio was significantly increased in the TBI group ($T_{1,35}$= -2,26, P=.03). Further analysis revealed a significantly higher ratio in patients with frontal brain damage (n=11) compared to patients with other lesion localizations (n=8) (T_{18}= 2,19, P=.045).

The results of the hand mental rotation test indicated a statistically significant effect of rotation angles on imagery movement times in both groups, with increasing angles resulting in increasing movement times ($F_{4,32}$.= 14,5, P<.001). Analysis of the test results showed a significantly slower execution of the imagined hand rotations in the TBI group ($F_{1,35}$ = 5,09 , P=.03) (Fig 2).

Figure 2. Reaction times of different rotation angles for traumatic brain injury patients and control subjects on the hand mental rotation task.



Discussion

This study was designed to assess motor imagery ability in patients with a moderate to severe TBI. Before starting mental practice in neurological rehabilitation, it is necessary to establish whether patients are still able to imagine movements and thus benefit from motor imagery training. Therefore MIQ-RS questionnaires, mental chronometry and mental rotation tasks were utilized to study motor imagery abilities in adults with TBI. The results obtained provide evidence that the ability to internally represent movements is preserved after TBI but in our cohort, motor imagery was less vivid[10] and less accurate[26], with the process of imagining the movements performed more slowly[1] than the actual movement performance. To our knowledge, the present study is the first to assess the vividness of motor imagery in TBI patients. The visual and kinesthetic sub-scores of the MIQ-RS were lower in the patient group compared to the healthy controls (Table 3). These results appear to conflict with those studies investigating motor imagery ability after stroke. Malouin et al found the vividness of mental images after stroke to be similar to that in age-matched controls. However, motor imagery ability was not symmetrical, with an overestimation when imagining limb movements on the unaffected side[16]. Relying on the subjects' self report , Kimberly et al found no difference in motor imagery ability between subjects with stroke and healthy controls[29]. The dominance of visual motor imagery, usually observed in healthy adults, was not confirmed in the present study. Possibly, the use of an adapted scale with relatively simple motor tasks influenced the ease with which the kinesthetic component of the imagery task was performed.

The TDMI and the temporal congruence test have been standardized and their test-retest reliability has been confirmed[25]. The results of the present study support the relevance of these mental chronometry tests for use in a population requiring neurological rehabilitation. Imagery/actual movement time ratios offer a means to quantify the changes in the temporal characteristics of motor imagery. In all mental chronometry tasks, a significant correlation was found between executed and imagery movement times in both the TBI and the CTL group. In all tasks, however, the temporal coupling (imagery/actual movement time ratios) was significantly increased in the TBI group, with the imagined movement being performed relatively more slowly, indicating a temporal uncoupling between actual and imagery movements. These results are consistent with the findings of other studies. Malouin et al reported increased imagery/executed movement time ratios in patients with stroke[25] and Caeyenberghs et al, who investigated motor imagery ability in children with brain injury, found an inferior ability to imagine the time needed to complete goal-directed movements[30]. Johnson et al found no evidence that chronic limb immobility after stroke compromised the ability to internally plan movements of the paretic arm. In their study, both groups performed at a comparable high level of accuracy on a mental rotation task[31].

We also investigated the relationship between the different motor imagery measures and found no correlation between the results of the imagery questionnaires and those of the mental chronometry tasks in both groups. Possibly, anosognosia, a disturbance of self-awareness, limits the usefulness of these self-report questionnaires in a brain-injured patient group, since many patients underestimate the severity of their cognitive functioning deficits[32,33]. Moreover, as shown in table 2, many patients suffered from frontal lobe damage, which is known to be involved in anosognosia pathogenesis[33]. It was shown in this study that patients with frontal lobe damage had difficulties in assessing their motor imagery ability with overrated scores of the MIQ-RS, compared to the results of the temporal congruence tests. Frontal lobe damage is important in explaining many of the neuropsychological and behavioral problems of this patient group. For this reason we incorporated this specific patient group in our analysis. However, due to the fact that our subgroups were small and the results not consistent, we were careful not to overemphasize the significance of our results.

The performance of the mental chronometry and rotation tasks by the TBI patients in our study indicates a preserved ability to internally reproduce the motor action, although imagined movements were performed more slowly and less accurately. Brain imaging studies have shown that the pre-motor cortex, the pre-frontal cortex, the posterior parietal cortex, the cerebellum and the basal ganglia are all involved in motor imagery. Dominey et al found motor imagery to be asymmetrically slowed in hemi-Parkinson's patients, confirming that dysfunction of the basal ganglia not only affected motor execution but also the internal representation of motor sequences[14]. In a study of patients with unilateral cerebellar lesions, Battaglia et al showed a reduced ability to prepare and imagine sequential movements[12]. Since many brain areas involved in motor imagery, are frequently damaged in patients with a traumatic brain lesion, TBI is also expected to reduce motor imagery capacity. The present study confirms the reduced vividness of motor imagery in a TBI population, with a deterioration of temporal coupling and accuracy of motor imagery. Motor imagery training might help to improve the vividness of motor imagery and the internal representation of intended movements, and hence promote motor skills relearning in this patient group.

Study limitations. The heterogeneous nature of a TBI patient group makes it difficult to draw general conclusions from such a study. However, we attempted to address this by including only patients with a moderate to severe traumatic brain injury, as indicated by the coma and post traumatic amnesia duration. Grouping of the TBI patients in this study was based on approximate MRI data. A further refining of lesion localization, and extending the number of patients to improve statistical rigour in each group according to pathology would be areas for focus in similar studies. Furthermore, the use of self-awareness measures to determine accuracy of self-ratings seems necessary to gain more insight into the influence of lesion localization on Motor Imagery ability in traumatic brain injury.

Conclusions

The present findings indicate that, while TBI patients may still perform motor imagery, our cohort showed a decrease in the three motor imagery modalities, with a decrease of motor imagery vividness, temporal congruence and accuracy. Our results however, suggest that patients with TBI retain ability for motor imagery and hence may benefit from motor imagery training to improve their motor preparation and execution of movement and thus their functional ability. However, due to the limited information available thus far, we stress that further research is essential in order to fully evaluate the potential contribution of motor imagery in patients with traumatic brain injury.

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Chapter 3

Mental Practice with Motor Imagery in gait rehabilitation following stroke.

Influence of Motor Imagery training on gait rehabilitation in sub-acute stroke:
a randomized controlled trial.
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Abstract

Objectives: To evaluate the effect of mental practice on motor imagery ability and assess the influence of motor imagery on gait rehabilitation in sub-acute stroke.

Design: Randomized controlled trial.

Subjects: Forty-four patients with gait dysfunction after first time stroke were randomly allocated to a motor imagery training group and a muscle relaxation group.

Methods: The motor imagery group received 6 weeks of daily mental practice. The relaxation group received a muscle relaxation program of equal duration. Motor imagery ability and lower limb function were assessed at baseline and after six weeks of treatment. Motor imagery ability was tested using a questionnaire and mental chronometry test. Gait outcome was evaluated using a 10m walk test (near transfer) and the Fugl-Meyer Assessment (far transfer).

Results: Vividness of kinesthetic imagery improved significantly more in the motor imagery group compared to the muscle relaxation group. Significant between group differences were found with the motor imagery group improving more than the muscle relaxation group in the walking test. We obtained no group interaction effect for the far transfer outcome score.

Conclusions: These results suggest that motor imagery training has a beneficial task-specific effect on gait function in sub-acute stroke but longer term confirmation is required.

Introduction

Mental practice (MP) can be defined as ‘the process of imaging and rehearsing the performance of a skill with no related overt actions’ (1). Several authors have reported that mental practice, in combination with physical therapy, can improve motor performance in stroke patients (2-7). Because the process of imagery is not dependent on the ability to execute a movement, mental practice can be implemented early in rehabilitation to train motor preparation and thus facilitate physical recovery. Furthermore, this training method can be performed by the patient alone after some familiarization and instruction (5).

Patients with impaired motor imagery (MI) ability should be identified as being suitable for imagery training. However it remains uncertain whether or not a high level of MI ability is necessary for therapy response before commencing MI therapy (8). Unrelated to cerebral damage, there are individual differences in motor imagery ability. Hall et al. classified subjects as high or low imagers based on their Movement Imagery Questionnaire (MIQ) scores and demonstrated that individual differences in motor imagery ability can influence motor task performance (9,10). Moreover, since motor imagery and motor execution are believed to share a similar underlying neural network, any structural damage to the brain could affect both motor performance and motor imagery (11). Malouin and co-workers found the vividness of motor imagery in stroke patients to be similar to that of age-matched healthy persons, although they reported a better motor imagery vividness for the unaffected side (12). Given the higher variance of MI ability in stroke patients, the first aim of the current study was to assess motor imagery ability in patients in their sub-acute rehabilitative phase and less than one year following stroke and to evaluate if this ability could be trained and stimulated to a higher level of performance to maximize the potential rehabilitative effect. We assessed motor imagery vividness in our patients using an MI questionnaire and mental chronometry paradigms. Several studies indicate that ratings from imagery questionnaires provide a good indication of the ability to generate vivid images of movements (12,13). Mental chronometry paradigms measure the temporal coupling between actual and imagery movements (14,15). Because temporal characteristics of motor imagery should be screened for the task to be trained, we introduced a walking trajectory test to quantify imagery of gait. This validated test demonstrated a high temporal congruence between actual and imagined walking in a healthy population (15).

Stroke patients rank the restoration of walking as one of the most important goals of their rehabilitation (16). In a prospective cohort study, Kollen et al. showed that independent gait was regained by only 62% of stroke patients six months post stroke onset (17). Although many patients regain some ability to walk eventually, independence in moving about the community often remains compromised (18). Given its clinical importance, therapeutic interventions that assist in gait recovery are highly relevant. The incorporation of mental practice into rehabilitation of the lower limb in a chronic phase after stroke has been assessed by several authors. For example, Dickstein and colleagues reported on a series of case studies where gait was trained using a home-based motor imagery program (5,19) and found an enhancement in gait speed in their stroke population. Recently, Cho et al. found that adding motor imagery to gait training enhanced balance and gait ability in their patients during the chronic phase post stroke (20). The second purpose of our study was therefore to confirm and extend these findings and examine if motor imagery training in combination with physical practice is also beneficial in improving gait function in the sub-acute phase following stroke.

Methods

Participants

This study was a single-centre, randomized controlled trial. Patients who were eligible for the study were invited to participate. Those who volunteered and gave written consent were then randomly allocated into one of two different treatment groups using a process of blinded random number allocation. Forty-six patients were eligible and forty-four gave written consent and 2 patients did not want to take part. Twenty-one were placed in the motor imagery training (MIT) group and twenty-three in the muscle relaxation (MR) group. To compare patients' performance with neurologically intact participants, 27 healthy age-matched control subjects (CTL) were recruited.

The flow of participants through the trial is presented in Figure 1 and the demographic variables of all participants are provided in Table 1.

Additionally, the physician responsible for the assessment of patients throughout the study remained blinded to the patients' group allocation for the full duration of the trial.

All patients sustained their stroke between August 2009 and June 2013. The patients were recruited via the University Hospital and from hospitals in East and West Flanders to the Rehabilitation Centre, University Hospital of Ghent.

Participants were eligible if they: (1) had experienced a first time stroke less than one year before entering the study; (2) were able to walk 10 m with minimal assistance (Functional Ambulation Category ≥ 3); (3) were able to pass the Time Dependent Motor Imagery screening test (TDMI, see paragraph below); (4) were between 16 and 70 years old and (5) did not suffer from psychiatric symptoms or any other neurological disease.

The TDMI was developed and validated by Malouin (14) and requires the examiner to record the number of movements imagined over 3 time periods (15s, 25s and 45 s) and specifically only involves imagined movements. The test indicates whether a person is able to understand instructions and simulate movements.

The study was approved by the Ghent University Hospital Ethics committee.

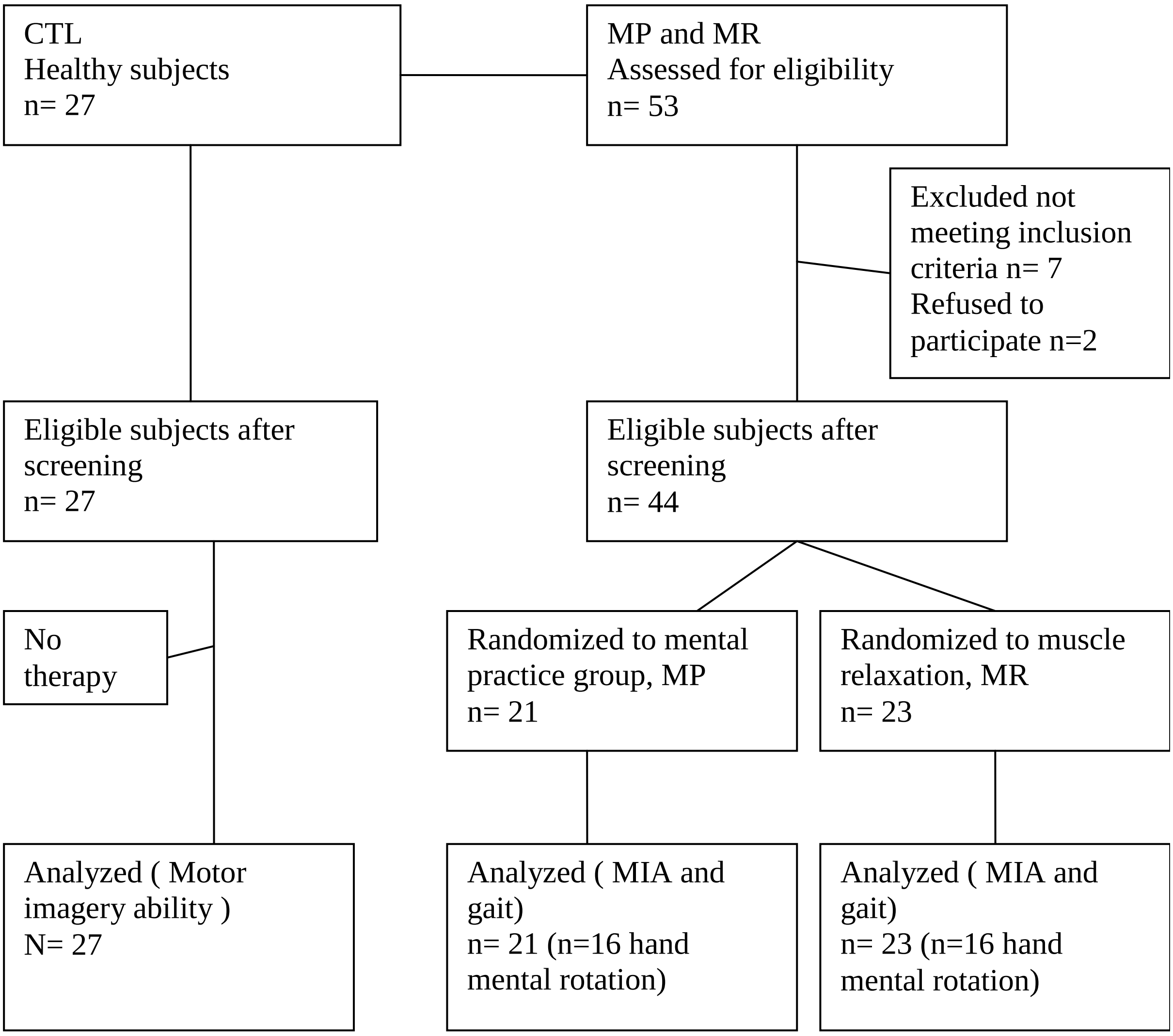

Figure 1. Flow of participants through the trial
Abbreviations: CTL, control; MP, mental practice; MR, muscle relaxation; n, number; MIA, motor imagery ability

Table 1. Participants' characteristics: mean (SD)

Characteristics	MIT group n=21	MR group n=23	p-value (MIT vs. MR)	CTL group n=27	p-value (patients vs. CTL)
Sex (♂:♀)	15:6	14:9	.46	14:13	.24
Age (years)	50.3(12.8)	53.7(12.0)	.38	47.3 (12.3)	.12
Disease duration (months)	4.7 (3.1)	3.6 (2.0)	.15	NA	
Hemiplegic side			.38		
Right	11	10		NA	
Left	10	13		NA	
Cause Hemiplegia			.82		
Ischemic	13	15		NA	
Hemorraghic	8	8		NA	
LE-FM (/34)	19.1 (5.6)	19.8 (5.6)	.73	NA	

Abbreviations: n, number; SD, standard deviation; MIT, motor imagery training; MR, muscle relaxation; CTL, control; NA, not applicable; LE-FM, lower-extremity Fugl-Meyer.

Procedures

All patients (MIT and MR) received a standard rehabilitation program, consisting of 2 hours of physical therapy and 1 hour of occupational therapy daily, five days per week. Physiotherapy was based on the Bobath concept using facilitation and guidance techniques. Additional physiotherapy and occupational therapy consisted of task-specific functional training including transfer and balance practice and walking incorporated in different daily activities.

In addition to standard training, the MIT group received 30-minute daily mental practice treatment sessions, based on the protocol described by Dickstein et al. (19). Each session was individually delivered in a quiet room in the hospital by two experienced therapists, who were not involved in any other part of the study. Every session started with 2 minutes of relaxation to promote a relaxed state preceding the actual imaging session. During motor imagery practice participants were seated in a (wheel) chair and were instructed to keep their eyes closed. The practice was performed from an internal perspective with both a visual (‘viewing’ themselves performing the task) and kinesthetic mode (‘feeling’ the experience of performing the task), with emphasis on the latter. During the first week the MIT participants were familiarised with the MI technique whereby the therapist gave visual, auditory and sensory cueing to each patient, focusing on imaging of environmental situations well known to the patient. During the second week MI training was focused on the individual patients’ gait problems such as forefoot landing, absence of knee loading response, knee hyperextension in stance and stiff knee gait. Gait specific lower limb movements (hip flexion/extension, knee flexion/extension, ankle flexion/extension) were thus guided by the results of the patient’s individual gait analysis (n=15). Additionally information concerning the patient’s gait problem areas was provided to the MI therapist by the treating rehabilitation therapist. During the third and fourth weeks, gait symmetry and velocity were rehearsed using different (motor imagery) walking tasks, focusing on integrating the components practiced previously into the (mental) gait cycle. Participants were asked to pay specific attention to step-length and walking velocity. Auditory cues were used to guide walking speed. During the last 2 weeks of practice, gait exercises were embedded in daily life activities. Patients were instructed to ‘view’ and ‘feel’ themselves walking in different situations and environments and on different terrains. Throughout the MI sessions, patients were asked open questions about the content of motor imagery sensations to verify their involvement in mental practice. Their feedback was used by the therapist to optimize further instructions regarding movement exercise and associated sensory perceptions.

The MR group, on the other hand, received the same amount of muscle relaxation therapy over and above the standard rehabilitation training. Muscle relaxation was used to control for therapeutic attention and consisted of relaxation therapy of daily 30-minute one to one sessions. Relaxation followed the principles of progressive muscle relaxation according to Jacobson (21). The basic principle of this technique is to begin by instructing participants to physically tense particular muscle groups in a given order and then to relax and let go of the contraction. During the same session the subjects were asked to concentrate on using diaphragmatic breathing to aid relaxation.

The motor imagery ability of the healthy control group (CTL) was also assessed to provide aged matched reference data.

Outcome measures

All participants (patients and healthy volunteers) were assessed at baseline and both patient groups (MIT and MR group) were reassessed after 6 weeks by the same assessor. A brief description of the tests used is provided below.

The first two tasks were used to assess aspects of motor imagery ability.

The Movement Imagery Questionnaire. The Movement Imagery Questionnaire-revised (MIQ-R) is a self-report questionnaire developed and validated by Hall et al. in order to assess visual and kinesthetic modalities of movement imagery (9). A revised version, the MIQ-RS was developed and validated by Gregg et al (22). The MIQ-RS is composed of 2 sub-scales of 7 relatively simple movements (like bending forward or pulling on a door handle) for use in people with limited mobility. For each item, 4 steps are required. First, the starting position of the movement is described by the examiner and the subject is asked to assume it. Second, the movement is described and the subject is asked to perform it. Third, the subject is asked to reassume the starting position and imagine producing the movement (no actual movement is made). Finally, the subject is instructed to rate the ease/difficulty with which he/she imagined the movement on a 7-point scale, where 1 is very difficult and 7 is very easy to picture (the visual sub-scale, $\text{MIQ-RS}_{\text{vis}}$) and feel (the kinesthetic sub-scale, $\text{MIQ-RS}_{\text{kin}}$).

Walking trajectory test. For this test, the participants were seated in a chair in front of a computer screen that displayed photographs of 3 walking trajectories. The walking trajectories had a varying length of 2, 5, and 10 m. The beginning of the walking trajectory was marked with a blue line and the end with a cone. There were 2 practice sessions, an imagery session referred to as the imagined walking time (IWT) and an actual walking session known as actual walking time (AWT). These two times were then expressed as a ratio: IWT/AWT which, if a subject took exactly the same time to actually walk as to imagine that they are walking, then the ratio would be equal to 1. Each imagery session started with the presentation of a photograph of a walking trajectory. The subjects were then asked to imagine walking at comfortable speed along the path and indicate when they had reached the cone.

The examiner recorded the duration of each trial. Subsequently, the subjects performed the actual walking trial. The actual walking session was always performed after the imagery session to minimize the amount of tacit knowledge about the time it actually took to walk along the trajectory.

Clinical outcome was assessed using validated and reliable tools for lower limb function after stroke: the 10 m walk test and the Lower-extremity Fugl-Meyer Assessment Scale (LE-FM) (23,24). The former test was used to assess an immediate training response of MI on walking and thus represents a near transfer effect of MI training. The latter test investigates possible far transfer effects of motor imagery since it encompasses a more general evaluation of lower limb function and is not just restricted to gait.

10 m walk test. Gait velocity was measured by asking the patient to walk a 10 m distance at comfortable speed. Times were recorded with a stopwatch after 2m, 5m and 10 m respectively. The patients performed this test with their usual assistive device and/or brace, using the same device at the pre and post training assessment.

Lower-extremity Fugl-Meyer Assessment Scale. This instrument measures distinct parameters of motor recuperation such as reflexes, voluntary control of isolated movement, co-ordination, speed and balance. The lower-extremity component of the scale was applied in this study. It consists of a total score of 34 points with 17 items scored on a 0 to 2 scale.

Statistical analysis

Statistical analysis was performed using SPSS Statistics 21.0 software. Data are expressed as median and interquartile range. For nominal scale data, Pearson’s Chi-square tests were used. Related-samples Wilcoxon Signed-Rank tests were used to investigate within-group differences and independent samples Mann-Whitney U tests were used to examine between-group differences. Analysis of variance was used to assess the interaction effect between group and pre-post measurements. Significance was accepted at $p \leq 0.05$.

Results

None of the participants dropped out during the study. The results are based on all 44 patients and 27 healthy controls. Individual participant characteristics are summarized in Table 1.

There were no statistically significant differences between the MIT and MR groups in demographic or clinical variables. At the start of the treatment, independent sample Mann Whitney U-tests showed that MIQ-RS$_{vis}$ and MIQ-RS$_{kin}$ scores were significantly ($p=.005$ and $p=.004$ respectively) higher in the control group than in the patient group (MIT and MR combined as 1 patient group). However, temporal coupling between imagined and actual walking (Imagery Walking Time/Actual Walking Time) revealed no differences between patients and controls (Table II).

Table 2. Descriptive statistics for the motor imagery ability variables (patients vs. controls): median (IQR).

Variables	Patients (MIT + MR) n=44 median (IQR)	Controls n=27 median (IQR)	Sig.
MIQ-RS Visual scale (/49)	35 (17)	41 (9)	.005
MIQ-RS Kinesthetic scale (/49)	30 (15)	39 (15)	.004
IWT/AWT	.95 (1.03)	1.11(1.94)	.44

IQR: Interquartile Range; Sig: significance level; MIT: motor imagery training; MR: muscle relaxation; MIQ-RS: Movement Imagery Questionnaire-Revised second version; IWT: imagery walking time; AWT: actual walking time.

More importantly, independent sample Mann-Whitney U-tests also revealed that the 2 treatment groups did not differ with respect to performance in baseline motor imagery ability performance, as MIQ-RS$_{vis}$, MIQ-RS$_{kin}$, and IWT/AWT ratios appeared very similar (Table III). Related-samples Wilcoxon Signed-Rank tests were used to evaluate the effect of treatment in general, that is comparing the pre-post assessment for the entire patient group (n=44). Main effects of session were found for MIQ-RS$_{kin}$, actual walking over 10m, and the lower-extremity Fugl-Meyer score (Table 3). Since the treatment by session effect cannot be captured in a nonparametric design, we used analysis of variance (ANOVA) to assess the interaction effect of treatment condition on the MI ability variables. Group (MIT, MR) was entered as between-subject factor, and session (baseline, final) was included as within-subject factor. A main effect of session was found for MIQ-RS$_{kin}$ and a group by session interaction effect revealed that after treatment the MIQ-RS$_{kin}$ scores had improved significantly more in the MIT group than in the MR group ($p < 0.05$) (Table III). Analysis revealed that the MIQ-RS$_{kin}$ scores of the MIT group after training showed no statistical difference from those scores of the healthy control group, indicating that the former were now within the normal range. The IWT/AWT ratio did not change statistically after the treatment and there was no group interaction effect. Finally, we similarly assessed the effect of the treatment condition on lower limb function. The 10-m walk scores and lower extremity Fugl-Meyer assessment (LE-FMA) scores improved significantly in both groups after treatment ($F_{(1,43)} = 42.0$, $p<0.001$ and $F_{(1,43)} = 34.3$, $p<0.001$ respectively). We also found a significant group interaction effect for the 10-m walk test ($F_{(1,43)} = 4.5$; $p<0.05$) revealing a significantly reduced walking duration in the MIT group compared to the MR group. There was no significant interaction between session and group for the LE-FMA score ($F_{(1,41)} = 34.2$, $p=0.35$).

In order to assess the possible influence of initial MI-vividness on gait improvement, we investigated the association between baseline MIQ-RS scores and walking speed. No significant correlation between initial MIQ-RS scores (nor of pre-to-post changes of the MIQ-RS scores) and gait velocity improvement after treatment was found.

		MIT group n=21		MR group n=23		
	inclusion median(IQR)	after 6 weeks median(IQR)	inclusion median(IQR)	after 6 weeks median(IQR)	sig*	sig**
MIQ-RS $_{vis}$ (/49)	35 (15)	40 (9)	37 (17)	33 (21)	.102	.08
MIQ-RS$_{kin}$ (/49)	28 (13)	35 (9)	30 (15)	30 (22)	**.021**	**.044**
IWT/AWT	1.12 (1.17)	1.12 (.64)	.84 (.83)	1.0 (.45)	.56	.82
AW 10m(s)	33.4 (27.0)	19.3 (21.3)	29.1 (30.6)	18.0 (19.1)	**<.001**	**.04**
LE-FM (/ 34)	17.0 (11.0)	21.5 (12.0)	18.5 (9.0)	22.5 (10.0)	**<.001**	.35

Table 3. Patients' performance and treatment effects in all outcome measures: median (interquartile range; IQR) and comparison of treatment effects between the experimental and control group after 6 weeks.

* Main effect of assessment (pre-post), within-group comparisons, significant values according to the Wilcoxon signed-rank test are in bold.
** Interaction effect between treatment type (MIT/MR) and assessment time (pre-post),
between-groups comparisons, significant p-values are in bold.
IQR: Interquartile Range; MIQ_{vis}: Movement Imagery Questionnaire-Revised second version visual subscale; MIQ_{kin}: Movement Imagery Questionnaire-Revised second version kinesthetic subscale; IWT: imagery walking time; AWT: actual walking time; AW: actual walking; FM-LE, lower-extremity Fugl-Meyer; MIT: motor imagery training; MR: muscle relaxation.

Discussion

Effect of Motor Imagery training on MI ability

Motor imagery ability can be affected by stroke. It is not known if being able to perform MI tasks is necessary to gain benefit from it in clinical practice (8,9). Moreover, Confalonieri et al. report that motor imagery stimulates sensorimotor and pre-motor areas even in poor imagers with stroke (25). In our study we found no correlation between motor imagery ability (as reflected by initial MIQ-RS scores) and our outcome measure of gait velocity improvement after motor imagery training. This suggests that those with poor motor imagery seemed to have the same improvement as those who were the better imagers. When using the MIQ-RS questionnaire, we found that both the visual and kinesthetic imagery modalities differed significantly from normal data in our stroke study population. Although frequently used, the questionnaire scores remain a subjective reflection of the estimated motor imagery vividness. In a further study by Malouin and colleagues, motor imagery vividness was measured using the Kinesthetic and Visual Imagery questionnaire (KVIQ-20) (12). They found a continuum of good to bad imagers similar to a normal age-matched population. The results of our study also indicate that MI vividness responded well to MI training with a significant increase in the kinesthetic subscale scores. This may be important as kinesthetic imagery from the first-person perspective has been shown to best activate the mental processes involved during motor task training (26). Our study results indicate that patients with poor imagery vividness pre-treatment should not be excluded from mental practice. However, the technique should first be taught, incorporating a training period at the start of the intervention period and to provide an extended learning period for poor imagers to become familiar with the procedure.

In our cohort the temporal organization of motor imagery measured by the imagined/actual walking ratio did not differ from the data of the healthy control subjects. Task instructions and the use of two-dimensional photographs might have influenced the results in both groups so they all slightly overstated the time to imagine. However a strong relationship was found between imagery and actual walking times in both groups. Stroke patients were markedly slower on the imagery condition but their actual walking was slowed to the same extent, indicating a preserved MI performance. These results concur with the findings of Malouin and co-workers who also found that the temporal representation of a complex locomotor task (Timed ‘Up and Go’ Test) was retained following stroke (2). The close temporal relationship between actual and imagined walking revealed that subjects were able to imagine walking in an environment in which they were not actually present.

Effect of motor imagery training on gait

More importantly, our study addressed the hypothesis that a combination of physical practice and motor imagery training is more effective than physical practice alone in gait rehabilitation in the sub-acute phase following stroke. The main outcome of this study indicates that there is modest but clear evidence supporting the additional benefit of mental practice in gait rehabilitation in the sub-acute phase after stroke, with a positive effect of a motor imagery intervention on gait velocity measures. We found a significant group interaction effect for gait velocity, measured by the 10 m walk test in that, the MIT group, although having initial lower (non-significant) gait velocities, their velocity improved more than that of the MR group at 6 weeks. Although gait velocity does not give an indication of the quality of movement, it is a valid and reliable measure and sensitive to change in walking capacities (27).

Several studies using mental practice in stroke populations have reported significant positive effects on motor function (5-7). Dunsky and colleagues investigated the feasibility of a home-based motor imagery training program for gait rehabilitation in chronic stroke and demonstrated a positive effect on gait performance (5). A locomotor imagery training with a five-stage protocol was described by Hwang et al. (28). Their subjects received a videotape-based motor imagery showing a young adult with a normal gait. Problem identification was an important part of the treatment protocol. Although no videotape was used in this study, we also focused on individual gait problems, if available guided by gait analysis data. Cho and co-workers combined treadmill training and MI training to investigate the effect of MI in chronic stroke (20). Gait training with motor imagery training improved balance and gait abilities significantly more so than gait training alone. The results of the current study concur with these findings.

In a review paper Langhorne and co-workers report that interventions including high intensity therapy and repetitive task training can improve gait (29). Mental practice includes both of these intensive and repetitive aspects. Additionally, brain imaging studies have confirmed the functional similarity between real walking and imagined walking (30). The literature further suggests that MI shares cortical circuitry with the preparation and execution of motor tasks and increases motor excitability (31,32). The inclusion of motor imagery alongside physical practice may therefore promote learning by reinforcing processes at the cortical level and by priming neuromotor pathways required for walking performance.

Motor recovery, independent of treatment group, was evident in our study but we found no statistically significant group interaction effect for motor recuperation, as measured by the Fugl-Meyer Assessment. These results contradict results from other studies (7,33). In the current study both groups improved, supported by an intensive rehabilitation program, and so perhaps the contrast between the two experimental protocols was not large enough to detect a possible effect of motor recuperation. In addition, the Fugl-Meyer assessment includes several other aspects of motor function that were not addressed in our training protocol. Due to task-specificity of motor learning, this could explain the absence of a significant ‘between group’ improvement of this parameter. In their study Ietswaart et al. found no effect of motor imagery training in upper extremity function in sub-acute stroke patients (34). Unlike other studies they did not combine physical and mental practice which may be essential for a possible benefit of this therapy (35). Thus imagery training may represent a complementary technique to actual motor training but may not replace it. In our study patients were involved in a standard rehabilitation program which included intensive actual gait training, thus linking the appropriate kinesthetic information directly to the MI. When gait velocity and symmetry were practiced in this study (especially weeks 3 and 4) we also included auditory cueing to guide motor imagery performance. Kim et al. compared four imagery protocols and found that the kinesthetic imagery, combined with auditory cueing, provided the largest treatment effect (36). The use of rhythmic auditory cueing may assist in co-ordinating sequential movements such as walking.

MI training was well tolerated by all participants. Patients involved in MI highly appreciated the training and were very motivated. They frequently revealed the further use of MI as a strategy in daily activities after finishing the study. Engagement in MI may increase self-efficacy, thus having a positive effect on motivation and self-confidence.

This study has its limitations in that it involved a relatively small number of patients. It is important to also be aware that the study included a young sub-population of stroke patients. The full potential of MI in older participants has been investigated and imagery capacity seems to decrease with age (37). The inclusion of a younger group of stroke patients may therefore, compromise generalisation of our results. Additionally, due to the absence of longer term follow-up in our patient cohort as yet, we could not report on this aspect. Finally, although current best practice for motor imagery was applied, detailed descriptions of MI training elements in neurorehabilitation are still lacking and further research is warranted (38,39).

In conclusion, the results of this study indicate that patients in a sub-acute phase following stroke have a preserved temporal coupling between real and imagined walking movements. We found significantly lower MI vividness scores in our study cohort but our results demonstrate that MI vividness can be trained and stimulated to a higher level of performance. These results concur with other studies in chronic stroke regarding motor imagery training as an adjunct to physical practice in gait rehabilitation. Mental practice appears to be an additional gait rehabilitation method in a sub-acute phase following stroke but further studies are required to examine the long-term benefit of this treatment.

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Chapter 4

Neural correlates of motor imagery ability following stroke.

Damage to fronto-parietal networks impairs motor imagery ability after stroke:
A voxel-lesion symptom mapping study.
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Abstract

Background: mental practice with motor imagery has been shown to promote motor skill acquisition in healthy subjects and patients. Although lesions of the common motor imagery and motor execution neural network are expected to impair motor imagery ability, functional equivalence appears to be at least partially preserved in stroke patients.
Aim: to identify brain regions that are mandatory for preserved motor imagery ability after stroke.
Method: thirty-seven patients with hemiplegia after a first time stroke participated. Motor imagery ability was measured using a Motor Imagery questionnaire and temporal congruence test. A voxelwise lesion symptom mapping approach was used to identify neural correlates of motor imagery in this cohort within the first year post-stroke.
Results: poor motor imagery vividness was associated with lesions in the left putamen, left ventral premotor cortex and long association fibres linking parieto-occipital regions with the dorsolateral premotor and prefrontal areas. Poor temporal congruence was otherwise linked to lesions in the more rostrally located white matter of the superior corona radiata.
Conclusion: This voxel-based lesion symptom mapping study confirms the association between white matter tract lesions and impaired motor imagery ability, thus emphasizing the importance of an intact fronto-parietal network for motor imagery. Our results further highlight the crucial role of the basal ganglia and premotor cortex when performing motor imagery tasks.

Keywords

Motor imagery, stroke, lesion symptom mapping, basal ganglia, white matter

Introduction

Motor imagery can be defined as a dynamic state during which a person mentally simulates a given action without actually performing it (Decety, Jeannerod,1996). Mental practice is the cognitive process through which a person repeatedly mentally rehearses a specific task without performing any actual body movement. Mental practice through motor imagery has been shown to promote motor skill acquisition in healthy subjects and in patients (Grouios, 1992; Heremans et al, 2012; Burianova et al, 2013; Kraeutner et al, 2015).

A combination of mental practice and physical practice has been recommended to improve upper and lower limb function in stroke patients and to promote relearning of daily tasks in neurologic rehabilitation (Schuster et al, 2011; Liu, 2004; Page et al, 2007; Malouin, Richards 2010; Cho et al, 2012). Especially patients in an early stage after stroke may benefit from motor imagery training. Mental practice can re-activate sensorimotor networks and induce neuroplasticity, thus preventing maladaptive non-use reorganization (Lotze, Cohen, 2006; Butler, 2006; Page, 2009).

Despite general optimism, recent negative trials have shown that not all patients may benefit from mental practice (Ietswaart M et al, 2011; Timmermans et al, 2013). Ietswaart and co-workers (2011) investigated the effect of 4 weeks of mental practice without any specific related physical practice in a large cohort of stroke patients. Their results showed that mental practice alone did not enhance motor recovery in stroke patients early post-stroke. As a result, more information about the relationship between motor imagery ability, brain damage, and motor training outcome remains warranted. Neuroimaging studies have revealed that imagination of an action and actual motor execution share many common motor and motor-related regions (Sharma et al, 2009; Gerardin et al, 2000; Szameitat et al, 2012; Kraeutner et al, 2014). Motor imagery and physical practice networks are not completely overlapping but appear to be functionally equivalent (Di Rienzo et al 2014; Lotze , Halsband, 2006).

The parts of the neural system that are most frequently reported to be involved in motor imagery are the supplementary motor area, the premotor area, posterior parietal regions, the basal ganglia and the cerebellum (Munzert et al, 2009; Liepert et al, 2012; Hétu et al 2013).

Several investigators have explored motor imagery ability in stroke populations. Due to the loss of integrity of the motor planning network (including premotor, posterior parietal and prefrontal regions), motor imagery ability is expected to be impaired accordingly in these patients. Damage to the parietal cortex has been shown to impair the generation of movement images (Sirigu et al, 1996; McInnes et al, 2015).

However research provides evidence that motor imagery ability is at least partially preserved in most stroke patients with motor imagery profiles paralleling actual motor impairments (Lotze, Halsband, 2006). In a study by Liepert et al. (2012) it was shown that patients with somatosensory deficits were more impaired in their ability to perform a mental chronometry task than stroke patients with pure motor deficits. The impairment of mental chronometry seemed to be the result of a reduction in somatosensory input from the affected upper limb. Malouin and co-workers (2008) found that the level of motor imagery vividness following stroke was similar to that of healthy subjects with good and bad imagers in both groups, although they reported a better motor imagery vividness for the unaffected side. Using the Movement Imagery Questionnaire-Revised second version (MIQ-RS), we have shown in a previous study that both the visual and kinaesthetic imagery modalities differed significantly from normal data in our stroke study cohort. However, motor imagery vividness responded well to motor imagery training with a significant increase in kinesthetic subscale scores (Oostra et al, 2015). Confalionieri and colleagues (2012) confirmed the shared neural circuitry between motor imagery and motor execution, involving a widely distributed frontoparietal network and subcortical structures, in chronic stroke patients. Moreover, low kinesthetic imagery ability was correlated with more activation of the contralesional primary motor cortex and ipsilesional primary somatosensory cortex in their study cohort.

Currently, lesions in the parietal cortex, left prefrontal area and basal ganglia have been reported to result in a loss of motor imagery ability in stroke patients (Sirigu et al, 1995; Li, 2000). In an extensive review Di Rienzo (2014) recently concluded that cerebral activity during motor imagery is highly correlated to structural and functional neuroplasticity. However a specific lesion localization that was unequivocally correlated with impaired motor imagery ability could not be identified.

Therefore, our goal in the present study was to clarify which brain regions are necessary for intact motor imagery ability after stroke. To evaluate motor imagery ability two behavioural tests were combined. To measure motor imagery vividness - both the clarity/sharpness of images and the intensity of sensations during motor imagery - a motor imagery questionnaire was used. The ability to preserve the temporal characteristics between the physical movement and motor imagery movement was measured using a temporal congruence test (McAvinue,2008). We examined the relationship between perceived motor imagery vividness of stroke patients, reflected by their score on the MIQ-RS and brain lesion localization on the one hand and temporal congruence between real and imagined movements and brain lesion localization on the other. To test whether impaired motor imagery ability was significantly associated with certain lesion locations in the brain, we conducted a voxel-based lesion-symptom mapping analysis, a technique that statistically assesses the lesion’s affect on behavioural scores on a voxel-by-voxel basis (Bates et al, 2003). The technique allows us to conduct a statistical test in each lesioned voxel to determine if a difference exists between the lesioned and non-lesioned group for a certain behavioural measure (Rorden et al, 2007).

Materials and Methods

Method

Participants

Thirty-seven patients with hemiplegia after a first time stroke participated in this study. Twenty-five males and twelve females were included. The average age was 53 years with a range of 17 to 68 years. The time from stroke varied from 1 to 12 months, with a mean disease duration of 4 months. Most patients (n=34) underwent formal neuropsychological testing. Rather than presenting all these data, we selected a measure of attention, the Test of Attentional Performance, as marker of general information processing speed as this ability is likely to be most reflective of the cognitive demands required by the behavioral tasks in this study. The Test of Attentional Performance comprises simple reaction time paradigms with the patient reacting selectively to non-verbal stimuli with a simple key-press (Zimmermann et al, 2012). The results of this neuropsychological test are presented as Z-scores in Table 1. The average Z-score of.86 reflects that most patients performed within one standard deviation (SD) below the normative mean on the attention task. Only five patients performed more than 2 SD below the norm and no one exceeded the 3 SD limit. To measure motor recuperation the Fugl-Meyer Assessment Scale was used. This instrument measures distinct parameters of motor recuperation such as reflexes, voluntary control of isolated movement, co-ordination, speed and balance. The lower-extremity component of the scale consists of a total score of 34 points, the upper-extremity component comprises a total score of 66 points with all items scored on a 0 to 2 scale (Fugl-Meyer et al, 1975). The results of the Fugl-Meyer scale are presented in Table 1. For a more detailed account of the individual data summarized in Table 1, the reader is referred to supplementary Table 1.

The patients were recruited via the University Hospital and from hospitals in East and West Flanders to the Rehabilitation Centre, Ghent University Hospital. Participants were eligible if they: (1) had experienced a first time stroke less than one year before entering the study; (2)

were between 16 and 70 years old and (3) did not suffer from psychiatric symptoms or any other neurological disease.

Table 1. Patients' characteristics

Characteristics	
Age (years)	53 (range 17-68 yrs)
Gender (♀: ♂)	12:25
Side hemiplegia	
right	15
left	22
Cause hemiplegia	
ischemic	21
hemorrhagic	16
Time since stroke (months)	4 (range 1-12 mths)
Fugl-Meyer Assessment Scale Upper Extremity (/66)	30.1±10.3 (mean±SD)
Fugl-Meyer Assessment Scale Lower Extremity (/34)	19 ±6.2 (mean±SD)
Test of Attentional Performance	-0.86 ±0.9 (Z-score, mean±SD)

All subjects provided written informed consent according to the Declaration of Helsinki. This study was approved by the Ethical Committee of the Ghent University Hospital (registration n° B67020084961).

Materials and procedures

Motor imagery ability

Motor imagery vividness was assessed using a self-report questionnaire, developed and validated by Hall et al. in order to assess visual and kinesthetic modalities of movement imagery (Hall, 1997). A revised version, the MIQ-RS was developed by Gregg et al. (Gregg et al, 2010) for use in people with limited mobility and validated by Butler and co-workers (2012) for evaluating motor imagery ability in stroke populations. The MIQ-RS is composed of 2 sub-scales of 7 relatively simple movements (like bending forward or pulling on a door handle). For each item, 4 steps are required. First, the starting position of the movement is described by the examiner and the subject is asked to assume it. Secondly, the movement is described and the subject is asked to perform it. Thirdly, the subject is asked to reassume the starting position and imagine producing the movement (no actual movement is made). Finally, the subject is instructed to rate the ease/difficulty with which he/she imagined the movement on a 7-point scale, where 1 is very difficult and 7 is very easy to picture (the visual sub-scale, MIQ-RS_{vis}) and to feel (the kinesthetic sub-scale, MIQ-RS_{kin}).

When administering the kinesthetic subscale, subjects were encouraged to imagine the tasks from a first person perspective and feel themselves moving. For the visual subscale, the subjects were instructed to see themselves moving from a third person perspective as if looking from a distance to themselves.

Mental chronometry tests measure the temporal coupling between real and imagined movements and evaluate motor imagery accuracy. The temporal congruence test was developed by Malouin and co-workers and measures the temporal correspondence between imagined and actual stepping movements (Malouin, 2008). The patients are seated in a chair and instructed to first imagine and then to physically perform 5 stepping movements, placing their foot on a board in front of them. During the imagery task, the subjects have their eyes closed. The examiner records the duration of real and imagined stepping movements. According to the mental chronometry paradigm, it is expected that movement times in both conditions will be similar with the imagined/actual movement time ratio equalling one.

Analysis of imaging data

Structural brain images were obtained using MRI scans, which were performed on clinical indication in the sub-acute phase after stroke. Thirty-one patients were scanned in the Ghent University hospital on 1,5 T Siemens Trio scanners (Siemens, Erlangen, Germany). Due to initial hospitalisation in another setting, the remaining 6 patients were scanned with 1.5 T MRI scanners in different hospitals.

For each subject a whole brain T1-weighted anatomical image that was obtained in the sagittal orientation and a FLAIR image in the transverse plane was available. Clinical T1 images were scanned with a pixel spacing around 0.45 x 0.45 mm and slice thickness between 4-6 mm, clinical FLAIR volumes were scanned with a pixel spacing around 0.9 x 0.9 mm and slice thickness between 4-6 mm.

Brainvoyager software was used for MRI data processing and normalisation (Goebel, 2012). All T1 and FLAIR scans were isovoxelized to a 1 x 1 x 1mm resolution using sinc interpolation. We used sagittal T1 MPRAGE images for AC-PC orientation of the isovoxelized anatomical scan. Following co-registration of the isovoxelized T1 and FLAIR 3D volumes, AC-PC transformations were applied to the FLAIR scan and this transverse scanned volume was warped into standard Talairach space. Lesion demarcation was based on the FLAIR images that were uploaded in MRIcron. The lesioned areas were manually traced by the first author, using MRIcron to draw the regions of interest (Rorden, Brett, 2000). The extension and location of the lesion shapes were controlled by an experienced radiologist, who was blinded to the performance of the subjects on the motor imagery ability tests.

We applied Voxel-Lesion Symptom Mapping analyses to the lesion and behavioural data (Rorden et al, 2007). We used the non-parametric Brunner Munzel test with the significance level set to $p< 0.01$. In the current study, an ‘a priori’ minimum lesion density threshold was set at 20%, i.e. analyses were confined to those voxels in which there were at least seven patients with and seven patients without a lesion, in order to avoid running analyses in voxels in which very few patients had lesions. To define a ‘significant’ voxel, a statistical threshold cut-off was determined based on permutation testing (n=2000). With permutation testing the patients’ behavioural scores are randomly reassigned across the voxels 2000 times. For each permutated dataset, the statistics are re-run and the top 5% of t-values calculated.

Brain regions corresponding to the significant voxel locations were determined using the Talairach and Montreal Neurological Institute and Hospital (*MNI) co-ordinate* systems where appropriate. For the identification of white matter structures, a white matter reference atlas was used (Oishi et al., 2011). All reported coordinates are presented in MNI co-ordinates in Table 3.

Results

Behavioural results

The behavioural results from 37 subjects with sub-acute stroke are summarized in Table 2. The vividness of motor imagery was measured using a validated motor imagery questionnaire, the MIQ-RS. The mean total MIQ-RS score was 60.84 (SD +/- 20.13). The mean score for the MIQ visual subscale was 32, with a range of 11 to 49. The mean score for the MIQ kinesthetic subscale was 29 with a range of 8 to 47. We found a significant correlation between kinesthetic and visual MIQ-RS subscales ($r = .82$, $p<.001$).

According to the MI Ability Assessment Scale a total MIQ-RS score ≤ 48 indicates MI inability, a score between 49 and 73 indicates MI impairment, whereas a score ≥ 74 indicates preserved MI ability (Mc Innes et al, 2015).

The temporal congruence test scores revealed a statistically significant correlation between imagery stepping time and actual stepping time ($r = .78$, $p<.001$).

The MIQ-RS_{tot} score was not significantly correlated with the results of the mental chronometry test ($r =.004$, $p=.98$)

Table 2. Performance of stroke patients on behavioural motor imagery ability tests.

Measures	N	minimum	maximum	mean	SD
MIQ-RS					
Kinesthetic scale	37	8	47	32.1	10.4
Visual scale	37	11	49	28.7	10.7
Total scale	37	22	96	60.8	20.1
Temporal congruence stepping test					
Ratio IS/AS	37	.00263	.7717	.2506	.176

MIQ-RS: Movement Imagery questionnaire-revised second version; IS: imagined stepping; AS: actual stepping

Neuroimaging results

Figure 1 shows the lesion overlay map for all 37 stroke patients with brighter regions indicating a greater degree of lesion overlap. Although the distribution of lesions involved both of the hemispheres, lesions and lesion overlap were larger in the right hemisphere where they also encompassed more anterior regions.

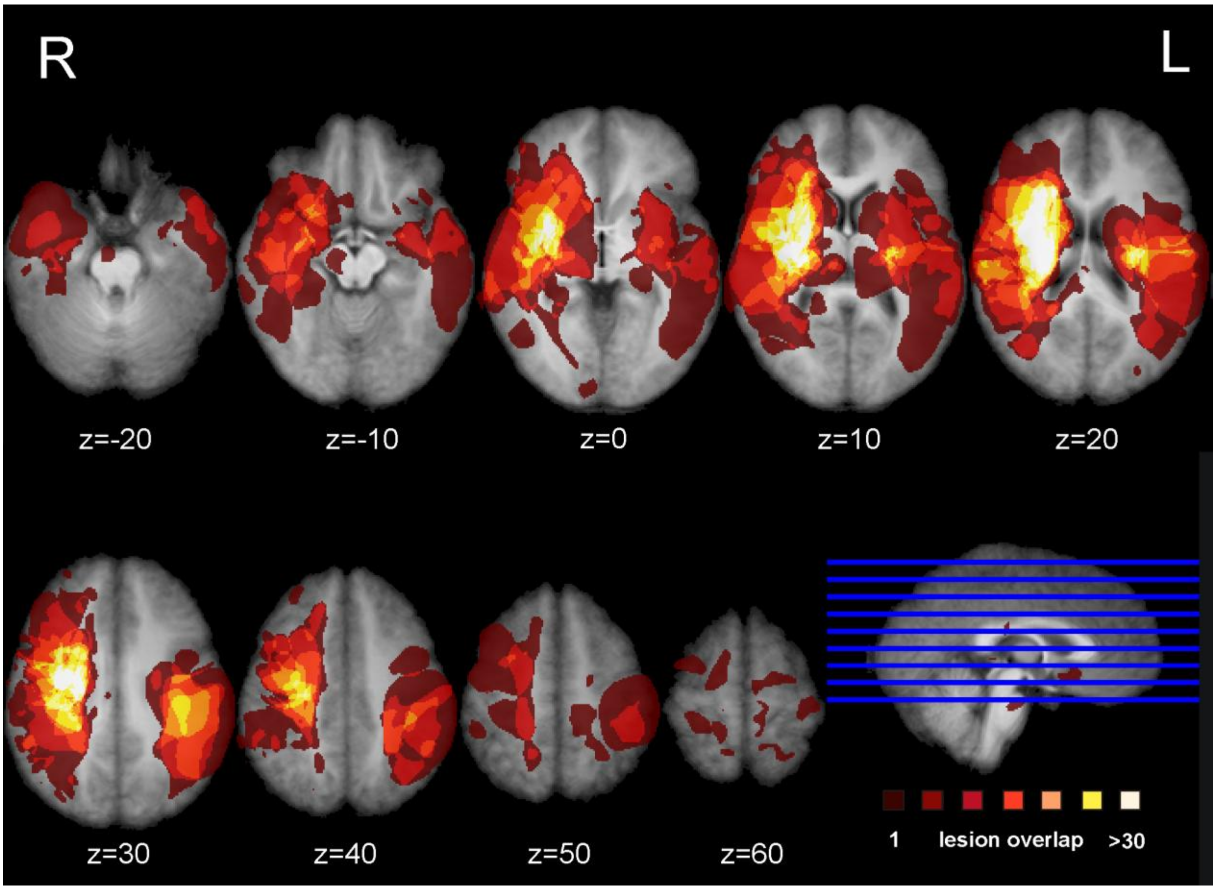

Figure 1. Lesion overlap map. Overlap of the binarized lesions of the 37 stroke patients included in the study. Lesions are displayed over horizontal sections parallel to the AC-PC line. Brighter regions indicate a greater degree of overlap of lesions.

Significant voxels associated with poor motor imagery vividness were identified in the left hemisphere, with significant foci in the putamen, the left ventral premotor cortex and the underlying white matter, connecting frontal and parietal/occipital regions (superior fronto-occipital fasciculus and claustrum region).

The mapping of the temporal congruence score (imagined/actual stepping ratio) on the lesioned brains through VLSM revealed the involvement of an area, localized in the superior part of the corona radiata. The results of the VLSM Brunner-Munzel test are presented in Table 3 below and show significant voxels, to be present in at least 7 patients, marked with MNI coordinates.

Table 3. Results of the VLSM analyses on motor imagery vividness and temporal congruence performance indices. Location of significant peak voxels based on MNI coordinates.

Brain region	Hemisphere	MNI coordinates		
		x	y	z
Motor imagery vividness				
Putamen	L	-27	1	-4
Gyrus frontalis inferior pars opercularis	L	-38	-4	3
External capsule/extreme capsule/claustrum*	L	-29	-18	13
		-29	-21	14
Superior Fasciculus fronto-occipitalis (sFOF)	L	-20	19	21
		-18	21	18
		-20	11	26
		-22	13	24
		-25	14	21
Anterior Corona Radiata	L	-18	23	18
		-18	27	15
Temporal congruence score				
Superior Corona Radiata	L	-26	-16	40
		-29	-14	38
		-24	-14	40
		-20	-6	34
		-18	-8	35
		-22	-4	34
		-27	14	21

L=left; x co-ordinate=right/left; y coordinate=anterior/posterior; z coordinate=superior/inferior

* Cannot be resolved with current resolution

Discussion

The present study used a voxel-based lesion-symptom mapping analysis to explore the relationship between motor imagery ability and brain lesion localization after stroke. Motor Imagery, being an internal process, is inherently difficult to assess in an objective manner. It is difficult to determine to what extent a person is able to generate vivid mental representations of movements and adhere to motor imagery training. Moreover, because motor imagery and motor execution are believed to share the same underlying neural network, any structural damage to the brain could affect both motor performance and motor imagery ability. Although the ability to perform motor imagery seems to be at least partially preserved after stroke, motor imagery vividness and accuracy can be hampered. Sharma and co-workers (2006) refer to this disturbed motor imagery accuracy as ‘chaotic’ post-stroke motor imagery. The predictive value of motor imagery ability tests to determine who might be the best potential candidates for mental practice, has not been fully established yet. Moreover, in a previous study we found no significant correlation between initial MIQ-RS scores, changes of the MIQ-RS scores and motor improvement, indicating that poor imagers can equally benefit from motor imagery training (Oostra et al, 2015). However it seems important to screen for motor imagery ability, to be able to estimate the need to teach motor imagery practice through an individually tailored initiation program, before starting mental practice. We are aware that screening for motor imagery ability on the basis of lesion localization is insufficient, but it may possibly give an indication which stroke survivors are potentially poor imagers.

Our present study results indicate that lesions in the left hemisphere, more specifically the left putamen and left ventral premotor cortex were associated with poor motor imagery vividness in stroke patients as measured with the MIQ-RS questionnaire. We further demonstrated the importance of an intact frontoparietal functional network for motor imagery. More specifically, lesions in the transition area between the anterior corona radiata and the superior fronto-occipital fasciculus and the more ventrally situated fibres near the claustrum were shown to be associated with impaired motor imagery vividness. Poor temporal coupling between real and imagined movements was solely associated with lesions in the white matter tracts, localized in the superior part of the corona radiata of the left hemisphere.

Basal ganglia. The results of our study further highlight the role of the basal ganglia in motor imagery. We found a correlation between putamen lesions and poor motor imagery ability, a finding which is corroborated by the work of Li (2000). They included patients with lesions of the putamen and compared the results to those obtained in patients with motor cortical lesions. Li found that lesions of the putamen as well as motor cortical lesions impaired movement imagery. Moreover a recent meta-analysis highlighted that damage to the putamen drives the impairment in MI after basal ganglia damage (Mc Innes et al, 2015). The role of the putamen in the planning and execution of a self-generated defined action has been demonstrated by several investigators (Monchi et al, 2006; Doyon et al, 2009). Lacourse and co-workers (2005) provided evidence for a substantial overlap of the functional neuroanatomy maps of movement execution and motor imagery in both early and skilled learning. This investigator showed that congruency between motor imagery and motor execution became increasingly similar in the skilled condition, with putamen activity increasing nearly a hundredfold in the skilled phase of learning.

We found significant voxels related to poor motor imagery ability in both the posterior and anterior part of the putamen, with the latter being more robust. Guillot et al (2008) showed that good and poor imagers differed in putamen function, with poor imagers activating anterior associative regions while good imagers were showing a more posterior activation in the sensorimotor region of the putamen.

Finally, the left putamen has been shown to take part in working memory, more specifically the putamen appears to hinder irrelevant information from entering the working memory (Baier et al, 2010). While performing motor imagery, subjects are generating and maintaining an internal model of motor action within the working memory, and the vividness of the imaging experience appears to be associated with the formation and maintenance of the image in working memory. Working memory impairment has clearly been shown to have a negative impact on motor imagery performance (Malouin, 2004).

The gyrus frontalis pars opercularis (BA 44). We further defined significant voxels in the left opercular part of the inferior frontal cortex to be associated with poor motor imagery vividness. The crucial role of this area in motor imagery and performance of visually guided movements is in agreement with Binkofski et al. (2000). They demonstrated that a left hemispheric activation of this region was associated with motor imagery from a first person perspective, while the imagery of a moving target was associated with activation of the right ventral opercular cortex. Our aim was to focus on motor imagery from one’s own movements and activation of the left ventral premotor cortex (vPMC) was confirmed.

The superior fronto-occipital fasciculus (sFOF)/claustrum. Our results further revealed a cluster of significant voxels in the transition area between the sFOF and anterior corona radiata that were correlated with poor motor imagery. Prefrontal and parietal regions are shown to form a functional network for motor imagery and disconnections in this network could account for impaired motor imagery ability (Mc Innes et al, 2015). An activation likelihood estimation meta-analysis by Hétu et al (2013) demonstrated that a large frontoparietal network is involved when a person imagines himself moving from a first person’s perspective. Lorey et al (2011) further showed that the extent of neural activation of the parieto-premotor areas was closely linked to perceived motor imagery vividness.

The sFOF or fronto-occipital fasciculus is one of the long association systems of the dorsal visual stream (Makris et al, 2007). According to Forkel et al (2014), the sFOF probably represents an occipital extension of the superior longitudinal fasciculus, running in the outermost region of the corona radiata. Our results indicate that lesions in this region of the long associative fibres mediating the integration of visual and sensory information for motor planning and control, are associated with poor motor imagery vividness. Kraeutner and co-workers (2015) recently demonstrated the importance of the left inferior parietal cortex (IPL) for MI performance. A preserved function of the IPL was shown to be critical for learning the cognitive aspects of a skill via MI practice.

Vry and colleagues (2012) describe a similar dorsal network, activated during motor imagery and motor execution in a healthy population. However they localize the dorsal network more laterally, corresponding to those fibres of the superior longitudinal fasciculus. These authors further describe an imagery-specific left hemispheric network with more ventrally localized fibres converging into the subinsular white matter near the claustrum, assigned to the extreme/external capsule. This finding could be relating to those voxels that we identified in the claustrum region.

Although MI has been shown to activate a widespread and bilateral neural network, we observed in particular a left hemispheric contribution for motor imagery tasks in this study cohort. Left brain dominance for motor planning of complex movements is in agreement with previous findings (Stinear et al, 2007; Bakker et al, 2008). Gerardin (2000) found that activation in the parietal cortex during imagination was predominant in the left hemisphere, while actual movement execution activated both parietal lobes symmetrically. Sabate and colleagues (2004) showed an increased performance time in both real and virtual movements in their stroke patients but velocity of imagined movements in both hands only decreased in patients with left-brain lesions.

Superior corona radiata. In our patient cohort a disturbed temporal coupling between real and imagined movements - as reflected by the results of the temporal coupling test - was solely associated with lesions in the superior part of the left corona radiata. Our results indicate that motor imagery questionnaires and temporal coupling tests address different MI modalities that involve different brain areas. While motor imagery vividness seems to reflect the movement-related anticipatory cognitive processes that precede movement, the temporal congruency between real and imagined stepping movements seems to be more related to pure motor action. Using lesion symptom mapping, Lo and co-workers (2010) showed that a lesion at the junction of the corona radiata and the corticospinal tract was critical for maintaining complex motor performance in their stroke population. Diffusion Tensor Imaging (DTI) study results identified that this area was connected with the premotor cortex, sensory cortex and primary motor cortex, with fibres converging to form the corticospinal tract, superior to the internal capsule.

Study limitations. We used the Motor Imagery Questionnaire-Revised second version to classify our patients into high or low imagers. Although MI questionnaires have been shown to be reliable and valid tools to screen for MI vividness and allow us to distinguish between high and low imagers, the scores remain a subjective reflection of the motor imagery capacity of the individual and this subjectivity remains an important disadvantage of this motor imagery measure (Malouin et al, 2008; Hall, 1997; Guillot, Collet, 2005). Nevertheless, a study by Lorey (2011), examining brain activation patterns during the imaging of movements, has shown a close relationship between the motor imagery vividness scores and the level of brain activation.

The use of an implicit motor imagery measure such as the hand laterality test would have been a more objective measure of motor imagery ability. On the other hand, de Vries and co-workers (2013) demonstrated that implicit and explicit motor imagery were differently affected in stroke patients. The patients in their study cohort scored below controls for both aspects (visual and kinesthetic) of the MIQ-RS while accuracy scores of an implicit motor imagery task did not significantly differ from the control group.

There are further limitations in the interpretations of our study that relate to the involvement and connectivity of white matter tracts. A complementary DTI study, allowing more precise identification and reconstruction of the involved white matter tracts, seems essential to enable us to gain a greater understanding of our findings.

Finally the small sample is a limitation of this study. Although 37 subjects were included, not all brain regions were sufficiently covered. Only one patient with a cerebellar lesion was included. Given the variability in lesion location coupled with the small sample size, it is possible that the distribution of MIQ scores is not completely reflective of the true distribution that would be observed in a larger sample.

Conclusion

Our results confirm the importance of an intact functional fronto-parietal network for preservation of motor imagery ability after stroke. Voxel-lesion symptom mapping further identifies the role of the basal ganglia and premotor cortex when performing motor imagery tasks.

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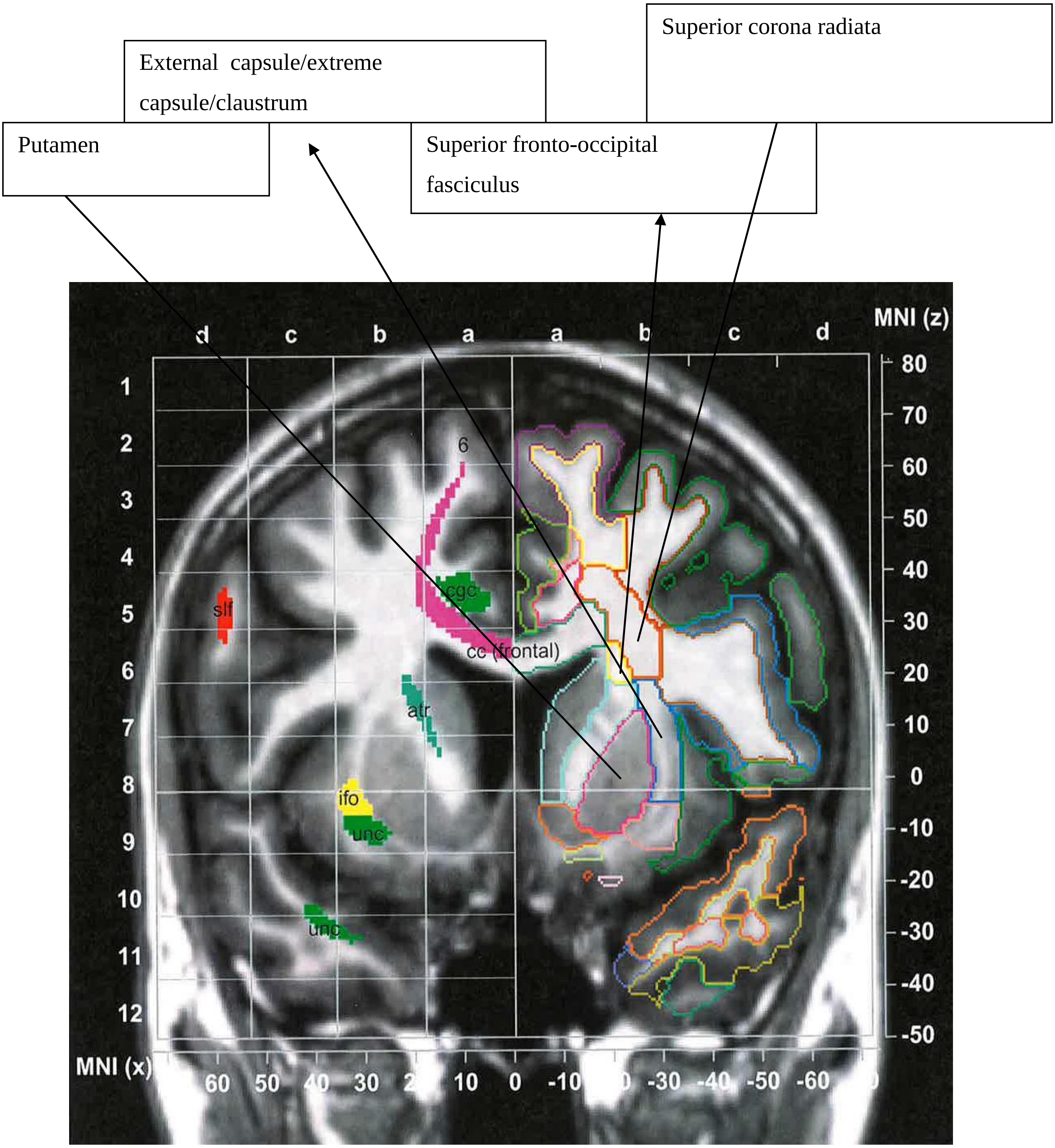
Supplementary material

Supplementary Table 1. Patients' characteristics.

Patient number	Age (years)	Gender	Time since stroke (months)	Cause hemiplegia	FM-UE Score /66	FM-LE Score /34	TAP visual reaction time	Aphasia	Brain localization
1	41	F	11	hem	4	8	-2.33	None	R thalamus
2	52	M	3	ischemic	11	18	-0.31	None	R capsula interna
3	51	F	5	ischemic	36	28	-0.31	None	R frontotemp
4	53	M	3	ischemic	21	27	.1	Motor aphasia	L lenticulostriatal
5	58	F	2	ischemic	47	23	0	None	L lenticulostriatal
6	45	F	4	hem	62	28	-1.18	None	R parietotemp
7	44	M	6	ischemic	54	29	-2.33	Conductive aphasia	L parietotemp
8	51	F	4	ischemic	6	17	-1.08	None	R parietotemp
9	64	M	5	hem	52	24	-0.2	None	R thalamus
10	61	M	7	ischemic	19	26	-1.28	Global aphasia	L frontotemp+capsula interna+putamen
11	59	M	3	ischemic	8	12	-2.37	None	R lenticulostriatal
12	62	M	2	ischemic	60	24	-2.37	None	R temporo-occip, thalamus
13	35	F	2	ischemic	20	16	-0.2	None	R lenticulostriatal, insular
14	62	M	1	ischemic	62	27		None	L putamen
15	41	M	7	ischemic	24	17	-0.5	None	L lenticulostriatal
16	67	M	3	ischemic	37	18		None	L cerebellum, medulla obl
17	53	F	2	ischemic	27	25	-1.65	Motor aphasia	L frontoparietotemp
18	53	M	3	hem	17	15	-1.41	None	R front, capsula interna
19	49	M	2	ischemic	62	29	-0.5	None	R frontopar, insular
20	63	F	4	ischemic	15	18	-1.08	None	R lenticulostriatal
21	17	F	3	hem	46	13	.39	Amnestic aphasia	L n.lentiformis, thalamus
22	35	M	9	hem	19	21	0	Verbal apraxia	L frontoparietal
23	62	M	2	hem	15	16	-0.1	N	L thalamus
24	37	M	8	hem	16	13	-.71	Motor aphasia, verbal apraxia	L frontoparietal
25	61	M	3	hem	17	23		None	R lenticulostriatal
26	53	M	2	ischemic			.1	None	L pons

27	68	M	2	ischemic	64	21	-1.48	None	R pons
28	48	M	7	hem	13	19	-2.05	None	R frontoparietotemp
29	60	M	12	hem	4	9	-1.18	None	R thalamocapsul
30	57	F	1	ischemic	54	25	-0.2	None	R frontal, insular
31	53	M	4	haem	42	21	-1.18	None	R parietal
32	60	M	1	ischemic	65	23	.31	None	L capsula interna
33	64	M	2	ischemic	15	12	.2	None	R pons
34	60	M	2	hem	10	17	-.2	Motor aphasia	L frontal
35	46	M	3	hem	17	14	.1	None	R lenticulostriatal
36	39	F	4	hem	4	7	-1.75	None	R frontoparietotemp
37	65	F	4	ischemic	39	17	-2.37	None	R frontopar, insular

TAP: test of attentional performance; M:male; F:female; L:left; R:right; hem: hemorrhagic
FM-UE: Fugl Meyer Scale- Upper Extremity; MF-LE: Fugl Meyer Scale-Lower Extremity


Superior corona radiata

External capsule/extreme capsule/claustrum

Putamen

Superior fronto-occipital fasciculus

This figure was published in MRI atlas of human white matter, second edition.

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Chapter 5

General discussion and conclusion

In this chapter the main results of this thesis will be presented, discussed and linked to recent literature findings. Simultaneously, the strengths and limitations will be discussed. Finally, directions for further research will be described.

5.1 General discussion

Stroke is the leading cause of impairment resulting in long-term disability and handicap in the Western world. Impaired walking function greatly contributes to functional disability and gait impairments may lead to restriction in the stroke patients' participation and social integration at home and in the community setting. Restoration of walking function is therefore one of the most important goals of post-stroke rehabilitation. Over the last two decades Mental Practice with motor imagery has been proposed by many researchers as a non-invasive, cost-effective rehabilitation method.

5.1.1 Motor Imagery Ability

The first aim of this thesis was to investigate if MI ability was preserved in a study cohort of people with acquired brain injury. MI ability has been investigated in several neurological populations. Patients with stroke, Parkinson's disease, cerebral palsy and multiple sclerosis have been shown to have specific MI profiles. To our best knowledge MI ability in persons with traumatic brain injury has not been investigated before, although this patient group constitutes an important part of our neurorehabilitation population. Therefore MI ability of a group of patients (N=20), suffering from a moderate to severe traumatic brain injury (TBI) was assessed and compared with age-matched controls (N=17). An MI test battery with complementary MI measurements was used, including measures of MI vividness, temporal coupling, and mental rotation. The implementation of different complementary MI evaluation methods to assess MI ability added to the strength of our study design. Standardized behavioral tests were combined with self-report questionnaires. We used the MIQ-Revised second version to classify our patients into high or low imagers. This questionnaire, used to assess MI vividness, was developed for people with limited mobility and had already been validated for people with stroke [1,2]. Although the visual and kinesthetic subscales share common characteristics, they represent two distinct aspects of MI. For the kinesthetic subscale, we instructed patients to 'feel' themselves moving from a first person's perspective.

When administering the visual subscale, patients were instructed to watch themselves from a third person's view (as if watching themselves on a TV screen).

The dominance of visual MI, usually observed in healthy adults, was not confirmed in the present study. Possibly, the use of an adapted scale with relatively simple motor tasks influenced the ease with which the kinesthetic component of the imagery task was performed. Despite its self-report nature, MI questionnaires have been shown to be reliable and valid tools to screen for MI vividness and allow us to distinguish between high and low imagers. Using a modified version of the Parsons’ laterality judgement test, we further measured mental rotation times [3]. This test provided valuable information about the patients’ ability to mentally rotate a body-part. However, we agree that, due to changed instructions -participants were explicitly asked to rotate the hand – the implicit character of the hand laterality test was lost, since the participants were aware of the mental simulation of the movement.

We demonstrated that patients with a TBI show a reduced MI vividness. Patients with TBI reported more difficulties in performing imagined motor actions, regardless of the absence or presence of a limb paresis. The impaired MI profile was further characterized by a deterioration of MI accuracy with a decrease of temporal congruence and mental rotation times. Imagery /actual movement time ratios were increased in the TBI group, with the imagined movement being performed relatively more slowly, indicating a temporal uncoupling between actual and imagery movements. The mental rotation tests showed that mental rotation of the hand was performed more slowly and less accurately by patients than by the control group. As expected, increasing angles led to increasing movement times but analysis of the results indicated a slower execution of the imagined hand rotation in the patient group. More specifically, patients with frontal lobe damage after acquired brain injury were reported to show this impaired MI profile. These findings corroborate the results of brain imaging studies that have shown that the pre-motor and prefrontal cortex are important brain areas, involved in motor imagery [4,5].

In a second study MI ability was assessed in a cohort of stroke patients (N=44) and compared to age-matched healthy controls (N=27). The visual and kinesthetic sub-scores of the MIQ-RS were lower in our stroke patients, compared to healthy controls. The difficulty of imagining actions involving the impaired or paralyzed limbs following acquired brain injury was confirmed by other researchers [6-8]. Patients often reported a type of ‘indolent’ feeling when trying to move the affected hand. On the other hand people in a sub-acute phase after stroke seem to be able to imagine moving the affected hand normally, depending on the given instructions (‘move your limb as if not paralyzed’).

Although MI vividness was shown to be reduced, we also demonstrated that MI ability was at least partially preserved with a preserved temporal coupling between real and imagined movements in our stroke cohort. In a recent review Di Rienzo reported on 49 studies, describing MI ability in stroke patients [9]. Results of these studies showed three MI profiles post stroke. A large group showed a high MI performance (equivalent to healthy persons), another group showed selective MI deficits corresponding to the actual motor deficits and a small group showed impaired MI regardless the motor deficit. Psychometric and behavioral tests showed a large prevalence (85 %) of either preserved or selective MI deficits corresponding to the motor impairments. The results of our study on stroke patients corroborate these findings.

We used the Temporal Congruence stepping test, developed by Malouin for patients with stroke, to measure the temporal relationship between imagined and executed motor actions [10]. Because temporal characteristics of MI are task-dependent, we also introduced a walking trajectory test to assess the relationship between actual and imagery walking [11]. These temporal congruence tests provided a quantitative measure of the temporal organization of MI, using movement times and imagery movement time/ actual movement time ratios. We found a preserved temporal congruence with a significant correlation between imagery stepping/walking time and actual stepping/walking time. Stroke patients were markedly slower on the imagery condition but their actual walking was slowed to the same extent, indicating a preserved MI performance. These results concur with the findings of Malouin and co-workers who also found that the temporal representation of a complex locomotor task (Timed ‘Up and Go’ Test) was retained following stroke [12].

Because mental chronometry, mental rotation, and questionnaires assess different domains of imagery, they provide complementary information about MI ability. All three domains were assessed in our study cohort and no correlation was found between the different measurements, which seems to confirm that they are complementary. Previous research acknowledges that each type of evaluation addresses a different component of MI and a full assessment of MI requires at least a combination of psychometric and behavioral methods. Ideally a neurophysiological method should have been added for completeness [13].

Despite all research, it remains unclear if one needs a preserved MI ability to benefit from MP. Hall and co-workers [14] investigated three imagery ability groups: low visual/low kinesthetic, high visual/low kinesthetic and high visual/high kinesthetic. They demonstrated that the low visual/low kinesthetic group required most trials to learn the movements. In our study, on the other hand, no significant correlation between initial MIQ-RS scores, changes of the MIQ-RS scores and gait velocity improvement after treatment were revealed, indicating that poor imagers can equally benefit from MI training. Moreover MP has been proven to stimulate relevant motor neural pathways, even in people with poor motor imagery [15]. Differences in imagery ability could be the combination of experience interacting with individual disposition. Therefore, it seems important to screen for MI ability, to be able to estimate the need to teach MI practice through an individually tailored initiation program, before starting MI training.

5.1.2 Motor Imagery Ability training

The second question to be addressed in this study was to investigate if MI ability can be trained to a higher level of performance in patients with acquired brain injury. In a randomized controlled trial patients with stroke were randomly allocated to one of two treatment groups.

One group received MP added to standard therapy while the other group received standard therapy, combined with muscle relaxation.

Both groups were assessed with an extensive MI ability test battery before and after 6 weeks of training. Kinesthetic MI vividness improved significantly after 6 weeks of MP. These results corroborate and extend the findings of Deutsch who reported in a single case study, an improvement in imagery skills attributable to imagery practice in a woman with chronic stroke [16]. We therefore suggest that people with an initially poor motor imagery ability can be trained to a higher level of MI performance and that they should not be excluded from MP. In his study de Vries showed a ‘spontaneous’ recovery of MI ability between 3 to 6 weeks after stroke in patients who followed an unaltered rehabilitation program. In our study, patients only improved after specific motor imagery training, no recovery was noted in patients who received the usual rehabilitation program [17]. These findings probably reflect the fact that subjects in the early stage of rehabilitation have a greater potential for recovery of cognitive function (3-6 weeks versus average 3-6 months in our study).

We feel that there is a need for more studies that follow MI ability during the course of rehabilitation to elucidate the relationship between spontaneous recovery of MI ability and the results of MI training.

In our stroke cohort the temporal organization of motor imagery measured by the imagined/actual walking ratio did not differ from the data of the healthy controls. A strong relationship was found between imagery and actual walking times in both groups. Stroke patients were markedly slower on the imagery condition but their actual walking was slowed to the same extent. Conversely, imagery/actual movement time ratios were increased in the TBI group, with the imagined movement being performed relatively more slowly, indicating a temporal uncoupling between actual and imagery movements. We did not administer MI training in this traumatic brain injury patient group but it could be beneficial to train this temporal congruence aspect of MI ability. Indeed, motor planning normally takes into account the actual capabilities of the motor system and the environmental conditions were the behavior has to be displayed. Real-virtual temporal congruency could thus be considered as a requirement for realistic motor planning, especially for complex movement patterns [18]. An accurate timing is an important feature of coordination and dexterity [19].

5.1.3 Mental Practice in gait rehabilitation after stroke

The third question to be addressed in this thesis was to investigate if MP can be administered to patients in a sub-acute phase after stroke and if adding MP to PP results in a better outcome of gait velocity and motor recovery. From a theoretical view point MP offers an intensive, repetitive rehabilitation technique, that has been shown to engage neural networks and can be used by the patient in an autonomous way without creating undue physical fatigue.

In a recent review Malouin collected 25 studies of MP in patients with stroke, of which 9 investigated the effect on mobility or gait [20]. Overall, beneficial effects were found for training motor functions in persons with stroke, although integration of MP in rehabilitation programs seemed to be hampered for unclear reasons so far. Bovend'Eerdt reported poor therapist and patient compliance when MP was promoted through an integrated MI program [21]. Most studies reported by Malouin (20/25) included patients in a chronic phase after stroke, the remaining studies were carried out in the sub-acute phase but none of these investigated gait or mobility.

The primary outcome measure used in our study protocol was gait velocity (10 m walk, self-selected walking speed), while global motor recovery was measured using the lower-extremity Fugl-Meyer assessment (FM-LE) [22]. Gait velocity is known to be a very robust outcome measure for walking capacity [23]. Our study results demonstrate that the 10 m walk scores improved significantly in both groups after treatment with a significant group interaction effect. Compared with baseline measures, gait velocity improved more for the MP group than for the MR group, 0.21±0.18 m/s vs. 0.16±0.15 m/s. These results concur with those of Hwang who found an increase of walking velocity of 0.07 m/s in a group of chronic stroke patients after four weeks of MP [24].

Although this gain in gait velocity appears rather small, gait velocity improved significantly in both groups, indicating that both therapy regimes led to clinically important gains. Despite the large improvement in both groups, we were able to show a supplementary effect of the MP treatment, which is in agreement with the presumed reinforcing function of motor imagery to physical practice.

Perera et al [25] investigated a cohort of subacute stroke survivors and reported that a small meaningful change for gait speed is estimated between 4 and 6 cm/s. Most substantial change estimates ranged from 8 to 14 cm/s. On the other hand, Tilson and co-workers [26] report a minimal detectable change for gait speed among patients with subacute stroke and severe gait impairments in a range of 5 cm/s to 8cm/s, while the minimal clinically important difference is situated around 16 cm/s. This gain in gait velocity resulted in a clinically meaningful improvement in disability according to the modified Rankin Scale.

In their studies Deutsch and colleagues report an effect size of .64 and Dickstein demonstrated an effect size of .7.

When calculating the sample size at the beginning of this study project, a robust effect size= .8 was assumed [27]. To achieve this effect size, a sample size n= 25 was premised. However, this sample size was not reached due to slow patient recruitment. It is recommended that in future multi-centre studies a larger study population should be recruited where possible.

Further, we found no significant interaction between session and group for the Fugl-Meyer Lower Extremity (FM-LE) result, indicating that motor recovery was not enhanced by the combination of mental and physical practice. These results appear to conflict with those of other studies where motor recovery did improve after MP [28,29]. However, most of these studies were performed in people with chronic stroke where motor recovery is thought to be stable. In the current study both groups improved, supported by an intensive rehabilitation program, and so perhaps the contrast between the two experimental protocols was not large enough to detect a possible effect on motor recuperation. Cho and co-workers, exploring the use of mental practice in gait rehabilitation, measured motor recovery outcome with the FM-LE assessment. An improvement in the experimental group of 6 points on the FM-LE subscale was found in this study cohort of chronic stroke patients [29].

On the other hand the results of our study confirm the findings reported by Dunsky and colleagues, who developed a home-based MP program to improve gait in chronic stroke patients. The performance of the lower limb as measured with the FM-LE subscale remained unchanged although a clear effect on gait velocity was found [30]. Motor recovery post-stroke is difficult to measure and Bowden and co-workers previously reported a lack of relationship between the FM-LE and hemiparetic walking performance [31]. We hypothesize that the Fugl-Meyer assessment, although a very reliable global score of motor performance, may not relate to the specific gait improvements that our MP program aimed at.

In this study gait velocity was chosen as the primary outcome ‘near transfer’ measure and the Fugl-Meyer Assessment for the lower limb as ‘far transfer’ measure. Consequently, we measured the training effect of MP on motor recovery and walking indoors. Nevertheless, the use of mobility tasks related to function in the community, like walking long distances, around obstacles and over uneven floor might have provided important additional information about the training result [32,33].

Moreover, given the possible effect of motor imagery training on self-worth and motivation, the use of outcome measures reflecting these issues could provide complementary information about the effect of MP [34]. Furthermore improvement of balance, movement strategy and navigation skills could be important secondary effects that further enhance walking capacities [20].

Finally, in further studies both short- and long term effects of MP should be measured, incorporating follow up measuring points of the above mentioned outcome parameters [34,35].

As highlighted by different reviews regarding the use of MP in neurorehabilitation, differences between study results may be related to the MP training method used. In her review Malouin describes three modes of MP delivery [20]. The first two procedures include protocols combining MP and PP, whereas the third includes only MP without any specific physical training. Because MP is an adjunct to PP, we assume that patients receiving MP in addition to PP, will demonstrate the larger gains.

Although current best practice was applied in this study, including individual, task-specific supervised sessions added after physical therapy, detailed descriptions of MI training elements in neuro-rehabilitation were still lacking at the beginning of the study. Although further research needs to address these issues, task analysis with problem identification, as well as a close relationship between MP and PP in an embedded program, could be important for optimal implementation of MP [36,37]. One could consider that combining MP and overt movements in one training protocol would have supplied our subjects more effectively with the appropriate kinesthetic information and hence would have resulted in larger gait speed gains. Combining MP and PP in one training session could have optimized the priming function of MP. Moreover, as MP is thought to enhance the cognitive aspect of the skill, repeating MP after PP could potentially have contributed to the consolidation of the trained action.

To our knowledge, the optimal timing of MP delivery has not been described yet. MP has been applied in the chronic phase after stroke and to a lesser extent in a sub-acute phase post-stroke. Many authors further suggest the possibility of delivering MP at a very early stage, before motor recovery is eminent. However, further research seems warranted to clarify the optimal timing for MP. We demonstrated that MP in a sub-acute phase after stroke is feasible and possibly enhances gait training poststroke.

Furthermore, a combination of different treatment approaches could have optimized therapy outcome. Combining different neuromodulatory strategies has proven to be effective in scientific research [38]. In a subsequent study protocol we will examine if the use of transcranial Direct Current Stimulation (tDCS) can lead to a boost of the MP effect by increasing the brain’s potential to benefit from this training. Recently motor imagery-based skill acquisition was shown to be disrupted following inhibitory rTMS of the left inferior parietal lobule [39]. Research suggests that the parietal cortex , including the inferior part, is the key structure in the dorsal visual pathway, responsible for visuospatial integration. Stimulating this region with tDCS while performing motor imagery training is thus expected to reinforce the training effect.

5.1.4 Motor imagery and lesion localization

The fourth and final question of our study was to investigate if MI ability after stroke is predictable and related to brain lesion localization. We used voxel-based lesion-symptom mapping (VLSM) to analyze the relationship between brain tissue damage and MI behaviour on a voxel-by-voxel basis [40-42]. Voxel is a portmanteau for ’volume’ and ‘pixel’. A voxel represents a value on a regular grid in three-dimensional space.

So far, research does not unambiguously reveal a specific lesion localization or lesion severity that hampers MP efficacy in stroke patients [9]. Using the VLSM technique, we tried to identify brain regions that are essential for a preserved MI ability after stroke. We found that poor MI vividness, as measured with an MI questionnaire, was associated with lesions in the left putamen, left ventral premotor cortex and long association fibers linking parieto-occipital regions with the dorsolateral premotor and prefrontal areas. Poor temporal congruence was otherwise linked to lesions in the more rostrally situated white matter of the superior corona radiata.

Neuroimaging findings in healthy persons provide evidence that MI and executed movement recruit overlapping brain regions, including pre-motor, parietal, primary somatosensory and motor cortices [43]. Hetu et al performed an ALE meta-analysis and, combining the data of 75 papers, revealed that MI recruits a large fronto-parietal network in addition to subcortical and cerebellar regions [44]. Our voxel-based lesion symptom mapping study revealed that lesions, linked with poor MI ability, were part of this fronto-parietal network. Moreover, significant lesions were shown to be part of two anatomically distinct association fiber systems, both the dorsal fronto-parietal network, shared by imagined and executed movement, and an imagery-specific ventral fronto-parietal network. This ventral network seems to support cognitive action control and allows interaction between prefrontal and parietal areas via fibers near the external capsule/claustrum [45].

Our results are consistent with previous findings that show a link between perceived motor imagery vividness and the extent of activation of these premotor-parietal areas [46].

Our results further confirm the hypothesis, stated by Hetu, that fronto-parietal regions form a functional network during MI. We showed that a brain lesion that interrupts this network can potentially impair MI performance. In a recent meta-analysis McInnes and co-workers [47] confirmed these findings, identifying three structures that were shown to impair MI ability when damaged: the parietal lobe, frontal lobe and basal ganglia. More specifically, MI ability seemed most impacted by parietal lobe damage and damage to the putamen.

We found lesions of the left putamen to be related to poor motor imagery vividness. This finding agrees with recent findings that highlight the role of the left putamen for the cognitive planning of an action [48].

Finally, although MI has been shown to activate both left and right hemisphere [49,50], our study findings demonstrate a left hemisphere dominance for motor imagery. This hemispheric asymmetry for motor imagery and motor planning has been reported previously [51,52].

Taking into account the results of our imaging study, we have to be aware that patients with a left hemisphere lesion are possibly less good candidates for MI training or, at least need more time to learn MI, before commencing training. Of note, patients with lesions in the left putamen and left fronto-parietal network seem to be potentially less good imagers and hence less suitable candidates for MP.

5.2 Conclusions and recommendations for further research

In daily rehabilitation practice we continuously feel the need for new effective evidence-based rehabilitation techniques. Although, so far, no technique has proved to be superior, increasing insights into the phenomenon of neuroplasticity seem to highlight the importance of intensive, repetitive practice incorporated into daily activities, to effectively guide neuroplasticity and long term potentiation. During the last two decades several investigators have shown that MP through MI is a therapeutically relevant new technique in neurorehabilitation.

Through this thesis we have explored some of the remaining questions about the impact of neurologic disorders on MI ability and how MP should be applied in a neurologic population for it to be beneficial.

The key issues, addressed in this thesis, can be summarized as:

° the measurement of MI ability in people with TBI, using an extensive MI test battery, has shown that MI vividness, temporal coupling and MI accuracy are at least partially preserved in this population. Although the predictive value of these MI ability tests has not been fully established yet, people with TBI appear to be potential candidates for MP.

° MI ability is a skill that can be trained to a higher level of performance. We suggest that people with initial low imagery ability after stroke, should not be excluded from MP but be directed to an individually tailored initiation program, to improve their level of MI ability, before starting MP.

° MP can be embedded in regular rehabilitation practice and can be considered as an effective gait rehabilitation technique that results in an additional gain of gait velocity.
° VLSM has demonstrated the relationship between lesions in the left frontoparietal network, connecting prefrontal and parietal regions, and poor motor imagery vividness. The potential role of the left putamen, when performing motor imagery tasks, has further been highlighted.

Whilst the present work has addressed some of the remaining questions regarding the implementation of MI training in neurorehabilitation, there is definitely a need for further research that could enhance patient and treatment selection when MP is considered as a treatment option. Recommendations for further research are identified below:

Additional research to investigate MI ability in people with TBI is warranted. To scrutinize the effect of the brain injury localization on MI ability and response to MP, MI ability in this subgroup of neurorehabilitation patients needs further attention.
Overall, research investigating the effect of MP in people with stroke and TBI should include larger groups of patients to enable sub-groups to be formed that have different lesion localizations. Such a study would allow additional comparisons between responders and non-responders to be made.

Further, the effect of different MP techniques in neurorehabilitation should be compared, including content and quantity of MP regimes, to identify respective advantages of each mode of MI delivery. More specifically, it seems essential to investigate the importance of the close relationship between mental and physical practice, within one therapy session. Moreover the possible enhancing effects of other neuromodulatory techniques such as tDCS need further investigation.

Finally, studies investigating the effect of MP should include short- and long-term follow-up testing, focusing on locomotor and motivational outcome measures, to clarify the behavioral, cognitive and locomotor long-term effect of MP training.

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Chapter 6

Summary

Mental practice (MP) using motor imagery (MI) is considered to be a promising rehabilitation technique in patients following acquired brain injury. During MP a motor task is repeatedly mentally rehearsed without any overt movement. Since MI and overt movement share many common behavioral characteristics and activate common neural pathways, mental practice using motor imagery can potentially be used to prevent learned non-use and maladaptive cortical reorganization even early in rehabilitation, before any motor recovery is present. This thesis was designed to further clarify the potential benefits of MP in a study cohort of patients with acquired brain injury.

The first objective was to examine if MI ability is preserved in patients with an acquired brain injury. The three aspects of MI, MI vividness, temporal congruence and MI accuracy, were closely looked at. We found that patients with a traumatic brain injury, especially those with frontal lobe damage, showed an impaired motor imagery ability with imagined movements being performed slower and less accurate than executed movements.

In our stroke cohort on the other hand, MI vividness was shown to be reduced, but we demonstrated a preserved temporal coupling between real and imagined movements.

Our second study aim was to examine if MI ability can be trained. MI is a skill and like any skill, we expect that it can be rehearsed and thus brought to a higher level of performance. Therefore, we examined MI ability in patients with a first-ever stroke and included these patients in a 6 weeks MI training program. Although patients initially reported a low motor imagery vividness, MI vividness responded well to MI training with a normalization of kinesthetic motor imagery vividness scores after training. This finding highlights the need to familiarize patients with the mental practice technique before applying it in rehabilitation practice.

Recovering independent gait is considered one of the most important rehabilitation goals by stroke patients and given its clinical importance, developing rehabilitation techniques that help gait recovery seem highly relevant. Therefore our third study objective was to examine the effect of a gait rehabilitation program based on Mental Practice. Our study results support the evidence that mental practice has an additional benefit in gait rehabilitation post stroke. Moreover, we did not find a relationship between initial low MI ability and gait velocity improvement after MP, indicating that people with initial low MI ability scores can equally benefit from MP.

Finally our fourth study aim was to clarify if MI ability after stroke is predictable and related to a specific brain lesion localization. Using voxel lesion-symptom mapping, we found that lesions in the left hemisphere were related to poor imagery ability. Voxel-lesion symptom mapping results identified the importance of an intact functional fronto-parietal network for a preserved MI ability.

We further elucidated the crucial role of the basal ganglia, more specifically the left putamen, when performing motor imagery tasks.

In conclusion, this work has aimed to further clarify motor imagery ability in patients with an acquired brain injury. Results have revealed that both patients with stroke and a traumatic brain injury have an (at least) partially preserved MI ability and are potential candidates for mental practice in neurorehabilitation. Moreover mental practice was shown to have an additional task specific benefit in gait rehabilitation in a sub-acute phase after stroke.

Finally voxel lesion-symptom mapping indicated a left hemisphere dominance for motor imagery, emphasizing the importance of the need for an intact fronto-parietal network and subcortical structures for preserved motor imagery ability.

Chapter 7

Samenvatting

Mentale training door het toepassen van motorische verbeeldingsstrategieën wordt de laatste 2 decennia voorgesteld als een potentiële revalidatietechniek bij patiënten met een verworven hersenletsel. Bij de toepassing van mentale training wordt een motorische handeling herhaaldelijk mentaal ingeoefend zonder de beweging echt uit te voeren. Deze techniek beroept zich op het gegeven dat motorische voorstelling en motorische activiteit dezelfde psychometrische eigenschappen delen en blijken beroep te doen op dezelfde zenuwbanen. Daarom kunnen motorische voorstelling en motorische activiteit worden beschouwd als ‘functioneel equivalent’. Het voordeel van mentale training op basis van motorische verbeeldingsstrategieën is dat de techniek kan worden aangewend tijdens neurorevalidatie, in een vroeg stadium na het herseninsult, zelfs vooraleer motorische recuperatie is opgetreden. Men neemt aan dat op die manier aangeleerd niet-gebruik van het aangedane lidmaat kan worden vermeden.

Met deze doctoraatsthesis hebben we geprobeerd een antwoord te formuleren op een aantal vragen betreffende de toepassing van mentale training door motorische verbeeldingsstrategieën waarop in de literatuur nog onvoldoende antwoord voorhanden bleek.

Met een eerste studie gingen we het vermogen tot motorische voorstelling na bij een groep patiënten met een verworven hersenletsel. Daarbij werden verschillende klinische tests afgenomen om de drie deelaspecten van motorische voorstelling, namelijk de levendigheid, de temporele congruentie en de accuraatheid van de motorische voorstelling, nader te bekijken. We konden aantonen dat patiënten met een traumatisch hersenletsel moeilijkheden ondervinden bij de voorstelling van motorische handelingen waarbij de bewegingen mentaal trager en minder accuraat worden uitgevoerd. Vooral bij patiënten met een hersenletsel gelegen in de frontale hersenkwab, bleek dit het geval. Bij onze studiepopulatie met een CVA was de levendigheid van motorische voorstelling eveneens gedaald doch de temporele koppeling tussen de eigenlijke beweging en de ingebeelde beweging bleek bewaard.

Bij een tweede studie gingen we na bij patiënten met een CVA of de capaciteit tot een levendige motorische voorstelling kan worden getraind.

Omdat het motorische voorstellingsvermogen een vaardigheid betreft, verwachten we dat deze vaardigheid- zoals elke vaardigheid- kan worden geoefend en verbeterd. Bij onze groep patiënten met een CVA konden we aantonen dat de capaciteit tot motorische voorstelling naar een hoger niveau kan worden gebracht door training en dat na training het niveau van motorische verbeeldingscapaciteit van de gezonde populatie wordt benaderd.

Gangrevalidatie vormt een belangrijk onderdeel van de neuromotorische revalidatie na een verworven hersenletsel. Het herwinnen van mobiliteit is een prioritaire doelstelling van de revalidant en het revalidatieteam. Met ons derde studieopzet konden we aantonen dat patiënten met een CVA in de subacute revalidatiefase gunstig reageren op gangreëducatie met bijkomende training op basis van mentale training. We noteerden bij de behandelde groep een taakspecifieke verbetering van de gangparameters ten opzichte van de controlegroep.

Meer nog, ook patiënten met een initieel laag motorisch voorstellingsvermogen konden een meerwaarde putten uit deze behandeltechniek.

Ten slotte gingen we na of een gestoorde motorische verbeeldingscapaciteit is gerelateerd aan een bepaalde hersenletsellokalisatie. Hiertoe maakten we gebruik van de techniek van ‘voxel-lesion symptom mapping’. Onze studieresultaten duiden op een dominantie van de linker hemisfeer voor wat betreft het motorische voorstellingsvermogen, waarbij een intact frontopariëtaal neuraal netwerk noodzakelijk blijkt voor een bewaarde motorische verbeeldingscapaciteit. Ook de basale ganglia, meer bepaald het putamen, maken deel uit van het aan motorische voorstelling gerelateerde neurale netwerk.

Globaal kunnen we uit ons onderzoek besluiten dat de capaciteit tot motorische voorstelling bij patiënten met een verworven hersenletsel althans gedeeltelijk is bewaard en dat deze patiënten kandidaten zijn voor een bijkomende behandeling met mentale training in de subacute revalidatiefase.

Vooral bij patiënten met een linker hemisferisch hersenletsel moeten we echter rekening houden met een potentieel gedaalde motorische verbeeldingscapaciteit en kan een geïndividualiseerde initiatie en training van het voorstellingsvermogen zich opdringen vooraleer met mentale training kan worden gestart.

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