Chapter 1

General introduction

1. Introduction

Stroke occurs when the supply of blood to part of the brain is disrupted, and brain tissue degenerates as a result of a lack of oxygen and nutrient.[1] Infarctions and haemorrhaging of cerebral arteries are the two main types of stroke, but the former are far more prevalent (roughly 90% vs 10%, respectively).[2] In the Netherlands alone, the prevalence of stroke is estimated to be over 300.000, with approximately 41.000 newly registered cases each year.[3] Stroke is a major cause of death and disability: it is estimated that worldwide around 12% of all deaths in 2015 were the consequence of stroke.[1] For the approximately two-thirds of patients who do survive the first month post-stroke[4] its sequelae are often highly debilitating for daily functioning.[3] This occurs because stroke can profoundly impact motor (e.g., loss of muscle strength and coordination),[5] cognitive (e.g., deficits in language, attention, and memory),[6] and/or neuropsychiatric functioning (e.g. depression, fatigue, personality changes).[7] Patients therefore often receive intensive, multidisciplinary rehabilitative care to improve their (independence of) daily functioning and quality of life.

This thesis focuses on one particular problem at the interface of motor and cognitive functioning, one that many stroke patients experience and that many therapists find difficult to address: An impaired ability to concurrently perform additional cognitive tasks during moving – so-called motor-cognitive dual-tasking.[8] In this general introduction I will first highlight the impact of dual-task impairments on patients' daily functioning. Next, I will shortly go into stroke patients' specific impairments in dual-tasking in light of the dominant views on (successful) dual-task performance, and describe the possible interventions that might follow from these. This introduction will close with an argumentation as to why one specific intervention called implicit motor learning might be particularly effective to improve dual-tasking in people with stroke. This proposition will be further scrutinized in detail in this thesis.

1.1. Impaired dual-tasking after stroke

Although people often may not be aware of it, performing dual-tasks is integral to daily life. During every-day tasks like crossing a street, for instance, we concurrently need to monitor the environment for upcoming cars or cyclists, and sometimes also talk with someone else, listen to music, or – increasingly so – busy ourselves with our smartphone. Fortunately, for many (healthy) people, walking is largely automated* such that dual-task performance can generally be achieved relatively safely and without much effort. Stroke patients, however, often have great difficulty with performing dual-tasks while standing or walking. In fact,

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*   Please note that gait is likely never fully automated. Even in young, fit, healthy adults walking will require some level of conscious control (Woollacott M, Shumway-Cook A. Attention and the control of posture and gait: a review of an emerging area of research. Gait Post 2002; 16(1): 1-14.)

although most stroke patients regain some degree of walking ability,[9] their capacity for dual-tasking does not substantially improve throughout rehabilitation.[8] Postural control[10] and gait[8] often strongly deteriorate when an additional cognitive task is to be performed, even years after discharge from rehabilitation.[11–13] This has significant repercussions for patients' mobility, safety, and daily functioning.[14] For example, many stroke patients can no longer walk fast enough to safely cross a street[15] when required to perform an additional cognitive task.[13,16] Further, a reduced dual-tasking ability may also increase their risk of falling.[17,18]

1.2. Underlying mechanisms of successful and impaired dual-tasking after stroke

In order to find interventions to address patients' dual-tasking impairments, it is important to consider the mechanisms at play. The dominant perspective on explaining dual-task performance revolves around the so-called capacity sharing hypothesis[19–21] and working memory model.[22] Shortly, capacity sharing posits that a performer's attentional resources are inherently limited, and that during dual-tasking both tasks thus compete for these resources. Hence, a prerequisite for successful dual-task performance is that the performer's attentional capacity is large enough to accommodate the combined task demands.[19] By itself however, a large attentional capacity is not sufficient. The performer also needs to be able to appropriately allocate the available attentional resources to each of the two tasks – a role which Baddeley assigned to the "central executive" in his working memory model.[22,23]

In people with stroke, the abovementioned prerequisites for successful dual-task performance are often not met. First, patients' capacity is often limited - up to half of all patients experiences persistent attentional deficits,[24,25] primarily in the form of reduced information processing speed and impaired sustained and selective attention.[26] Further, impairments of executive function are highly prevalent as well.[24,27] Adding to this, stroke patients seem generally strongly predisposed to consciously control and monitor their movements, far more so than healthy peers.[28,29] As a result, for many patients motor skills such as walking require a substantial amount of attentional capacity, leaving fewer resources available for the performance of additional tasks.

Put together, dual-tasking impairments after stroke may arise through a combination of increased demands placed on a reduced attentional capacity that itself often cannot be deployed optimally.

1.3. Possible interventions to improve dual-tasking after stroke?

Based on the above, there are two logical ways to address dual-tasking impairments after stroke. The first is to improve patients' working memory *functioning*, by increasing their available attentional resources and/or optimize their ability to strategically deploy these. The last decade has seen a surge in studies that investigated whether dedicated cognitive

training programs result in generic improvements in attention and working memory capacity. Although initial results seemed promising,[30,31] recent systematic reviews[32,33] concluded that interventions are generally not effective. Improvements are short-lived, and largely restricted to the tasks trained. Melby-Lervåg et al.[32] therefore proposed that improving particular working memory functions – such as dual-tasking – can only be achieved with highly task-specific interventions.

A prime example of such a highly task-specific intervention is dual-task training. The rationale is that by practicing two tasks simultaneously, patients can improve their ability to strategically divide attention during moving.[34] Preliminary evidence does suggest beneficial effects of dual-task training in stroke.[35,36] However, improvements do not seem to generalize beyond the practiced dual-task combinations. For example, in the case-series by Plummer et al.[37] sub-acute stroke patients completed 12 sessions of gait-related exercises (e.g., walking with narrow base of support, crossing obstacles) with simultaneous cognitive tasks (e.g., naming as many words as possible starting with specific letter). Patients' gait speed was significantly more robust to dual-task interference after the intervention compared to baseline, but mostly in dual-task conditions that involved executive function – similar to the practiced cognitive dual-tasks. No or minor improvements were observed in untrained visuospatial and spontaneous speech dual-task conditions. Limited transfer of training effects, which is also a common finding in healthy elderly,[38,39] is a significant drawback: It implies that patients need to practice each motor task in combination with the potentially very large number of dual-task combinations that are relevant to daily life. Another limitation of dual-task training is that the high task complexity makes it less suitable for people with severe cognitive or motor deficits.[35]

This leads us to an alternative approach to enhance dual-tasking, namely to reduce the *load* placed on patients' working memory by increasing their automaticity of movement. The rationale is simple: when motor skills become more automatic, motor performance requires less working memory involvement. As a result, more residual capacity remains available for the performance of a second (motor or cognitive) task. In theory, when compared with dual-task training, a main benefit of this automatization approach is that it should improve dual-tasking across a wide range of dual-task combinations. Also, interventions that promote automatization should be less cognitively demanding, making them potentially more suitable for patients with severe cognitive deficits.

In spite of the rationale presented above, in current rehabilitation practice automatization of motor skills may actually be hindered. This because there seems to be widespread use of explicit motor learning strategies. Such explicit learning heavily relies on the processing and storing of the movement-related rules conveyed in the therapists' instructions – a process that is highly working memory dependent.[40,41] For example, therapists have been reported to predominantly use verbal instructions and feedback that prescribe how movements should be

performed. This stimulates patients to consciously control movements.[42,43] The high frequency of explicit learning sessions during rehabilitation is thought to contribute to patients' strong conscious control tendencies, and thereby may exacerbate their dual-task impairments.[28]

This thesis explores the merits of the alternative *implicit motor learning*[41] approach for stroke rehabilitation. Implicit motor learning is considered to require no or minimal working memory involvement,[40,44] and thereby result in relatively automatic movements that are robust to dual-task interference. However, notwithstanding its theoretical potential, very little is known about implicit motor learning in people with stroke. Before entering studies on implicit motor learning in people with stroke, the remainder of this introduction describes the core concept of implicit motor learning as well as converging lines of evidence in healthy adults and elderly that indicate that implicit motor learning fosters movement automaticity and, consequently, dual-task performance.

2. What is implicit motor learning?

The concept of implicit motor learning is best understood in relation to traditional views on skill acquisition.[45,46] These hold that in the early verbal-cognitive phase of motor learning, motor performance requires considerable involvement of a performer's working memory; adult novices must accrue and employ verbal movement-related rules and strategies to consciously control motor performance. In the course of learning, however, control gradually becomes less dependent on declarative knowledge and instead increasingly relies on procedural knowledge that directly links task-relevant information to the desired motor response.[45] Since procedural knowledge is inaccessible for consciousness, motor control becomes less reliant on working memory contributions. Finally, after extensive practice the automatic phase is reached, in which motor control has become fully procedural. This type of learning – involving a shift in motor control from based on declarative toward based on procedural knowledge – is typically referred to as explicit motor learning.[47]

When learning is intentional and unconstrained, adult learners typically engage in explicit motor learning from learning onset.[41,48,49] Nonetheless, motor learning can also be *implicit* right from the beginning of learning.[48,50,51] In contrast to explicit motor learning, implicit motor learning is characterized by improvements in motor performance with no or minimal use and aggregation of declarative movement-related knowledge.[47] Rather, performance improvements are the result of direct shaping and reinforcing of task-relevant information-movement linkages.[52] Thus, when learning a movement implicitly, one effectively 'skips' the declarative phase of learning and directly accrues procedural knowledge of the skill instead. As a consequence, implicit motor learning is presumed to not or only minimally load working memory.[40,41,48] This should benefit dual-task performance, as a larger share of capacity can be deployed for the execution of a secondary task than with explicit learning.

3. Implicit motor learning and its relation to working memory and dual-task performance: evidence from healthy adults and elderly

If implicit motor learning indeed results in (largely) automated motor control, empirical evidence should show that implicit learning is not dependent on working memory involvement. In line with this, different strands of evidence in healthy adults and elderly indeed show that: 1) preventing involvement of working memory during skill-acquisition is key to inducing implicit motor learning; 2) compared to explicit motor learning, the neural correlates of implicit motor learning overlap less with those underlying executive working memory control; 3) the rate of implicit motor learning is not related to working memory capacity; and most importantly 4) implicitly acquired motor skills are often less affected by performance of a concurrent task. These findings will be discussed in more detail below.

3.1. Minimizing working memory involvement is essential to induce implicit motor learning

The hallmark of implicit motor learning is that, although learners show substantial improvements in motor skill, they are generally remarkably unable to describe how they perform the learned skill.[41,51] This relative absence of declarative movement-related knowledge after practice suggests that there was minimal conscious processing of verbal rules of movement by working memory during practice.[53] In line with this, all paradigms that have been found to successfully induce implicit motor learning specifically try to prevent working memory from processing movement-related rules during skill acquisition. A classic example is unintentional or incidental learning, such as in the serial reaction time (SRT) task.[51] During this task, learners unknowingly practice a sequence of key-presses. Implicit learning is evidenced by the fact that reaction times shorten on the practiced repeated sequences, but not on randomly presented stimuli.[40,51] Yet, despite their improvements in performance, learners generally are unable to verbally describe how they perform the learned task: They usually cannot recognize or explicitly reproduce the sequence they just learned.[51]

Arguably, the SRT task only involves fairly simple movements (in terms of their dynamics), whereas stroke rehabilitation usually concerns more complex skills such as sit-to-stand transfers or balance tasks. Pure implicit learning may not be achievable for such skills, as learners likely will always have some explicit knowledge of how they should perform the task at hand. However, several paradigms have been validated that minimize conscious involvement during learning of more complex functional tasks. The following interventions are agreed upon to yield most reliable implicit learning effects:[47] minimizing errors during practice such that learners do not engage in working memory demanding hypothesis-testing behavior (errorless learning),[48] instructing patients with an analogy that encapsulates all relevant movement-related information (analogy learning),[54,55] performing an attention-demanding secondary

task during practice to minimize conscious control of the motor task (dual-task learning),[41,55] or triggering learners to focus on the effects of their movements (external focus learning).[56,57] In this thesis I will primarily focus on the current application and effectiveness of external focus instructions in motor learning in stroke rehabilitation.

3.2. Neural network underlying working memory overlaps more with explicit than with implicit motor learning

The neural network supporting working memory seems to be more involved in explicit motor learning than in implicit motor learning. Specifically, a fronto-striatal network is considered to be central to working memory function (see Figure 1.1).[58,59] Within this network, the prefrontal cortex functions as 'central executive' by modulating activity in other brain areas in order to enhance processing of task-relevant information. Based on the top-down input from the prefrontal cortex, the striatum (part of the basal ganglia) assists in this process, by filtering out task-irrelevant information.[60] It is highly task-dependent what other brain networks are "plugged into" this fronto-striatal network during working memory tasks. Verbal working memory tasks, for instance, mainly activate left-lateralized areas that are also engaged in phonological processing, whereas spatial tasks predominantly activate right-lateralized areas involved in visuospatial processing.[58,59]

Recently, a meta-analysis of functional imaging studies into motor learning in healthy adults has identified a cortico-striatal-cerebellar network to underlie motor skill acquisition (Figure 1.1).[61] While this network encompasses both implicit and explicit motor learning, these two learning modes differ in terms of their relative reliance on neural nodes within this network. That is, while the basal ganglia are considered to be more strongly involved in implicit motor learning,[52,62] explicit motor learning more heavily involves activity of the (dorsolateral) prefrontal[63–65] and premotor cortex.[66,67] Considering the executive role of the prefrontal cortex in working memory function, this indicates that top-down working memory control is less involved in implicit motor learning than in explicit motor learning. This is corroborated by EEG-studies that showed that explicit motor learning is associated with greater coherence between left-lateralized temporal areas involved in verbal-analytical processing and frontal motor areas involved in motor planning compared to implicit learning.[68,69]

3.3. Scores on working memory tests do not predict rate of implicit motor learning

Support for the working memory independence of implicit motor learning is also grounded in observations that learner's working memory capacity is not associated with the rate of implicit motor learning, while it does predict the rate of explicit learning. For instance, several studies have investigated the relation between improvements on the SRT task and neuropsychological working memory assessments. A recent review of these studies shows that working memory capacity positively correlates with improvement on the SRT task only

after explicit motor learning, but not after implicit motor learning.[40] These findings are corroborated by observations that, although working memory capacity decreases with age,[70] this deficit seems to primarily affect elderly's explicit motor learning ability, while leaving implicit motor learning relatively intact.[71] For instance, Chauvel and co-workers[72] trained healthy young and elderly participants on a golf-putting task either implicitly through errorless learning or explicitly through error-prone learning. Working memory capacity of the elderly participants was significantly reduced compared to a young control group. At the end of training, the group of elderly participants who had engaged in explicit motor learning was outperformed by their younger counterparts both in single- and dual-task conditions. By contrast, after implicit motor learning, elderly and young participants showed equal performance improvements. This suggests that reduced working memory capacity primarily impacted explicit motor learning, rather than implicit motor learning.[cf 73]
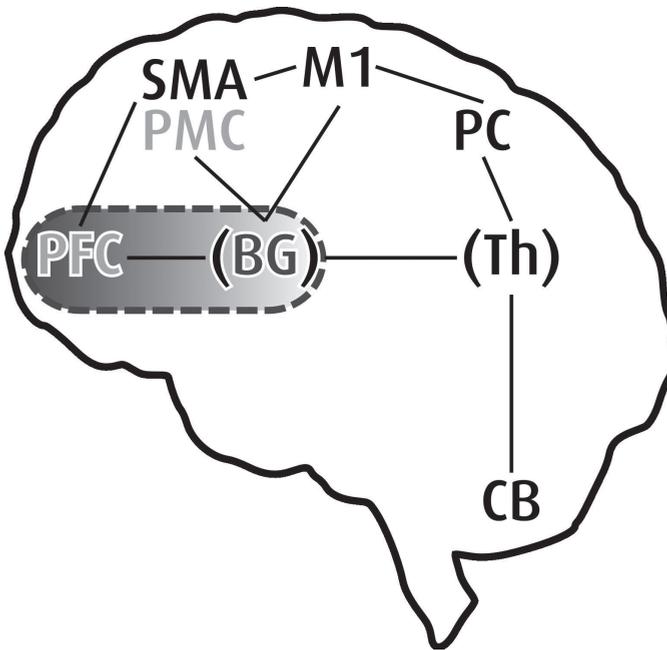

Figure 1.1. Schematic representation of the cortico-striatal-cerebellar network underlying motor learning in general[35]. Black interconnecting lines represent the functional connections within this network, and are not intended to be naturalistic representations of functional and anatomical interconnections. Neural nodes most active during explicit motor learning – highlighted in light grey – are the prefrontal cortex (PFC) and premotor cortex (PMC). The basal ganglia (BG) are especially active during implicit motor learning (highlighted in dark grey). The core of the fronto-striatal network of working memory (grey box) is superimposed on the motor learning network. Although working memory's network overlaps both with implicit (BG) and explicit (PFC) motor learning, explicit motor learning's reliance on PFC activity indicates greater reliance on executive working memory control. NB: BG = basal ganglia; CB = cerebellum; PFC = prefrontal cortex; M1 = primary motor cortex; PC = parietal cortex; PMC = premotor cortex; SMA = supplementary motor area; Th = Thalamus; () = subcortical structure

3.4. Implicit motor learning is associated with better dual-task performance

Finally, in healthy adults it has frequently been reported that the performance of implicitly acquired motor skills is robust to concurrent performance of a wide variety of cognitive tasks. Examples include counting aloud backwards during basketball shooting[54] and table tennis forehand strokes,[55] tone-counting while golf-putting,[56] and random-letter generation during rugby passing.[74] For example, Lam et al.[54] trained novice participants on a basketball free throw task, either implicitly through analogy learning by instructing them to shoot as if putting cookies in a jar on a high shelf, or explicitly by instructing them with several movement-related rules. Although both groups showed similar improvements in throwing accuracy in single task conditions, only implicit learners' performance was unaffected when they simultaneously needed to count backward in threes. Because counting accuracy and speed was similar in both groups, this difference in dual-task ability could not be attributed to differences in task-prioritization.

4. Outline of the present thesis

Recapitulating, in healthy adults there is converging evidence that implicit motor learning interventions minimally tax working memory, especially when compared to explicit motor learning interventions. Most importantly, implicit motor learning seems to result in superior dual-task performance. Nonetheless, very little is known about implicit motor learning in people with stroke. For instance, it is unclear whether stroke patients' capacity for implicit motor learning is preserved, and to what extent this applies to certain subgroups of patients. Also, there have been virtually no controlled studies that directly compared the effects of explicit and implicit interventions on motor learning and performance after stroke.[cf 75]

Hence, the main aim of this thesis is to address these issues, and explore the potential of implicit motor learning interventions as a means to improve movement automaticity and dual-task performance in rehabilitation after stroke. For a comprehensive assessment I aim to (1) systematically review the current state of the evidence regarding implicit motor learning in healthy adults and patients with stroke, (2) observe how implicit and explicit motor learning strategies are currently applied within rehabilitation practice, and (3) evaluate the effects of one specific implicit motor learning intervention in people with stroke, and explore the relation with specific individual patient characteristics. Hence, the thesis is divided in three main parts.

In the first part, I critically evaluate the current state of the evidence regarding the effectiveness of implicit motor learning interventions in healthy adults and stroke rehabilitation. Specifically, the systematic review described in **Chapter 2** assesses the effectiveness of four widely-accepted implicit motor learning interventions (analogy-, errorless-, dual-task-, and

external focus learning) for improving movement automaticity and dual-task performance in healthy adults. In **Chapter 3** an additional systematic review to is performed to determine whether the ability for implicit motor learning is actually preserved after stroke.

The second part of this thesis focuses on the current practices in stroke rehabilitation. The aim is to determine how patients and therapists use explicit and implicit strategies during rehabilitation. To this end, in **Chapter 4** I validated a self-report measure of stroke patients' inclination to consciously control their movements in daily life. Subsequently, the cross-sectional study described in **Chapter 5** investigates the relation between patients' conscious control preferences and their ability to perform motor-cognitive dual-tasks. In **Chapter 6**, it is determined how often physical therapists use instructions and feedback that promote explicit (internal focus) or implicit (external focus) motor learning during inpatient rehabilitation therapy. I also explore whether therapists adapt their use of these strategies based on specific patient characteristics, such as their conscious motor control preferences, and motor and cognitive functioning.

In the final and third part of this thesis the actual effects of implicit learning on dual-tasking in healthy adults and people with stroke are assessed. One particular implicit motor learning intervention is investigated: learning using external focus instructions. This particular intervention is chosen because it is the most widely used intervention in sports research and practice,[57,76,77] and is currently gaining significant attention in neurorehabilitation education and practice as well.[78–80] Further – if found to be effective – external focus learning would be a low-cost and easily implementable tool for daily practice; in essence, therapists would only need to change the wording of their instructions. Of note though, there is some debate as to whether external focus learning induces implicit learning.[47] I therefore first perform a comprehensive analysis of the effects of external focus instructions on movement automaticity and dual-task performance during leg-stepping in healthy adults in **Chapter 7**. In **Chapter 8** this same paradigm is used to determine the direct effects of external focus instructions on leg-stepping performance and dual-tasking in chronic stroke patients. Finally, in **Chapter 9** a randomized controlled trial is run to compare the effects of external and internal focus instructions on learning a new balance task in stroke patients involved in inpatient rehabilitation. The effects on single- and dual-task performance are evaluated. Additionally, both in **Chapters 8 and 9** it is investigated whether specific patient factors such as motor and cognitive functioning determined whether patients benefit most from implicit (external focus) or explicit (internal focus) motor learning interventions.

Chapter 10 (the epilogue) summarizes the results of the studies performed, and discusses the implications of the findings of this thesis for clinical practice and future research.