Retrograde interference and ballistic motor task learning

Behavioral and neurophysiological analysis

Fulfillment of the requirements for the
Master of Science in Sport Sciences
Health and research option

submitted by

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Fribourg, March 2023

Acknowledgments

I thank Matteo Bugnon for his help and support throughout the entire project. I am particularly grateful for his proofreading of my thesis and his advice.

I also thank Jan Ruffieux for his help during the measurements.

Finally, thank you to all the participants who kindly participated in the experiment and without whom this master thesis would not have been possible.

Abbreviations

aMT = active motor threshold

BT = ballistic task

CG = control groups

CS = conditioning stimulus

CSE = corticospinal excitability

CSP = cortical silent period

EMG = electromyography

FCR = flexor carpi radialis

LTP = long-term potentiation

M1 = primary motor cortex

MEP = motor-evoked potential

$\eta 2$ = eta-squared

RFD = rate of force development

RMSE = root mean square error

rMT = resting motor threshold

rTMS = repetitive transcranial magnetic stimulation

SICI = short-interval intracortical inhibition

TG = test groups

TMS = transcranial magnetic stimulation

TS = test stimulus

VMT = visuomotor task

Summary

Humans can learn movements and form memories of them. Sometimes when several memories are learned one after the other, they interact. It can result in various phenomena, including retrograde interference.

This master thesis had two main aims. First, to examine if the time interval between the initial learning of a ballistic task and its retention test is crucial to observe retrograde interference. Second, to better understand some neurophysiological mechanisms measured with transcranial magnetic stimulation (TMS) during the learning process.

Fifty-eight young, healthy adults participated. They were distributed into four groups: two control groups followed an *A1-A2* paradigm, and two test groups followed an *A1-B1-A2-B2* paradigm. The difference between the groups was the time interval between tasks *A1* and *A2*. Task *A* was a ballistic task, and task *B* was a visuomotor task. All tasks involved the non-dominant wrist and hand. TMS targeting the flexor carpi radialis (FCR) muscle was applied before and after the learning.

All groups significantly improved their performance during the initial learning of the ballistic and visuomotor tasks ($p<0.001$). For the retrograde interference, there was a significant TIMES x GROUPS interaction ($F_{3, 56} = 3.39$, $p = 0.024$, $\eta^2 = 0.004$). However, this significant interaction was due to the timing of the retention test (i.e., immediate vs. 48 hours later) and not to the training of the interference task. Thus, there was no retrograde interference. Among the neurophysiological parameters measured, only short-interval intracortical inhibition (SICI) task was influenced by the learning of a ballistic task and significantly decreased ($F_{1, 53} = 8.56$, $p = 0.005$, $\eta^2 = 0.032$).

It is possible that instead of retrograde interference, we observed generalization. It may be due to the SICI task that subjects performed during TMS measurements. Neurophysiological parameters measured by TMS do not seem relevant to assess motor learning, except perhaps SICI, but only when measured during the execution of a task similar to the learned motor task. In conclusion, more studies are needed before any clinically applicable conclusions can be drawn.

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1 Introduction

The human being can remember how to ski from one winter to another thanks to motor memory. Movements can be memorized as much as biomechanical lessons or the beginning of this sentence to understand its meaning while arriving at the point.

When everything goes smoothly, the creation of a motor memory follows a linear pathway: learning, consolidation, and retention (Doyon & Benali, 2005). However, it can also be a winding path that goes in one direction and then back in the other, that no longer exists or has dead ends. In other words, the different phases through which a memory passes are permeable. For example, following a disturbing event, a memory in the consolidation phase could return to the same level as it was at the beginning of learning, with a concomitant loss of the performance improvements that had been made. It would be an interference (Reis et al., 2008; Robertson et al., 2004). In contrast, this same memory could also be stabilized after a smooth consolidation phase, leading to a preserved or even enhanced performance without further training. This latter phenomenon is called offline gains (Krakauer & Shadmehr, 2006). As various consolidation or forgetting processes can happen with different conditions, more studies are needed to better understand the mechanisms underlying motor learning and memory. It, in turn, would help to optimize therapy for patients who need to relearn how to move after an adverse event such as a stroke or a fall that provoked a severe injury.

Motor learning and motor memory mechanisms can be observed at the behavioral but also at the neurophysiological level. Combining these two approaches allows for an exhaustive set of knowledge on the topic. It was also the case in this master thesis to better understand the interference phenomenon. While the performance analysis allowed the quantification of learning, the neurophysiological analysis was employed to evaluate how some neurophysiological processes evolved through learning a new ballistic motor task.

The following chapters review the current state of scientific knowledge on motor learning and memory. They provide the theoretical background for understanding this work and show where knowledge is still lacking.

1.1 Motor learning

1.1.1 Motor learning anatomy

Motor learning consists of repeating the same movement several times to improve its execution and to link this new knowledge with specific contextual clues, for example, to brake while

arriving at the bottom of a ski slope. This definition from Krakauer & Shadmehr (2006) shows that motor learning seems to depend not only on the motor system but also on the sensory system. It is required to perceive its own body to be able to move the correct segment at the right location, and it is also needed to perceive its environment to move at the right moment. The nervous system constantly processes motor (efferent) and sensory (afferent) signals to make the best possible adjustment and produce the best result possible at the right time. In this context, it is not surprising that the somatosensory system is essential and active during the early phases of motor learning (Bernardi et al., 2015). It may be related to the finding by Shadmehr & Holcomb (1997) that blood flow in the somatosensory cortex decreases through training.

Apart from the somatosensory cortex, several other brain regions are also involved in motor learning: the primary motor cortex (M1) (Doyon & Benali, 2005; Krakauer & Shadmehr, 2006; Reis et al., 2008), the premotor cortex (Doyon & Benali, 2005; Reis et al., 2008), the supplementary motor area (Doyon & Benali, 2005; Reis et al., 2008), the cerebellum (Reis et al., 2008; Wolpert et al., 2011), the basal ganglia (Reis et al., 2008), the thalamus (Reis et al., 2008; Shadmehr & Holcomb, 1997), as well as the medial occipital gyrus and the prefrontal dorsolateral cortex (Shadmehr & Holcomb, 1997). The hippocampus, which is a central part of declarative memory (Squire & Zola-Morgan, 1991), seems involved in motor learning too, but without being fundamental as patients with limbic lesions can normally acquire new motor skills (Doyon & Benali, 2005).

1.1.2 Motor learning at the neurophysiological level

At the neurophysiological level, people with a better modulation capacity of GABAergic pathways (i.e., GABA decrease) within M1 appear to learn faster in the short term (Stagg et al., 2011). These results were obtained with a reaction time task in which participants had to perform a sequence with their fingers in response to a visual signal. The modulation of the GABA neurotransmitter seems more critical than its concentration because GABA concentration at the beginning of the training could not predict learning ability (Stagg et al., 2011). After learning, an increase in GABA concentration may be possible to restore homeostasis. This process could regulate the early consolidation of motor memory (Robertson & Takacs, 2017). These results suggest that the modulation capacity of the GABA system may be essential for the (motor) learning process.

Several other neurophysiological processes behind motor learning can be measured with transcranial magnetic stimulation (TMS). As it is an important part of this master thesis, this topic is further developed in chapter 1.4.

1.2 Motor memory consolidation

After the learning stage is the consolidation stage. Indeed, once the memory is created from different information collected during the training, it has to be stored somewhere in the brain to be recalled later. Consolidation is an ensemble of processes by which a long-term memory becomes more robust with time (Krakauer & Shadmehr, 2006). Consolidation can be evaluated through interferences (Reis et al., 2008) because a consolidated memory is less, or not anymore, susceptible to interference. For this reason, retrograde interferences allow observing if and how the consolidation happened at the behavioral level by recording the performance during a motor task. There are two kinds of interferences: retrograde, also called retroactive, and anterograde, or proactive (Krakauer et al., 2005; Robertson et al., 2004). The terms retrograde and anterograde interferences were chosen for this master thesis. An interference is retrograde when the learning of task *B* disrupts the retention of task *A* previously learned (Brashers-Krug et al., 1996). On the contrary, interference is anterograde when the learning of task *B* interferes with the relearning of task *A* (Krakauer et al., 2005). These definitions show that interferences are usually tested with the *A1-B-A2* paradigm (Robertson et al., 2004), in which *A* and *B* are two different motor tasks. An important part of this master thesis focused on retrograde interferences, i.e., whether the learning of task *B* disrupted the consolidation of task *A* previously learned. This topic is developed later in the introduction and chapter 2 on methods.

1.2.1 Motor memory consolidation and anatomy

Motor memory consolidation depends on several anatomical structures, including the somatosensory cortex, cerebellum, basal ganglia, and perhaps M1. The role of M1 in motor memory consolidation seems to depend on the type of motor task. For example, Lundbye-Jensen et al. (2011) suggested that M1 is crucial because they applied 1 Hz repetitive TMS (rTMS) on M1 and that it provoked interferences after the learning of a ballistic task. On the opposite, Kumar et al. (2019) argued that M1 is not fundamental for motor memory consolidation of a motor adaptation task because the "suppression" of M1 with theta-burst TMS only had a small effect on retention.

A common point in the consolidation of these various motor tasks could be the somatosensory cortex. Indeed, motor memory consolidation is disrupted when theta-burst TMS suppresses the

somatosensory cortex (Kumar et al., 2019). It is likely that the consolidation of motor memory depends on both sensory and motor brain areas and that these regions are highly interrelated. Indeed, when Lundbye-Jensen and colleagues (2011) suggested that M1 is essential for motor memory consolidation, they applied suprathreshold rTMS over M1, which provoked a muscular response and sensory (re-)afference. In the same study, direct but superficial stimulation of the nerve innervating the muscle involved in the learned motor task also caused interference in the same way as stimulation of M1. It may signify that the unexpected sensory afferents caused indirectly by the stimulation were causing the interference and not a disturbance of M1. It would mean that, besides M1, sensory feedbacks and the somatosensory cortex that processes them are fundamental to consolidation.

Apart from the somatosensory cortex, consolidation may also depend on the cerebellum (Krakauer & Shadmehr, 2006). At least in associative motor learning, this dependence on the cerebellum is critical directly after learning and decreases with time. The cerebellum does not seem decisive for long-term memory (Krakauer & Shadmehr, 2006).

Finally, it has been speculated that motor skills could be stored (i.e., consolidated) in the basal ganglia and, more precisely, in the sensorimotor part of the striatum (Doyon & Benali, 2005). It is consistent with the principle of motor learning, which consists of linking new knowledge with specific contextual clues (Krakauer & Shadmehr, 2006). It emphasizes one more time the relevance of sensory perception in motor learning and motor memory consolidation.

1.2.2 Physiological processes behind motor memory consolidation

How does (motor) memory work? At the cellular (and synaptic) level, one possible mechanism for the long-term storage of information is long-term potentiation (LTP) (Nicoll, 2017). LTP is an immediate and lasting increase in the excitatory synapses' strength (Nicoll, 2017). It is the scientific term behind the image of the small path in the middle of a field that becomes a highway through training. This theory was initially developed by the observation of the neurons in the hippocampus (Nicoll, 2017). It is, therefore, primarily concerned with declarative learning and memory, which depends mainly on the hippocampus (Squire & Zola-Morgan, 1991). However, Rioult-Pedotti et al. (2000) showed that LTP also seems to extend to motor learning and memory.

LTP consists of two phases: tetanus and expression. Tetanus involves NMDA receptors, and expression involves AMPA receptors (Nicoll, 2017). LTP proceeds as follows: when the postsynaptic membrane is under depolarization, Ca_{2+} enters through NMDA receptors and activates calmodulin-dependent kinases II (CaMKII), which may be necessary and sufficient for

LTP. There is then a rapid accumulation of AMPA receptors at the synapse (Nicoll, 2017). Silent synapses in the hippocampus represent an interesting example to illustrate the physiological importance of LTP. These synapses do not have AMPA receptors, but they contain NMDA receptors. Therefore, LTP makes these synapses unsilenced by adding AMPA receptors.

1.2.3 Phenomena that can occur during motor memory consolidation

Ideally, we learn one task at a time and retain it. However, real life is more complex than that. It is common to learn several pieces of information or skills one after the other. In response to this complexity of life, many different phenomena can occur during consolidation, all of which have various consequences for the quality of the memory(s) involved. They can be observed during the recall (i.e., the retention test). These phenomena include savings, offline gains, generalization/facilitation, and interference. Savings increase the rate of readaptation (Reis et al., 2008) and allow for faster and more complete relearning than original (initial) learning of the same task (Krakauer & Shadmehr, 2006). Similarly, offline gains are an improvement in the quality of recall (i.e., performance improvements) without additional training (Krakauer & Shadmehr, 2006). Facilitation is a performance improvement at the beginning of the learning of a new motor task following the learning of a first (often related) motor task due to a better ability to adapt (Bock et al., 2001). Generalization, which makes facilitation possible, is the process that occurs when two memories link together and apply common rules to each other (Herszage & Censor, 2018). Finally, interference can also occur, which was the main theme of this master thesis. If the different phenomena possible during the consolidation of memory have been listed, although they are not directly the matter of this work, it is because the frontier between them is thin. For example, the same pattern of motor tasks, i.e., learning two tasks one after the other, is needed to observe interference or facilitation/generalization (Herszage & Censor, 2018; Robertson et al., 2004). Sometimes, retrograde interference and savings even seem to occur simultaneously (Krakauer et al., 2005). Moreover, interference and generalization may share common neural mechanisms, even though some specific synaptic mechanisms may differ (Herszage & Censor, 2018). Thus, a slight nuance in the experimental protocol is enough to obtain a different consolidation (or forgetting) phenomenon than expected.

1.3 Retrograde interferences

1.3.1 Retrograde interferences at the behavioral level

Interference, as well as other possible consolidation phenomena, are observed and defined at the behavioral level. For this purpose, the *A1-B-A2* paradigm is commonly used (Robertson et al., 2004). The first task, task *A*, is learned, then task *B*, which is different, is also learned, and finally, task *A* is trained again (Table 1). Performance is quantified and recorded throughout the entire process. This paradigm can be adapted to the needs of each experiment. For example, in this project, the control groups performed only task *A*, corresponding to *A1-A2*, while our test groups performed an *A1-B1-A2-B2* paradigm (see the *Methods* chapter for more details). In this model, whatever its final form, it is possible to play with different parameters: choice of tasks *A* and *B*, number of repetitions of *A* and *B* within each training block, the number of times tasks *A* and *B* are repeated, the time lapse between *A* and *B*, or between *A1* and *A2*.

Table 1

Visual representation of the A1-B-A2 paradigm

Task *A1*	→	Task *B*	→	Task *A2*
Learning task		Interference task		Retention test
Initial learning				Relearning of task *A*
First task				Recall
First learning session				

Note. Under the different tasks are names that are used to speak about the various tasks in this thesis to help the reader.

In this paradigm, it is mainly the difference in performance between the end of *A1* and the beginning of *A2* that indicates whether there is interference, offline gains, or some other phenomenon. It is a behavioral observation since the results come from an analysis of the performance. Interference occurs when performance evolution between the end of the initial training (*A1*) and the beginning of the retention test (*A2*) is significantly different between the interference (practicing the interference task) and control groups. For this reason, the measure of a control group is always necessary.

1.3.2 Retrograde interferences at the neurophysiological level

Retrograde interference is defined at the behavioral level. It is, therefore, necessary to have a behavioral measure to know if retrograde interference has occurred. However, it is possible to simultaneously collect neurophysiological data, for example with TMS, to learn more about the characteristics of interferences. The latter occur after learning, and many studies have already investigated the evolution of the parameters measurable by TMS during motor learning (see chapter 3.2). In contrast, the studies that have looked at the influence of retrograde interference on the parameters measurable by TMS are much less numerous and do not allow conclusions to be drawn at the present time. This master thesis has therefore attempted to complete the existing knowledge on this specific topic.

1.3.3 Requirements for retrograde interferences

Several conditions are necessary for retrograde interference to occur. As a reminder, there is retrograde interference when the learning of task *B* disrupts the retention of task *A* previously learned (Brashers-Krug et al., 1996). First, motor tasks *A* and *B* must be learning tasks (Egger et al., 2021; Lundbye-Jensen et al., 2011). Interference can occur shortly after learning when the newly trained skill is not yet stably encoded in the brain. Indeed, most, if not all, studies agree that there is no interference if at least six hours separate the learning of tasks *A* and *B* (Egger et al., 2021; Muellbacher et al., 2002; Robertson et al., 2004). Some studies suggest that there is no interference if more than four hours separate the two tasks (Brashers-Krug et al., 1996; Lundbye-Jensen et al., 2011). Formulated differently, it takes four to six hours for the memory of a new motor skill to be stable. Hence, the time between tasks *A1* and *B* is crucial for a proper consolidation of motor task *A*. What has yet to be discovered is whether the time between tasks *A1* and *A2* is also crucial for observing interference. To my knowledge, no study has directly addressed this question to date. The experimental designs of the various scientific studies vary from one another, with some projects having participants perform task *A2* shortly after task *A1* (Lauber et al., 2013; Lundbye-Jensen et al., 2011), while others have had them perform it 24 hours (Brashers-Krug et al., 1996; Egger et al., 2021; Krakauer et al., 2005), 48 hours (Krakauer et al., 2005) or one week (Krakauer et al., 2005) later. However, these different projects sought to answer other hypotheses, such as the time needed between learning tasks *A1* and *B* to avoid interference (Brashers-Krug et al., 1996; Lundbye-Jensen et al., 2011), or the characteristics of the tasks that cause interference (Egger et al., 2021; Lundbye-Jensen et al., 2011). It is, therefore, difficult to deduce anything about the time between learning task *A1* and performing task *A2* from these different studies. It is why this master thesis tried to fill this gap

by directly studying the time interval between tasks *A1* and *A2*. The aim was to find out if it is crucial to observe interference.

In order to answer this question, it seemed relevant to base the experiment on the *A1-B-A2* paradigm and to have tasks *A* and *B* with which interference can be observed. As in the studies by Lundbye-Jensen et al. (2011) and Lauber et al. (2013), where interference occurred under certain conditions, it was chosen that task *A* would be a ballistic task and task *B* a visuomotor task. These tasks allowed the same muscles to be used under slightly different conditions. It seems to be an important feature as Lundbye-Jensen et al. (2011) showed that there is interference if tasks *A* and *B* use the same muscle and in the same direction, but not if the two tasks use different muscles, such as agonist and antagonist. Similarly, Egger et al. (2021), who studied interference in balance exercises, argued that different balance exercises should require the same neural resources (i.e., "similar task-specificities"; for example, the same control of the center of gravity) to interfere. In addition, Lundbye-Jensen et al. (2011) were also able to induce interference with 1 Hz rTMS and superficial nervous stimulation instead of task *B*. In other words, either by directly stimulating the part of M1 or the nerve responsible for moving the primary muscle of task *A*. All these experiments imply that tasks *A* and *B* must be relatively similar and use the body in the same way to have any risk of interference.

Finding a suitable experimental protocol to obtain interference is a considerable challenge. However, one that must be overcome to modulate the time between tasks *A1* and *A2* to examine its implication in the appearance of interference. This master thesis has inspired its experimental protocol on the successful experiments of Lundbye Jensen et al. (2011) and Lauber et al. (2013). More details can be found in the *Methods* chapter.

1.4 Motor learning and transcranial magnetic stimulation

TMS is a non-invasive brain stimulation tool that can measure specific inhibitory and excitatory mechanisms. This method allows, for example, to increase or diminish brain excitability (Reis et al., 2008). However, it also helps to understand the mechanisms behind motor learning and memory formation (Reis et al., 2008). TMS provokes a muscular answer, called motor-evoked potential (MEP), when applied to M1 (Rotenberg et al., 2014). It is often assumed that the change in MEPs amplitudes shows M1 contribution during motor learning (Carson et al., 2016), even though the link between amplitude variations of MEPs and learning is not well known (Bestmann & Krakauer, 2015). Indeed, MEPs depend on many parameters: changes in cortico-spinal tract integrity, changes in M1, and top-down influence of cognitive processes on M1 (Bestmann & Krakauer, 2015).

1.4.1 Motor learning and corticospinal excitability

Despite the limitations mentioned above, studies on motor learning often use amplitude changes of MEPs, considered as corticospinal excitability, as a marker of motor learning. Different studies have obtained conflicting results regarding changes in corticospinal excitability during motor learning (Ho et al., 2022; Holland et al., 2015). Most studies did not find any correlation between corticospinal excitability changes and learning (Carson et al., 2016). Corticospinal excitability changes may depend more on the motor task itself than on the learning process Berghuis et al., 2017). Indeed, it seems that corticospinal excitability increases after a visuomotor task but not after a ballistic task (Berghuis et al., 2017). It could potentially explain why all the studies did not find the same results regarding the changes in corticospinal excitability. However, conflicting results were also observed for the same task: for example, and in contrast to the study mentioned above (Berghuis et al., 2017), Holland and colleagues (2015) found that learning of a visuomotor task is associated with a decrease in corticospinal excitability, where Paparella et al. (2020) did not find any change. The situation is also inconsistent for the learning of a ballistic task because, at the opposite of Berghuis et al. (2017), Paparella et al. (2020) found an increase in corticospinal excitability.

The situation still being unclear, this master thesis has examined the corticospinal excitability evolution during the learning of a new ballistic task and possible retrograde interference.

1.4.2 Motor learning and cortical silent period

Another parameter measurable by TMS is the cortical silent period (CSP), which is "an interruption of a voluntary muscle contraction by transcranial stimulation of the contralateral motor cortex" (Wolters et al., 2008, p.91). It lasts between 100 and 300ms and can represent cortical motor inhibition (Wolters et al., 2008). There are not many studies about the evolution of CSP through the learning of a new ballistic task, but according to Taube et al. (2020), CSP does not seem to change after a four-week ballistic task training.

It is interesting to look simultaneously at the corticospinal excitability and the CSP because it shows two sides of excitation-inhibition mechanisms: corticospinal excitability for excitation and CSP for inhibition. Corticospinal excitability and CSP are probably generated by different processes (Wolters et al., 2008). This hypothesis is supported (among other things) by the fact that CSP duration evolves linearly in response to the stimulus intensity, while MEP amplitude reaches a plateau at high intensities stimuli (Wolters et al., 2008).

1.4.3 Motor learning and motor thresholds

Resting motor threshold (rMT) and/or active motor threshold (aMT) are systematically measured at the beginning of a TMS session because this information is needed to choose the appropriate stimulation intensities. Therefore, some studies analyzed if the motor thresholds change through the learning of a motor task. In the case of a ballistic task, the rMT and aMT do not appear to evolve (Paparella et al., 2020; Taube et al., 2020).

1.4.4 Motor learning and short-interval intracortical inhibition

TMS can measure the parameters mentioned above, i.e., corticospinal excitability, CSP, rMT, and aMT, using single pulse stimulations. Furthermore, it can also measure other parameters, such as intracortical inhibition (SICI) with paired-pulses stimulation paradigms (Rotenberg et al., 2014). The first stimulation is called conditioning stimulus (CS), and the second one test stimulus (TS). In the case of the SICI protocol, the CS is subthreshold, meaning that it does not evoke a visible muscular answer. However, it activates the inhibitory interneurons (Di Lazzaro & Rothwell, 2014), which conditions the TS. The TS is, in turn, suprathreshold and usually provokes a muscular answer, i.e., an MEP. The CS and the TS are spaced from one to six ms (Rotenberg et al., 2014). A SICI protocol contains several single- and paired-pulses stimulations. It allows calculating the SICI value, which represents the amplitude differences between single- and paired-pulses MEPs expressed in percentage. As previously stated, MEPs are influenced by many factors, making their amplitude variations challenging to interpret (Bestmann & Krakauer, 2015). However, paired-pulses protocols give more information about the amplitude changes of MEPs as they enable to identify at which level the modifications happen (Bestmann & Krakauer, 2015). For example, SICI, as indicated in its name, show what happens at the intracortical level.

SICI does not seem to be correlated with motor learning and does not appear to change with the learning of a ballistic task (Berghuis et al., 2017). However, one study measured SICI under different conditions, i.e., at rest, during a ballistic task, and during a balance exercise, to see if the values changed after four weeks of training (Taube et al., 2020). They had one group that trained a lower body ballistic task and one group that trained a balance task. According to their results, neither training had an impact on resting SICI values, which is consistent with the results of Berghuis et al. (2017). More interestingly, Taube and colleagues (2020) observed a change in SICI when measured during a task and that this change is specific to the training being performed. That is, the SICI values of the ballistic task training group decreased when

SICI was measured during the ballistic task in the post-tests but not when SICI was measured during the balance exercise. And vice versa for the balance training group. These results suggest, therefore, that SICI is task specific.
However, more studies are needed to confirm these results. For this reason, another aim of this thesis was to investigate how SICI evolves through learning a new ballistic task and possible retrograde interference.

1.5 Aims and hypotheses

This master's thesis pursues two main aims. The first one is to examine if the time interval between the initial learning of the first task (*A1*) and its retention test (*A2*) is crucial to observe retrograde interference. The second one is to better understand some neurophysiological mechanisms measured with TMS during the learning of a new ballistic task. Below are the hypotheses formulated for all the questions answered in this master thesis. Only the alternative hypotheses have been formulated. The null hypotheses would negate the differences assumed in the alternative hypotheses.

1 Importance of the time between the first learning of a ballistic task (*A1*) and its retention test (*A2*) to observe retrograde interference

H_{1A}: Control and test groups will improve their performance during the first learning session of a ballistic task (*A1*).

H_{1B}: The test groups (i.e., *BT_VMT_48hRet* and *BT_VMT_ImmRet*) will improve their performance during the initial training of a visuomotor task (*B1*).

H_{1C}: Compared to the control groups (i.e., *BT_48hRet* and *BT_ImmRet*), the test groups (i.e., *BT_VMT_48hRet* and *BT_VMT_ImmRet*) will show retrograde interference.

H_{1D}: The test groups (i.e., *BT_VMT_48hRet* and *BT_VMT_ImmRet*) will show different levels of retrograde interference.

2 The evolution of TMS parameters during the learning of a new ballistic task

H_{2A}: The peak-to-peak amplitude of MEPs increases during the learning of a new ballistic task.

H_{2B}: The learning of a new ballistic task modifies the length of the CSP.

H_{2C}: The learning of a new ballistic task modifies the rMT.

H_{2D}: The learning of a new ballistic task modifies the aMT.

H_{2E}: The learning of a new ballistic task influences SICI active, i.e., SICI measured during a slight isometric contraction of the wrist.

H_{2F}: The learning of a new ballistic task has an effect on SICI task, i.e., SICI measured during a rapid isometric contraction of the wrist.

2 Methods

Fifty-eight adults recruited among sports students and relatives participated in the study (Table 2). Due to the neurophysiological recordings, people with neurological or psychiatric disorders were not included in this study, as well as people with electrical stimulators in the body and pregnant women. The participants had to be task naïve and give their written informed consent. Participants were randomly assigned into four groups (Figure 1).

Table 2

Characteristics of the participants according to their group

Characteristics	Only BT task		BT and VMT tasks	
	BT_48hRet	*BT_ImmRet*	*BT_VMT_48hRet*	*BT_VMT_ImmRet*
n (f/m)	7/7	6/8	7/8	7/8
Age (years)	23.2 ± 2.0	22.0 ± 3.3	22.5 ± 2.4	24.3 ± 1.7
Weight (kg)	65.6 ± 10.7	64.9 ± 10.2	70.4 ± 13.4	68.6 ± 10.6
Height (cm)	171.9 ± 7.6	172.1 ± 10.5	175.1 ± 8.8	171.9 ± 9.2

Note. BT = ballistic task (task *A*), VMT = visuomotor task (task *B*).

During each experimental session, the participants alternated between TMS and task practice (Figure 1). There were four groups: two control groups and two test groups. Both control groups, namely *BT_48hRet* and *BT_ImmRet*, only did task *A*, which was a ballistic task, as shown in Figure 1. They differed in the time interval between *A1* and *A2*: the group *BT_48hRet* had a 48 hours break between both tasks, whereas the group *BT_ImmRet* had 30 minutes rest. The test groups, i.e., *BT_VMT_48hRet* and *BT_VMT_ImmRet*, followed an *A1-B1-A2-B2* design inspired by the *A-B-A* paradigm. In other words, they learned task *A*, a ballistic task, and task *B*, a visuomotor task. The difference between both groups was the time interval between tasks *A1* and *A2*, which was 48 hours or five minutes. See below for more details.

Figure 1

Overview of the study design

BT_48hRet group

TMS 1	BT(35x) *A1*	TMS 2	48h →	TMS 3	BT(35x) *A2*

BT_ImmRet group

TMS 1	BT(35x) *A1*	TMS 2	30min →	TMS 3	BT(35x) *A2*

BT_VMT_48hRet

TMS 1	BT(35x) *A1*	TMS 2	VMT(50x) *B1*	48h →	TMS 3	BT(35x) *A2*	VMT(15x) *B2*

BT_VMT_ImmRet

TMS 1	BT(35x) *A1*	TMS 2	VMT(50x) *B1*	5min →	TMS 3	BT(35x) *A2*	VMT(15x) *B2*

Note. TMS = transcranial magnetic stimulation, BT = ballistic task (learning task), VMT = visuomotor task (interference task). *A1* and *B1* = initial learning, *A2* and *B2* = retention tests.

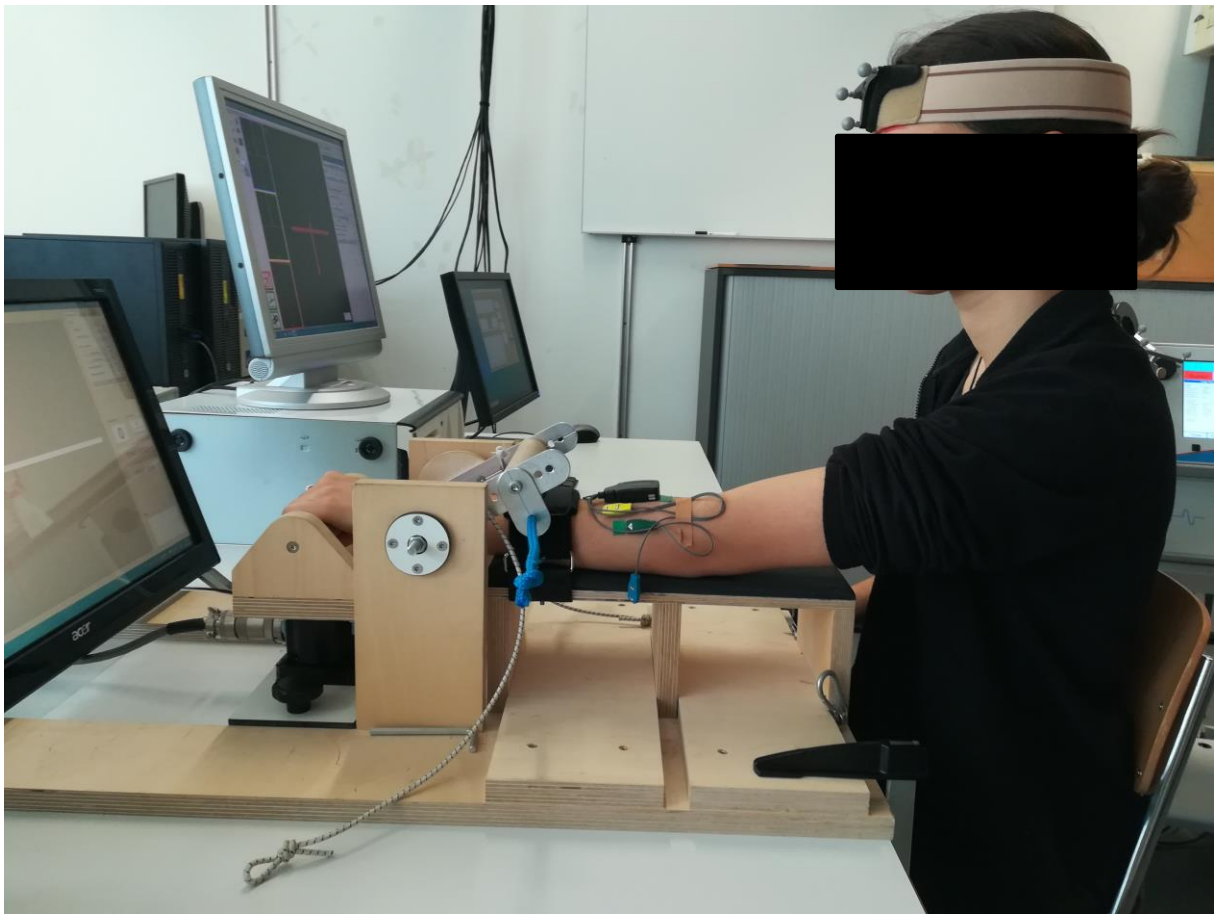
2.1 Ballistic task

The ballistic task consisted of producing maximal force as quickly as possible with the wrist flexor muscles. The participants sat in front of a computer screen and held a fixed handle with their non-dominant hand (Figure 2). A sound signal indicated the start of each trial. The participants heard three beeps followed by a fourth longer beep. Each participant was instructed to perform the wrist flexion during the fourth beep. This movement corresponded to a maximal explosive isometric contraction. There was no familiarization trial. A force transducer (MC3A-500, Advanced Mechanical Technology Inc., MA, USA) placed below the fixed handle recorded the force applied by the participants. Two feedbacks were provided on the computer screen: the force curve and the peak rate of force development (RFD), expressed in N/s (Figure 3). The peak RFD was obtained from the force curve and represented the capacity to increase force as quickly as possible from a resting level (Maffiuletti et al., 2016). A third feedback was

provided on another computer screen at the participants' right. This screen displayed the learning curve, i.e., the peak RFD values of all trials. The participants were motivated and explicitly encouraged to improve their performance (i.e., the peak RFD values) throughout each training session. The ballistic task corresponded to the learning task, namely task *A*.

Figure 2

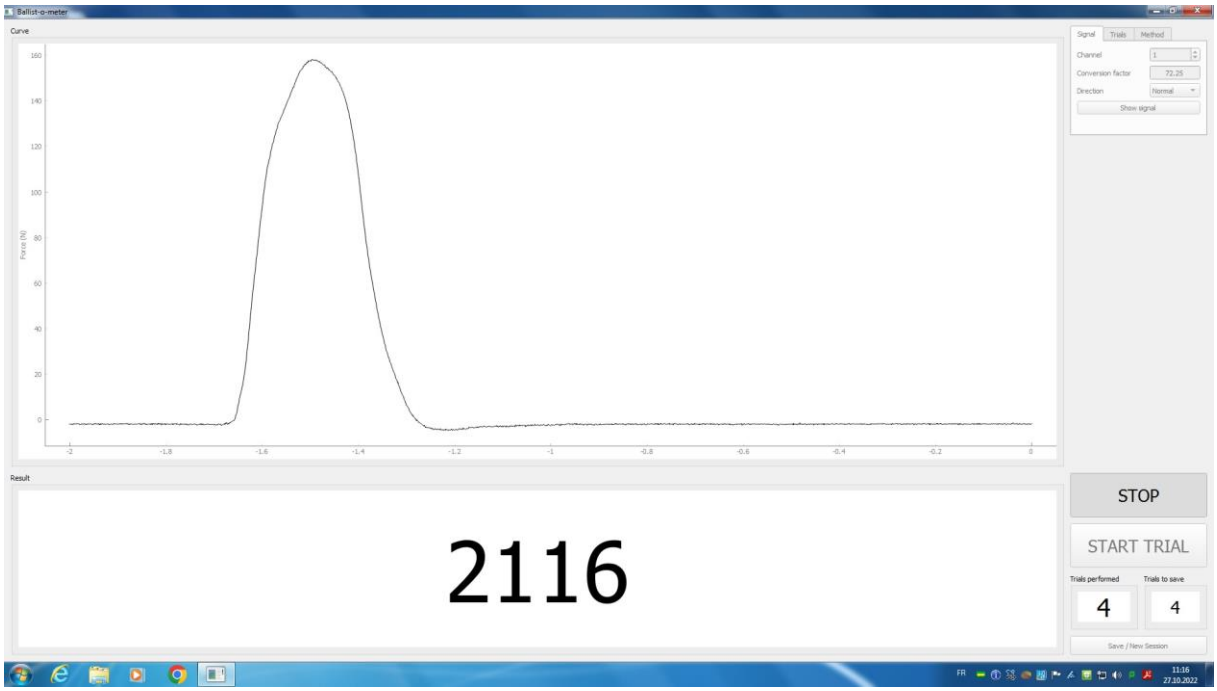
Installation for the ballistic task (task A)



Note. Each participant held the fixed handle with their non-dominant hand. The EMG device was stuck on their forearm. The headband with the three markers was part of the TMS neuronavigation system.

Figure 3

Feedback during the ballistic task (task A)



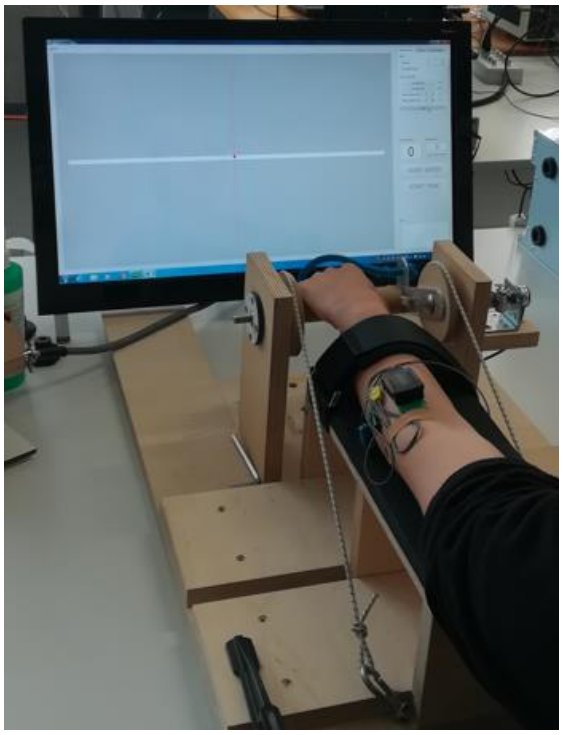
Note. This is an example of the feedback that one of the participants received for one of their trials. The curve is a visual representation of the force produced by the participant during the trial. The number in the *Result* rectangle (i.e., 2116) represents the peak RFD (N/s). It is the value that the participant is encouraged to improve.

2.2 Visuomotor task

The participants were in the same position as for the ballistic task. However, they held a mobile handle connected to two elastic bands instead of a fixed handle (Figure 4). The visuomotor task consisted of following a moving curve with a cursor controlled through a potentiometer (6639S-1-103, Bourns Inc., CA, USA) placed in the rotation axis of the handle. The cursor could go up with wrist flexion movements and down with wrist extensions. The experimenter warned participants before the start of each trial, which then lasted 11 seconds. The curve was always the same. The participants again received three feedbacks: the trajectory they made superposed with the curve they should follow, the root mean square error (RMSE; Figure 5), and the learning curve (i.e., the RMSE of all the trials). The RMSE is calculated from the difference between the curve to follow and the curve actually made. The participants were motivated and explicitly encouraged to improve their performance (i.e., the RMSE values) throughout each training session. The smallest the RMSE was, the better it was. The visuomotor task was the interference task, namely task *B*.

Figure 4

Mobile handle used for the visuomotor task (task B)



Note. Each participant held the mobile handle with their non-dominant hand. The EMG device was stuck on their forearm. The red point on the computer screen is the cursor controlled by the mobile handle, and the white line is the line to follow during the task.

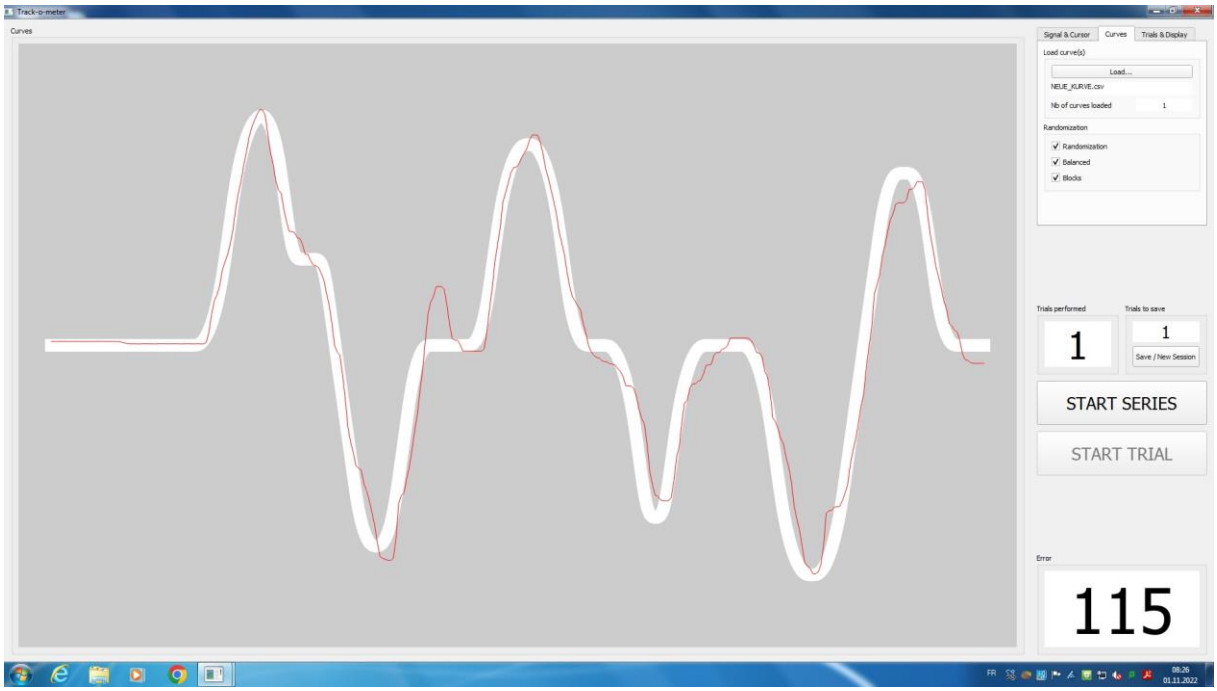
2.3 Neurophysiological recordings

2.3.1 Electromyography

The muscular activity of the flexor carpi radialis muscle (FCR) and a wrist extensor muscle of the non-dominant hand was measured using surface electromyography (EMG; Trigno Quattro Sensor, Delsys, MA, USA). Once the target muscles were found, the skin was rubbed and disinfected. Then two electrodes and a reference were stuck to the skin. Afterward, the EMG signals were visually controlled to ensure muscle activity during contractions was large enough compared to the background noise. The latter should be as close as possible to 0 μV and smaller than 0.5 μV to avoid the noise being confused with MEPs later. The position of the electrodes was marked with a permanent marker on the subjects taking part in two measurement sessions, i.e., the subjects of *BT_VMT_48hRet* and *BT_48hRet* groups, in order to stick the electrodes at the same place during both sessions.

Figure 5

Feedback during the visuomotor task (task B)



Note. The white curve is the curve that the participants must follow. The red curve is the curve that one participant actually made. The number in the *Error* rectangle (i.e., 115) represents the RMSE.

2.3.2 Peripheral nerve stimulation

Peripheral nerve stimulation (Digitimer DS7Q, Digitimer Ltd., Welwyn Garden City, England) is a non-invasive method that has been used to obtain the M-wave of the FCR muscle of the non-dominant hand. The median nerve innervates the FCR muscle. Therefore, the stimulation site was located on the inside of the upper arm, next to the biceps brachii tendon near the elbow. The electrode, consisting of an anode and a cathode, was pressed against the skin with gel. The location was tested, and when the right one was found, the M-wave was measured repeatedly. The intensity of the electrical stimulations was gradually increased until a plateau of the muscular response was reached. The maximum M-wave amplitude, called Mmax, was recorded and later used to normalize the MEP amplitude produced by TMS.

2.3.3 Transcranial magnetic stimulation

TMS is a non-invasive method of applying a magnetic field to M1 to depolarize neurons and elicit a muscular response within the target muscle. The muscular response is called MEP and

is recorded with EMG (Rotenberg et al., 2014). In this project, the part of M1 responsible for the FCR muscle was targeted.

During each session, the coil of the TMS device (MagPro with MagOption, MagVenture A/S, GA, USA), which was a figure-eight coil, and the neuronavigation system (Cameras: Polaris Spectra, Northern Digital Inc., Ontario, Canada. Software: Localite TMS Navigator Version 2.0.5, LOCALITE GmbH, Bonn, Germany) were calibrated. The neuronavigation system was used to stimulate the participants in the same place during and between sessions. Then the hotspot, i.e., the location where the stimulations produce the biggest MEP at a given intensity, was determined. Each participant underwent three TMS units: TMS 1, TMS 2, and TMS 3 (Figure 1). Each TMS unit was similar: it started with the determination of rMT and aMT and continued with five blocks of twenty stimulations during various conditions (Table 3).

Table 3

Content of each TMS unit

Name of the part	TMS 1	TMS 2	TMS 3
	Hotspot		
	rMT	rMT	rMT
	aMT	aMT	aMT
Block 1	1x20 single-pulse	1x20 single-pulse	1x20 single-pulse
Blocks 2 and 3	2x20 SICI active	2x20 SICI task	2x20 SICI active
Blocks 4 and 5	2x20 SICI task	2x20 SICI active	2x20 SICI task

Note. This table is intended to facilitate the understanding of the reader. TMS = transcranial magnetic stimulation, rMT = resting motor threshold, aMT = active motor threshold, SICI = short-interval intracortical inhibition.

For the rMT, the participants sat and had their non-dominant hand relaxed on the desk during the stimulations. The aim was to find the lowest stimulation intensity that evoked an MEP >50 μV in 5/10 stimulations (Rotenberg et al., 2014).

The aMT was then determined. For this purpose, the participants held the mobile handle (Figure 4) connected to the two elastic bands. During the stimulations, the participants were instructed to keep the cursor at a specific position indicated by a white line on the computer screen (Figure 4), causing a slight isometric contraction. The aim was to find the lowest stimulation intensity eliciting an MEP >200 μV in 5/10 stimulations (Rotenberg et al., 2014). The rMT and aMT were used to determine the stimulation intensities applied during the five blocks of twenty

stimulations. The first block aimed to determine corticospinal excitability and CSP. Therefore, only single-pulse stimulations were delivered. During the stimulations, the participants held the mobile handle, which was connected to a weight of 3.4 kg for females and 4.0 kg for males. As during aMT determination, the participants had to keep the cursor in the white line during the stimuli. SICI was measured during the remaining TMS blocks (i.e., blocks 2, 3, 4, and 5). During a SICI protocol, single- and paired-pulses stimulations are delivered. For the paired-pulses stimulations, stimulation intensities were initially set to 80 % of the aMT for the CS and 130 % of the rMT for the TS. During the second and third blocks, the participants performed the same task as during aMT determination, i.e., keeping the cursor in the white line with the elastic's resistance (i.e., SICI active). At the end of the second block of TMS 1, SICI was calculated to determine the percentage of inhibition during SICI active. If the value was between 40 and 60 %, the stimulation intensities were kept for the rest of the experiment. Otherwise, stimulation intensities were adapted. Finally, during blocks 4 and 5, SICI was measured during the execution of rapid wrist flexions (i.e., SICI task). For this purpose, the participants held the fixed handle. There were two beeps followed by a third longer beep. During the third beep, the participants had to perform the fastest possible wrist flexion. After five familiarization trials without TMS and with visual feedback, each participant performed two blocks of twenty trials with TMS and without visual feedback.

2.4 Statistical analysis

The statistical analysis was performed with the Jamovi software (version 2.3.0.0, Sydney, Australia). Four groups were compared: *BT_VMT_48hRet*, *BT_VMT_ImmRet*, *BT_48hRet*, and *BT_ImmRet*.

Before conducting two-way mixed design ANOVAs, the normality of the data and homogeneity of the variances were tested with Levene's and Shapiro-Wilk tests, respectively. If the ANOVAs reported significant results, post hoc tests were performed to find where the significant differences were. For all the statistical tests performed during the data analysis, the level of significance was set with $p<0.05$.

2.4.1 Statistical analysis of behavioral parameters

This section concerns the hypotheses H_{1A} to H_{1D} and, therefore, the behavioral analysis. Initial learning of the ballistic (*A1*) and visuomotor (*B1*) tasks were quantified by comparing the mean of trials 3-5 with the mean of the last three trials, i.e., trials 33-35, and 48-50, respectively. Two-

way mixed design 2x4, and 2x2, ANOVAs [*TIMES* x *GROUPS*] were conducted to verify that all groups had a similar learning rate during *A1* and *B1*, respectively.

The comparison between the first and the last trials of each training was inspired by the methods of Lundbye-Jensen et al. (2011). In their study, they used trials one to three, not three to five, but they had two familiarization trials that we do not have in our study. Hence, I chose to analyze trials three to five.

To observe whether retrograde interference had occurred, the last three trials of the initial learning of the ballistic task (*A1*) were compared with trials 3-5 of the retention test of the ballistic task (*A2*). This comparison was made using a two-way mixed design 2x4 ANOVA [*TIMES* x *GROUPS*].

Finally, if retrograde interference had occurred, I would have tried to find out whether the time interval between *A1* and *A2* might be crucial for the observation of the interference.

2.4.2 Statistical analysis of TMS parameters

This section concerns the hypotheses H_{2A} to H_{2F} and, thus, the analysis of corticospinal excitability, CSP, rMT, aMT, SICI active, and SICI task. For each of these parameters, the evolution between TMS 1 and TMS 2 was examined.

During each TMS unit, corticospinal excitability and CSP data were derived from the 20 single-pulse MEPs of the first block of the unit. Corticospinal excitability was measured as the peak-to-peak amplitude of MEPs. The CSP was calculated from the MEP onset to the end of the silent period. The 20 stimulations were averaged for each parameter and each participant. The means of the different participants recorded during TMS 1 were compared with the means recorded during TMS 2 with two-way mixed design 2x4 ANOVAs with the factors TIMES (*TMS 1, TMS 2*) x GROUPS (*BT_VMT_48hRet, BT_VMT_ImmRet, BT_48hRet, BT_ImmRet*).

The rMT and the aMT were measured at the beginning of each TMS unit. The values obtained during TMS 1 were then compared to those of TMS 2, using a two-way mixed design 2x4 ANOVAs [*TIMES* x *GROUPS*].

Finally, the SICI parameters were calculated as follows: 100 – (average amplitude of 20 paired-pulse MEPs / average amplitude of 20 single-pulse MEPs x 100). These parameters were obtained for SICI active and SICI task. Two-way mixed design 2x4 ANOVAs [*TIMES* x *GROUPS*] were then applied to compare the evolution between TMS units 1 and 2.

2.4.3 Operationalized alternative hypotheses, applied analyses, and interpretation plan

Table 4

Summary of operationalized hypotheses, as well as specific tests used to demonstrate them and the effect size computation method

N°	Hypotheses (H)	Tests	Effect size
H_{1A}	Performance ($A1_{3\text{-}5}$) < Performance ($A1_{33\text{-}35}$)	Two-way mixed design ANOVA	$\eta 2 \leq 0.01$ (small); $0.01 < \eta 2 < 0.14$ (medium); $0.14 \leq \eta 2$ (large)
H_{1B}	Performance ($B1_{3\text{-}5}$) < Performance ($B1_{48\text{-}50}$)		
H_{1C}	CG (($A1_{33\text{-}35}$)-($A2_{3\text{-}5}$)) ≠ TG (($A1_{33\text{-}35}$)-($A2_{3\text{-}5}$))		
H_{1D}	*BT_VMT_48hRet* ($A1_{33\text{-}35}$)-($A2_{3\text{-}5}$) ≠ *BT_VMT_ImmRet* ($A1_{33\text{-}35}$)-($A2_{3\text{-}5}$)		
H_{2A}	CSE (TMS 1) ≠ CSE (TMS 2)		
H_{2B}	CSP (TMS 1) ≠ CSP (TMS 2)		
H_{2C}	rMT (TMS 1) ≠ rMT (TMS 2)		
H_{2D}	aMT (TMS 1) ≠ aMT (TMS 2)		
H_{2E}	SICI active (TMS 1) ≠ SICI active (TMS 2)		
H_{2F}	SICI task (TMS 1) ≠ SICI task (TMS 2)		

Note. CG = control groups (*BT_48hRet*, *BT_ImmRet*), TG = test groups (*BT_VMT_48hRet*, *BT_VMT_ImmRet*), CSE = corticospinal excitability, CSP = cortical silent period, rMT = resting motor threshold, aMT = active motor threshold, SICI = short-interval intracortical inhibition, $\eta 2$ = eta-squared.

3 Results

3.1 Importance of the time between *A1* and *A2* to observe retrograde interference

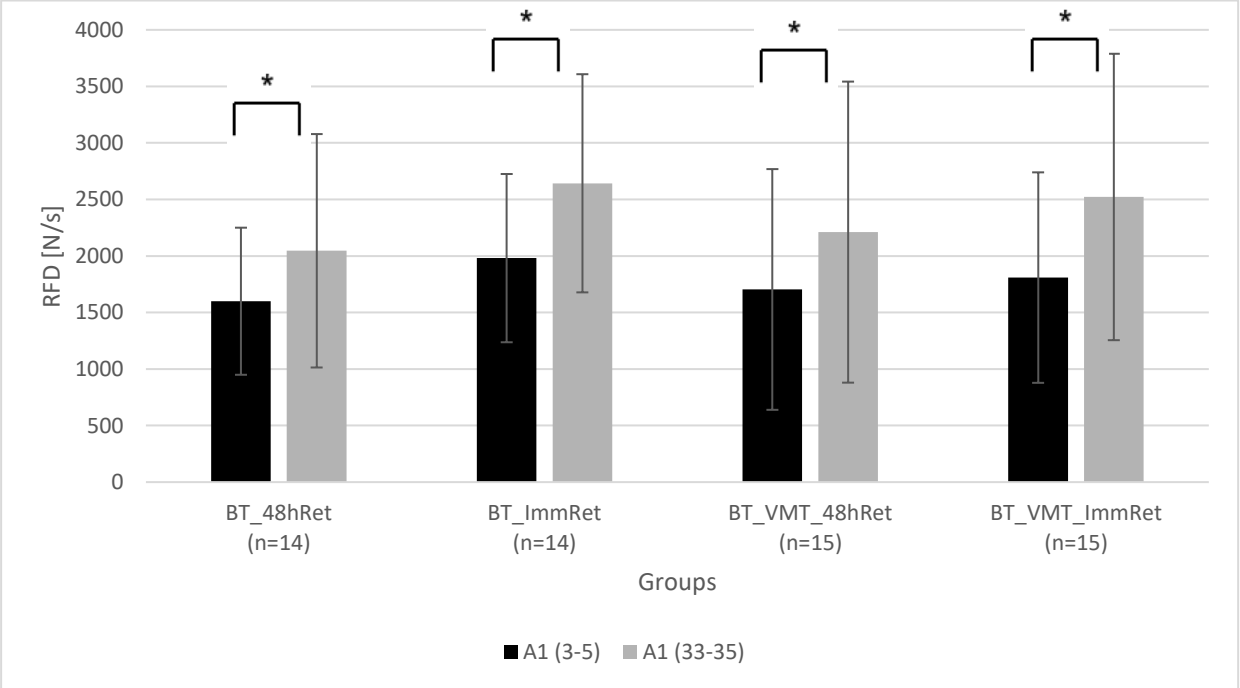
3.1.1 Motor learning

As shown in Figure 6, all groups significantly improved performance during the initial learning of the ballistic task (*A1*; main effect of TIMES: $F_{1, 56}$ = 74.21, p<0.001, η^2 = 0.077) and progressed in a similar way (TIMES x GROUPS interaction: $F_{3, 56}$ = 0.87, p = 0.463, η^2 = 0.003). Finally, no main effect of GROUPS was observed ($F_{3, 56}$ = 0.73, p = 0.541, η^2 = 0.032).

Performance of the groups *BT_VMT_48hRet* and *BT_VMT_ImmRet* groups, which trained the visuomotor task in addition to the ballistic task, improved significantly during the first training of the visuomotor task (*B1*) as indicated by the significant main effect of TIMES ($F_{1, 28}$ = 376.16, p<0.001, η^2 = 0.610; Figure 7). There was no significant main effect of the factor GROUPS ($F_{1, 28}$ = 0.35, p = 0.561, η^2 = 0.004) and no TIMES x GROUPS interaction ($F_{1, 28}$ = 0.45, p = 0.510, η^2 = 0.001).

Figure 6

Initial learning of the ballistic task (A1)

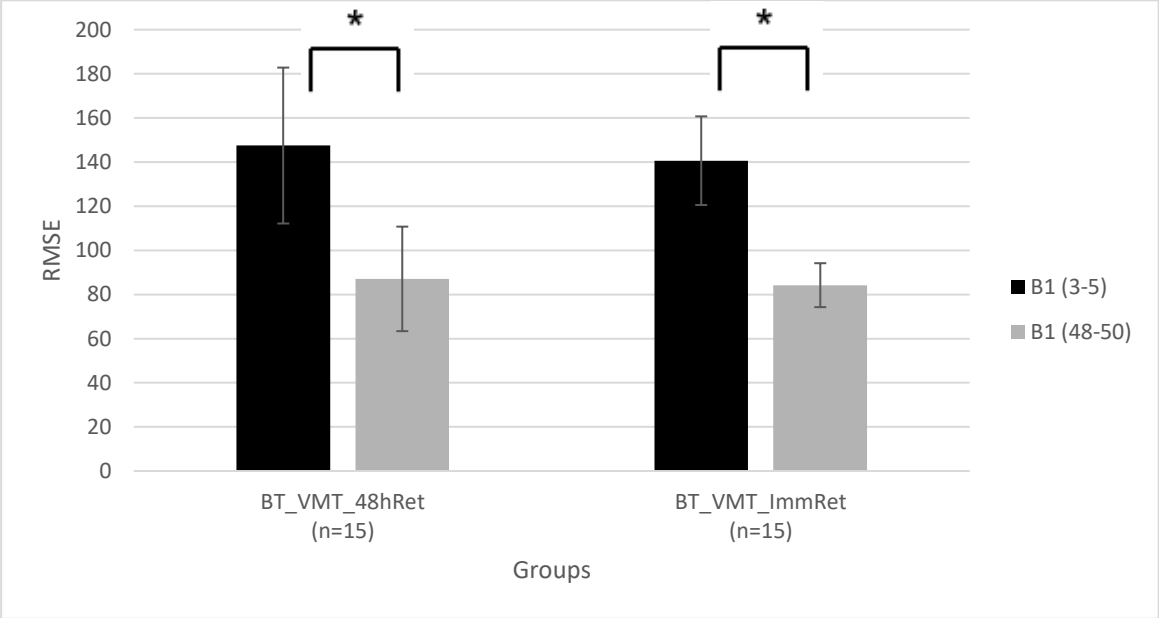


Note. This graph shows the evolution of the performance during the initial learning of the ballistic task (i.e., *A1*). The higher the rate of force development (RFD), the better the performance.

All groups significantly improved their performance on the ballistic task, for a mean increase of 32.88 %. More specifically, *BT_48hRet* increased its performance by 27.88 %, going from 1600 ± 650 N/s to 2046 ± 1032 N/s. The average performance of the *BT_ImmRet* group increased from 1981 ± 744 N/s to 2643 ± 965 N/s, representing an improvement of 33.42 %. The average performance of the *BT_VMT_48hRet* group increased from 1704 ± 1065 N/s to 2211 ± 1331 N/s, an increase of 29.75 %. Finally, the *BT_VMT_ImmRet* group improved by 39.41 % from 1809 ± 931 N/s to 2522 ± 1266 N/s.

Figure 7

Initial learning of the visuomotor task (B1)



Note. This graph represents the evolution of performance during the initial learning of the visuomotor task (i.e., *B1*). The lower the RMSE, the better the performance. Both groups significantly improved performance, for an average reduction in RMSE of 40.56 %. The group *BT_VMT_48hRet* went from an RMSE of 147 ± 35.3 to an RMSE of 87.1 ± 23.7, corresponding to a progress of 40.75 %. The performance of the *BT_VMT_ImmRet* group went from 141 ± 20.1 to 84.2 ± 9.96, an improvement of 40.28 %.

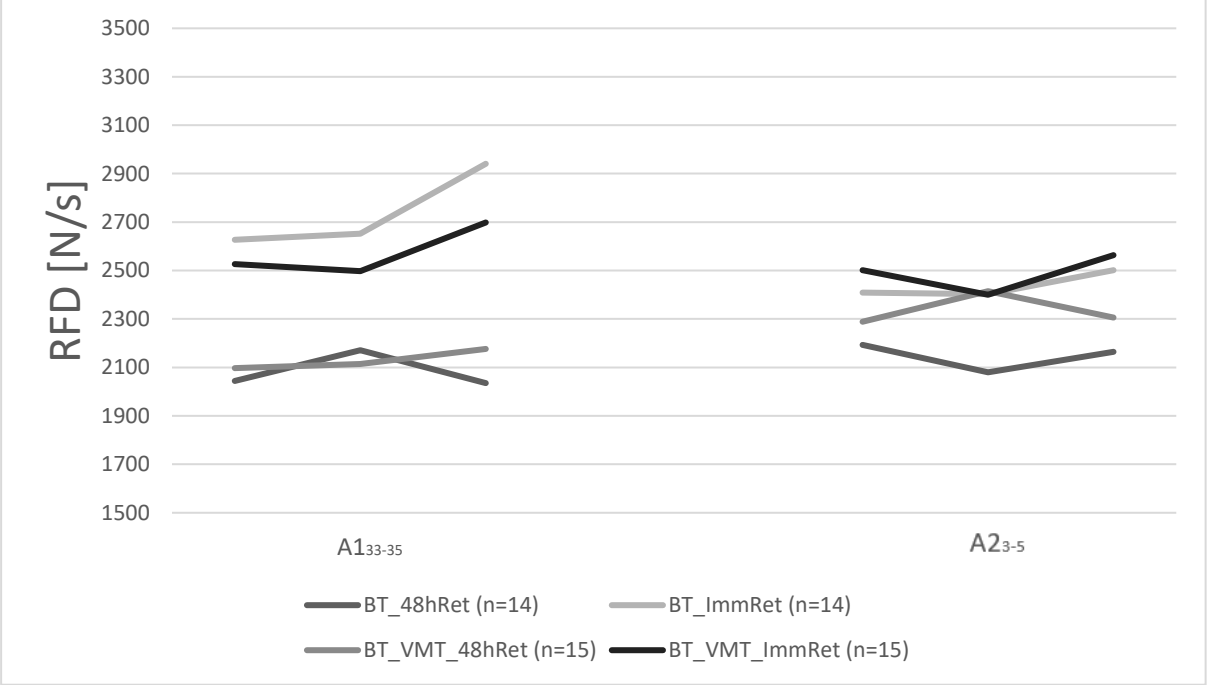
3.1.2 Retrograde interferences

One of the main purposes of the experiment was to observe retrograde interference to further investigate this mechanism. The two-way mixed design 4x2 ANOVA [GROUPS x TIMES] revealed a significant GROUPS x TIMES interaction ($F_{3, 56} = 3.39$, $p = 0.024$, $\eta^2 = 0.004$; Figure 8), while no significant main effects of the factors GROUPS ($F_{3, 56} = 0.46$, $p = 0.710$, $\eta^2 = 0.023$)

and TIMES ($F_{1, 56}$ = 0.64, p = 0.428, η^2 = 0.000) were observed. However, as can be seen in Figure 8, the significant interaction was due to the timing of the retention test (i.e., immediate vs. 48 hours later) and not to the training of the interference task. Overall, therefore, no retrograde interference was observed. It is confirmed by the results of two-way mixed design 2x2 ANOVAs [*TIMES* x *GROUPS*] performed separately for the immediate retention groups (*BT_VMT_ImmRet* vs. *BT_ImmRet*) and the 48 hours retention groups (*BT_VMT_48hRet* vs. *BT_48hRet*). In fact, in both cases, the ANOVAs showed no significant *GROUPS* x *TIMES* interaction (p = 0.245 and p = 0.667, respectively).

Figure 8

Overview of the learning of the ballistic task (A1 and A2)



Note. This graph shows the average evolution of performance when learning the ballistic task. The RFD of the *BT_48hRet* group increased from 2046 ± 1032 N/s to 2118 ± 885 N/s, corresponding to an improvement of 3.52 %. The performance of the *BT_ImmRet* group decreased by 9.84 % from 2643 ± 965 N/s to 2383 ± 1030 N/s. The RFD of the *BT_VMT_48hRet* group increased from 2211 ± 1331 N/s to 2337 ± 1400 N/s, corresponding to an increase of 5.70 %. Finally, the performance of the *BT_VMT_ImmRet* group went from 2522 ± 1266 N/s to 2434 ± 1224 N/s, a decrease of 3.49 %.

3.2 Evolution of TMS parameters during the learning of a new ballistic task

3.2.1 Corticospinal excitability

Corticospinal excitability (measured as MEPs peak-to-peak amplitude) did not vary between the beginning and the end of the initial training (*A1*) of the ballistic task, as indicated by the non-significant main effect of *TIMES* ($F_{1, 54}$ = 1.25, p = 0.269, η^2 = 0.001). No main effect of groups was observed ($F_{3, 54}$ = 2.23, p = 0.095, η^2 = 0.104). However, a TIMES x GROUPS interaction was found ($F_{3, 54}$ = 4.39, p = 0.008, η^2 = 0.011). Post hoc comparisons showed that this difference was only significant in the *BT_48hRet* group (p_{Holm} = 0.019) when comparing TMS 1 and TMS 2. More specifically, this group had an increase in corticospinal excitability of 19.1 % between TMS 1 and 2, from 46.7 ± 16.2 % to 55.6 ± 16.5 %. More descriptive statistics are presented in Table 5.

3.2.2 CSP

No main effect of TIMES was observed for the CSP, indicating that this parameter did not evolve through the initial learning of the ballistic task (*A1*; $F_{1, 54}$ = 0.054, p = 0.818, η^2 = 0.000). There was no main effect of GROUPS either ($F_{3, 54}$ = 2.19, p = 0.100, η^2 = 0.103), as well as no TIMES x GROUPS interaction ($F_{3, 54}$ = 1.02, p = 0.389, η^2 = 0.003). The CSP values are presented in Table 5.

3.2.3 rMT and aMT

rMT and aMT did not change between the beginning and the end of the initial training (*A1*) of the ballistic task (main effect of TIMES: rMT ($F_{1,52}$ = 1.40, p = 0.243, η^2 = 0.000) and aMT ($F_{1, 54}$ = 1.15, p = 0.289, η^2 = 0.000)). No significant main effect of GROUPS was observed for both rMT ($F_{3, 52}$ = 2.36, p = 0.082, η^2 = 0.118) and aMT ($F_{3, 54}$ = 1.62, p = 0.194, η^2 = 0.081). Finally, no interaction between the factors TIMES and GROUPS was observed, nor for the rMT ($F_{3, 52}$ = 0.59, p = 0.624, η^2 = 0.001), or the aMT ($F_{3, 54}$ = 1.55, p = 0.212, η^2 = 0.002). Descriptive statistics of the parameters rMT and aMT are presented in Table 5.

3.2.4 SICI

3.2.4.1 SICI active No main effect of TIMES was found for SICI active, indicating that this parameter did not change during the learning of the new ballistic task ($F1, 54 = 1.16$, $p = 0.286$, $\eta^2 = 0.002$). There was also no significant main effect of GROUPS ($F3, 54 = 2.62$, $p = 0.060$, $\eta^2 = 0.116$), as well as no TIMES x GROUPS interaction ($F3, 54 = 1.68$, $p = 0.183$, $\eta^2 = 0.007$). The SICI active values are presented in Table 5.

3.2.4.2 SICI task A significant main effect of TIMES was observed for SICI task, indicating that this parameter changed during the initial training of the ballistic task ($F_{1, 53} = 8.56$, $p = 0.005$, $\eta^2 = 0.032$). More precisely, the descriptive statistics indicate that SICI task decreased by 54.0% between TMS 1 and TMS 2, from 8.63 ± 12.0 % to 3.97 ± 13.0 %. In contrast, no main effect of GROUPS ($F_{3, 53} = 1.12$, $p = 0.351$, $\eta^2 = 0.045$), as well as no TIMES x GROUPS interaction ($F_{3, 53} = 0.49$, $p = 0.691$, $\eta^2 = 0.006$) were found. The SICI task values are presented in Table 5.

Table 5

Descriptive statistics of the TMS parameters

Parameters	*BT_48hRet*		*BT_ImmRet*		*BT_VMT_48hRet*		*BT_VMT_ImmRet*	
	TMS 1	TMS 2	TMS 1	TMS 2	TMS 1	TMS 2	TMS 1	TMS 2
Corticospinal excitability [%Mwave]	46.7±16.2	55.6±16.5	32.5±11.7	30.6±13.1	40.5±24.9	40.8±23.9	41.7±26.5	39.9±24.4
CSP [ms]	148.0 ±31.7	153.0 ±40.0	142.0 ±40.9	137.0 ±38.2	132.0 ±30.4	133.0 ±31.3	120.0 ±24.9	121.0 ±26.4
rMT [% Stimulator]	41.6±8.2	41.8±8.7	40.1±8.2	39.6±7.2	48.1±11.0	47.2±9.6	42.4±5.8	42.1±5.8
aMT [% Stimulator]	35.7±6.5	36.1±7.0	33.1±5.9	32.7±5.4	37.6±6.7	36.6±6.6	33.7±4.1	33.7±4.0
SICI active [%]	34.2±14.7	34.8±18.6	42.0±17.5	44.5±22.2	40.1±22.0	36.5±19.5	28.3±16.7	22.5±16.5
SICI task [%]	12.0±9.0	6.12±9.8	7.33±14.1	5.83±16.5	11.2±13.8	4.35±15.4	4.30±9.9	-0.14±9.2

Note. TMS = transcranial magnetic stimulation, CSP = cortical silent period, rMT = resting motor threshold, aMT = active motor threshold, and SICI = short-interval intracortical inhibition. Except for the CSP, which is in ms, all other parameters are expressed in percentages.

4 Discussion

This master thesis had two main aims: to examine if the time interval between initial learning of the first task (*A1*) and its retention test (*A2*) is crucial to observe retrograde interference and to better understand some neurophysiological mechanisms measured with TMS during the learning of a new ballistic task. Several hypotheses were then formulated to obtain the desired answers. These hypotheses are summarized in Table 6 and are accompanied by the results, i.e., whether they are correct or not.

Table 6

Overview of the operationalized hypotheses and their results

N°	Hypotheses (H)	Results
H_{1A}	Performance ($A1_{3\text{-}5}$) < Performance ($A1_{33\text{-}35}$)	Ok
H_{1B}	Performance ($B1_{3\text{-}5}$) < Performance ($B1_{48\text{-}50}$)	Ok
H_{1C}	CG (($A1_{33\text{-}35}$)-($A2_{3\text{-}5}$)) ≠ TG (($A1_{33\text{-}35}$)-($A2_{3\text{-}5}$))	X
H_{1D}	*BT_VMT_48hRet* ($A1_{33\text{-}35}$)-($A2_{3\text{-}5}$) ≠ *BT_VMT_ImmRet* ($A1_{33\text{-}35}$)-($A2_{3\text{-}5}$)	n/a
H_{2A}	CSE (TMS 1) ≠ CSE (TMS 2)	Ok / X
H_{2B}	CSP (TMS 1) ≠ CSP (TMS 2)	X
H_{2C}	rMT (TMS 1) ≠ rMT (TMS 2)	X
H_{2D}	aMT (TMS 1) ≠ aMT (TMS 2)	X
H_{2E}	SICI active (TMS 1) ≠ SICI active (TMS 2)	X
H_{2F}	SICI task (TMS 1) ≠ SICI task (TMS 2)	Ok

Note. CG = control groups (*BT_48hRet, BT_ImmRet*), TG = test groups (*BT_VMT_48hRet, BT_VMT_ImmRet*), CSE = corticospinal excitability, TMS = transcranial magnetic stimulation, CSP = cortical silent period, rMT = resting motor threshold, aMT = active motor threshold, SICI = short-interval intracortical inhibition. In the third column, a red cross indicates that the hypothesis was rejected, a green "Ok" that the hypothesis was confirmed, and n/a = not applicable means that it was not possible to answer the hypothesis since we did not observe any interference.

4.1 Behavioral results

As expected, learning was visible at the behavioral level, with a performance improvement, both for the ballistic and visuomotor tasks. This is in line with the literature (Lundbye-Jensen

et al., 2011; Muellbacher et al., 2002) and fulfills one of the necessary conditions for retrograde interference since two learning tasks are required (Egger et al., 2021; Lundbye-Jensen et al., 2011). However, no retrograde interference occurred in the test groups. It is, therefore, impossible to know whether the time interval between the initial learning (*A1*) and the retention test (*A2*) influences the occurrence of retrograde interference since the phenomenon was not present at all. The question is why there was no retrograde interference, although the baseline conditions were met. Several explanations are possible.

It is possible that no interference was obtained because of the use of TMS as a neurophysiological measurement tool. TMS has been used several times in studies of retrograde interference, but mainly in the form of rTMS to induce retrograde interference (Lundbye-Jensen et al., 2011; Muellbacher et al., 2002). That is, in the form of a stimulation tool that affects the nervous system (for example, by modulating the amount of GABA (Gröhn et al., 2019)) and can thus cause interference. It is rarer that TMS has simply been used as a neurophysiological measurement tool. It was the case in the study by Lauber et al. (2013), where they used single-pulse stimulation to assess corticospinal excitability. The authors were able to achieve retrograde interference with their experimental design. Therefore, the use of TMS as a measurement tool and the occurrence of interference are not mutually exclusive. It seems important to remind here that although single-pulse TMS has been little used as a measurement tool in studies examining interference, it has been widely used in studies looking at simple motor learning. In the latter, it is difficult to say whether TMS influenced the results obtained since there are not necessarily comparison points without TMS.

Since TMS is both an interfering and a neurophysiological measurement tool, it is necessary to know where the separation between the two lies and when the data obtained are influenced by the stimulations. It is relatively apparent that rTMS influences the state of the nervous system as it can modulate GABA levels (Gröhn et al., 2019) or cause interference (Lundbye-Jensen et al., 2011; Muellbacher et al., 2002). However, the situation is a little more unclear for single-pulse TMS and paired-pulse protocols (Carson et al., 2016). Bütefisch et al. (2004) showed that if single-pulse TMS is applied ipsilaterally and in synchronization with movement (in this case, voluntary thumb movements), then it seems to prevent the formation of motor memory. Furthermore, Hadipour-Niktarash et al. (2007) showed that forgetting could be faster if single-pulse TMS is applied to M1 contralaterally at the end of a reaching movement during the learning of an adaptation task. Thus, single-pulse TMS, which is generally considered only as a measuring tool, can influence motor memory and cause interference under certain conditions. Bütefisch et al. (2004) have shown that single-pulse TMS can also facilitate learning. According

to these authors, single-pulse TMS applied contralaterally at the same time as the movement facilitates memorization, more so than training alone, i.e., without TMS or with single-pulse TMS applied contralaterally between movements.

If we look again at the results of Lauber et al. (2013) with this new information on TMS, it is possible to realize that the occurrence of retrograde interference in their study was independent of the use of TMS as retrograde interference was observed both in groups with and without TMS. In this study, TMS was applied between the movements during the learning of a ballistic task (task *A*) and a visuomotor task (task *B*), which does not facilitate learning but does not seem to affect learning (Bütefisch et al., 2004). All scenarios are, thus, possible with single-pulse TMS: interference, facilitation, or no effect.
In our project, TMS was applied either before or after the ballistic task training. According to this temporal distribution and the literature consulted, TMS should not have influenced the absence of retrograde interference since it was not applied simultaneously as the movements performed by the participants during the different ballistic and visuomotor tasks (Bütefisch et al., 2004).

More than TMS, it is possible that the tasks performed during the TMS measurements prevented interference, mainly the SICI task. Indeed, the SICI task was very similar to the ballistic task in which we would have liked to observe retrograde interference. It is, hence, possible that the SICI task indirectly constituted an additional training to the ballistic task. As Krakauer et al. (2005) have shown, an increase in the training volume could prevent interference during the learning of a visuomotor adaptation task. In addition, and as explained in the introduction, the somatosensory cortex may be crucial for motor learning and motor consolidation (Kumar et al., 2019). More practice also implies more sensory feedback. This additional information obtained during the SICI task could help the nervous system to consolidate the ballistic task and make it less susceptible to retrograde interference.
It should be noted, however, that the SICI task and the ballistic task were not exactly the same tasks. Therefore, the sensory afferents received were not exactly the same either. Nevertheless, this is not necessarily problematic for facilitating sensorimotor consolidation. Indeed, Cuppone et al. (2018) have shown that gains in proprioceptive acuity following sensorimotor learning can generalize to untrained sensory regions of the workspace. In this study, a reaching task was learned during several training sessions. The participants had to reach five different targets with their hands and without visual feedback. Before and after the trainings, a wrist joint

proprioceptive test was performed using eight different positions: the five targets trained in the reaching task and three additional targets. Their results show that the participants improved their position sense not only on the trained targets but also on the untrained targets. It means that sensory learning from one task can generalize to a similar task. It is what potentially happened in our experiment between the ballistic and SICI tasks.

There is one more argument in favor of the SICI task protecting the ballistic task from retrograde interference. The memorization of a movement is facilitated, and its retention time is prolonged when single-pulse TMS is applied at the same time as the execution of this movement (Bütefisch et al., 2004). It is indeed what was done in the SICI task: participants received stimulation in the middle of the movement, which prolonged their voluntary contraction. The SICI protocol was used in this task, meaning the participants received single- and paired-pulses stimulation. Therefore, there were also single-pulse stimuli, as in the previously cited study (Bütefisch et al., 2004), which may have improved the consolidation and retention of the SICI task. And if generalization between the SICI task and the ballistic task occurred (via a phenomenon similar to that observed in the study of Cuppone et al. (2018)), it may have helped to consolidate the ballistic task as well.

In conclusion, based on our results and the literature, it may be that the combination of SICI task and TMS could have prevented the occurrence of retrograde interference for the ballistic task. Further experiments are needed to confirm this hypothesis. It would be possible to start by removing the SICI task and the simultaneous TMS stimulations while keeping the rest of the protocol and see if retrograde interference occurs. If so, it would be interesting to add a group that would follow the same protocol but without TMS during the SICI task. It would allow us to know if it is the SICI task - TMS combination that prevents the occurrence of retrograde interference or if the task alone (i.e., the contractions executed during SICI task) is sufficient.

4.2 Neurophysiological results

Corticospinal excitability did not change after learning a new ballistic task in three of our groups, but it increased significantly in the *BT_48hRet* group. These results are representative of the current literature, which is equivocal and does not help to clarify it. Indeed, Berghuis et al. (2017) and Ho et al. (2022) would agree that corticospinal excitability does not change following learning a ballistic task, which is in agreement with three of our groups. However, in contrast, Paparella et al. (2020) found an increase in corticospinal excitability when learning a ballistic task, which is consistent with the results of our fourth group. Further studies are therefore needed to provide more data and better determine the general trend.

CSP values remained similar before and after learning a ballistic task, as did rMT and aMT. These results are consistent with those of Taube and colleagues (2020), who found no changes in CSP, rMT, or aMT after four weeks of training on a ballistic task. It would therefore seem that these different parameters measured by TMS do not play a determining role in learning a ballistic task.

In our project, SICI was measured in two different tasks (SICI active and SICI task) to examine its evolution after learning a ballistic task. According to a systematic review and meta-analysis of 11 studies that measured SICI in different kinds of motor tasks and with different experimental designs, SICI should have stayed the same regardless of how it was measured (Berghuis et al., 2017). The results we obtained for SICI active are consistent with this paper, but not for the SICI task, which was significantly lower after learning the ballistic task. The latter result perfectly agrees with those of Taube et al. (2020), who also found a decrease in SICI after ballistic task training when SICI was measured during a (submaximal) ballistic contraction. The change in SICI task, but not SICI active following ballistic task training, could be explained by the same hypothesis as that put forward by Taube et al. (2020): SICI could be modulated in a task-specific manner. It would mean that values change following training of a motor skill only when SICI is measured in a sufficiently similar task. Future studies could define which conditions are necessary to observe a change in SICI following motor learning to understand better the mechanisms influencing intracortical inhibition.

4.3 Strengths and weaknesses

This master thesis contributed to a better understanding of the evolution of parameters measured by the TMS while learning a ballistic motor task. It also tried to provide new knowledge on the evolution of these neurophysiological parameters in case of retrograde interference. If interference had been observed, this study would have been among the first to analyze whether retrograde interference influences SICI. Unfortunately, we failed to observe any interference, although the experimental design was meticulously designed to do so. A revision of the protocol, as well as the measurement of new groups, is needed to access the knowledge initially desired. That is, whether the time interval between initial learning (*A1*) and the retention test (*A2*) is crucial for observing retrograde interference and whether specific neurophysiological parameters evolve differently under interference compared to simple motor learning.

5 Conclusion

This thesis aimed to learn more about the retrograde interference phenomenon and the learning of a ballistic task. We could see that the different parameters measurable with the TMS did not seem particularly relevant to quantify the learning of a ballistic task, except possibly SICI when measured in a task close to the trained one. Indeed, learning the ballistic task had no impact on corticospinal excitability, CSP, rMT, or aMT. SICI active did not change either. Only the SICI task was influenced.

The situation about retrograde interference was more interesting. Science being sometimes difficult to predict, we failed to observe this phenomenon despite careful planning of the experimental protocol. After analysis, it seemed that the SICI task may have prevented interference. It is indeed possible that a generalization phenomenon was observed where it was not expected, i.e., between the SICI task and the ballistic task, which protected the ballistic task from the expected retrograde interference. However, since we did not have the desired control over the results of our project, it is necessary to pursue the experiment with additional groups to understand better what happened. If our future tests confirm what has been argued in the discussion, further studies specific to generalization between two motor tasks will be needed to confirm our results. Hence, it is too premature to draw any clinically applicable conclusions.

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Appendix

Information and consent statement

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INFORMATIONS AUX VOLONTAIRES

Apprentissage et consolidation d'une tâche motrice balistique

Cette étude est organisée par: Prof. Dr. phil. Wolfgang Taube, Université de Fribourg

Madame, Monsieur,

Nous vous proposons de participer à notre projet de recherche, qui s'intéresse à la l'apprentissage d'une tâche motrice balistique. Cette feuille d'information décrit le projet.

1. Objectifs de l'étude

Notre cerveau a la capacité de former de nouveaux contenus de mémoire via de l'entrainement. On distingue deux phases lors de la formation d'un contenu mnésique : l'encodage, au début de l'apprentissage, et la consolidation, qui suit la phase d'encodage et qui nous permet de retrouver des contenus de mémoire longtemps après l'encodage. Ces deux phases seront étudiées dans le cadre de ce projet de recherche.
Plus précisément, cette étude vise à analyser les phases d'encodage et de consolidation de la mémoire motrice lors de l'apprentissage d'une tâche motrice balistique. Des mécanismes d'inhibition, mesurés au sein du cerveau et impliqués dans ces différentes phases, seront également évalués.

2. Sélection des personnes pouvant participer à l'étude

La participation est ouverte à toutes les personnes qui ont entre 18 et 45 ans, qui sont en bonne santé et qui **ne remplissent pas** l'un des critères d'exclusion suivants:

- Personnes ayant consommé de l'alcool dans les 24 heures précédant une session de mesure
- Personnes avec des implants cérébraux ou cochléaires
- Personnes avec un pacemaker
- Personnes avec un trouble neurologique ou psychiatrique diagnostiqué
- Personnes ayant des crises d'épilepsie ou des antécédents familiaux de crise d'épilepsie
- Personnes souffrant/ayant soufferts de lésions cérébrales
- Grossesse

3. Déroulement pour les participant-e-s

En cas de décision de participation à l'étude, chaque participant-e devra se rendre deux fois au laboratoire, avec une journée de repos entre les deux visites. La première session durera environ 2 heures, et la deuxième session environ 1 heure. Au début de la première session, vous devrez répondre au questionnaire reçu avec ce document pour déterminer si vous pouvez participer à l'étude (*Questionnaire d'admissibilité*).
Durant les deux sessions, chaque participant-e devra s'entraîner à la réalisation d'une tâche motrice balistique impliquant les muscles du poignet de la main non-dominante. De plus, divers

paramètres neurophysiologiques seront évalués à l'aide des méthodes de mesure présentées plus loin.

Voici le déroulement lors de la première visite :

- *Questionnaire d'admissibilité*: seuls les participant-e-s admissibles poursuivront le protocole
- Neurostimulation électrique transcutanée du nerf médian, un nerf de l'avant-bras innervant les muscles fléchisseurs du poignet
- Stimulations magnétiques transcrâniennes
- Entraînement de la tâche balistique. Cette tâche consiste à produire une force maximale avec les muscles fléchisseurs de votre poignet, et ce le plus rapidement possible. 35 essais sont effectués, avec 30 s de pause entre chaque essai
- Stimulations magnétiques transcrâniennes
- Fin de la première visite

Voici le déroulement lors de la deuxième visite :

- Neurostimulation électrique transcutanée du nerf médian
- Stimulations magnétiques transcrâniennes
- Entraînement de la tâche balistique
- Fin de la deuxième visite et de l'étude

La tâche motrice balistique sera effectuée sur l'engin de la figure 1.

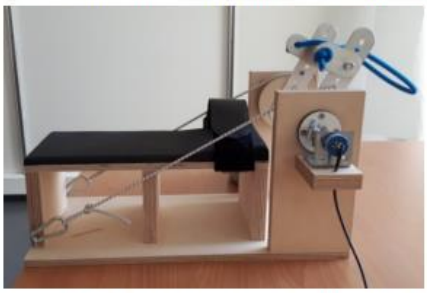

Figure 1. Engin utilisé dans cette étude.

En tant que participant-e, votre **objectif** est d'atteindre la **meilleure performance possible**. Il est donc très important de réaliser chaque **entraînement** avec une **concentration maximale**, afin de **maximiser l'apprentissage de la tâche motrice balistique**.

Présentation des méthodes de mesure :

- Electromyographie de surface (EMG).
  Les muscles, lorsqu'ils se contractent, génèrent une activité électrique. L'EMG de surface est une technique qui permet d'enregistrer cette activité électrique. Pour ce faire, des électrodes sont collées sur la peau, au-dessus du muscle ciblé, et l'activité électrique est enregistrée sur un ordinateur. Afin d'enregistrer un signal de bonne qualité, la peau doit être préparée avant la pose des électrodes. Cela consiste en un rasage, une application d'un gel abrasif et un nettoyage à l'alcool. Cette opération peut éventuellement conduire à des irritations cutanées superficielles. L'EMG est donc une technique non-invasive, pour laquelle il n'existe, à ce jour, aucun effet secondaire connu.

- Stimulation magnétique transcrânienne (SMT).
  La SMT consiste en de très brèves impulsions électriques déchargées au sein d'une bobine de stimulation placée sur la tête, au contact du cuir chevelu. Ces impulsions électriques génèrent un champ magnétique, qui traverse les os du crâne et pénètre dans le tissu cérébral superficiel. À cet endroit, ce champ magnétique génère alors de faibles courants électriques, ce qui permet de stimuler les neurones situés sous la bobine. Lorsque les impulsions de la SMT sont délivrées sur la zone du cerveau responsable de l'exécution des mouvements volontaires, cela provoque une petite contraction musculaire. La SMT est donc une méthode de stimulation cérébrale non-invasive.

- Neurostimulation transcutanée électrique.
  Un système de neurostimulation transcutanée électrique est composé d'une cathode et d'une anode. Ces deux électrodes sont collées sur la peau, à des endroits précis permettant de stimuler un nerf particulier. Pour ce faire, de brefs courants électriques sont émis et circulent de la cathode à l'anode, en passant par les tissus corporels. Ces courants électriques sont alors capables de stimuler les nerfs qu'ils traversent, engendrant une contraction des muscles innervés par ces nerfs. La neurostimulation transcutanée électrique est donc une méthode de stimulation nerveuse non-invasive.

4. Bénéfices pour les participant-e-s

Les participant-e-s ne tireront aucun bénéfice direct de l'étude.

5. Droits du participant / de la participante

Vous devez prendre part à cette étude uniquement selon votre propre volonté. Personne n'est en droit de vous y pousser ou de vous influencer de quelques manières que ce soit. Vous êtes donc libre d'accepter ou de refuser de participer à l'étude, sans justifications. Si vous décidez de participer à l'étude, vous signerez un formulaire de consentement, présent en fin de document. Même après avoir signé ce formulaire, vous restez libre de vous retirer de l'étude à n'importe quel moment, sans donner de raison. Vous n'avez donc pas à justifier vos décisions.
Si vous êtes étudiant ou employé à l'Université de Fribourg, la décision de vous retirer de l'étude ou de ne pas y participer n'a aucune conséquence sur vos études ou sur votre engagement à l'Université.

Vous pouvez à tout moment poser toutes les questions nécessaires au sujet de l'étude. Veuillez vous adresser pour ce faire à la personne indiquée à la fin de la présente feuille d'information.

6. Obligations des participant-e-s

Si vous décidez de participer à l'étude, vous êtes tenus de répondre de façon exacte aux questionnaires. De plus, vous devrez respecter les critères d'exclusion présentés dans ce document, et informer l'équipe de l'étude en cas de changement les concernant.

7. Risques et contraintes pour les participant-e-s

Stimulation magnétique transcrânienne
Bien que la stimulation magnétique transcrânienne soit une procédure de routine dans la pratique clinique, on ne peut pas l'appliquer sur tout le monde. Lors de la considération des conditions de participation, les personnes risquant des effets secondaires sérieux sont exclues (voir les critères d'exclusion au point 2).
En dehors de ces effets secondaires, les stimulations magnétiques transcrâniennes peuvent être accompagnées de maux de têtes passagers. Cela est dû à l'activation de muscles environnant du crâne lors des stimulations.

Neurostimulation électrique transcutanée
Les neurostimulations électriques transcutanées peuvent être inconfortables, voir un peu douloureuses. Ces douleurs disparaissent cependant rapidement. Il n'y a pas d'autres effets néfastes connus liés à cette méthode.

Électromyographie de surface
Hormis les irritations cutanées superficielles qui peuvent survenir dans certains cas, il n'existe, à ce jour, aucun effet secondaire connu pour l'électromyographie de surface.

8. Découvertes

L'investigateur vous avisera pendant l'étude de toute nouvelle découverte susceptible d'influer sur les bénéfices de l'étude ou votre sécurité.
Toute découverte fortuite survenant durant l'étude et pertinente pour votre santé vous sera communiquée.

9. Confidentialité des données

Nous serons amenés, pour les besoins de l'étude, à enregistrer vos données personnelles. Ces données seront toutefois codées. Le codage signifie que toutes les données permettant de vous identifier (nom, date de naissance, etc.) sont remplacées par un code, de sorte que les personnes ne connaissant pas ce code ne peuvent pas lier ces données à votre personne. Vos données sont ainsi traitées de façon anonyme. Au sein de l'Université de Fribourg, seules les personnes autorisées et clairement désignées auront accès à ces données, y compris sous forme non codée. Le code reste en permanence au sein de l'institution.
Toutes les personnes impliquées dans l'étude de quelque manière que ce soit sont tenues au secret professionnel et à une confidentialité absolue. Votre nom n'apparaîtra jamais sur Internet ou dans une publication.

10. Retrait de l'étude

Vous pouvez à tout moment vous retirer du projet si vous le souhaitez. Les données personnelles recueillies jusque-là seront analysées malgré tout.

11. Compensation des participant-e-s

Vous ne recevrez aucune compensation pour la participation à cette étude.

12. Réparation des dommages subis

Les dommages de santé que vous pourriez subir du fait de cette étude relèvent de la responsabilité de l'organisme qui l'a initiée et est en charge de sa réalisation (le promoteur). Les conditions et la procédure sont fixées par la loi.
L'université de Fribourg a conclu une assurance auprès de la compagnie *Bâloise Assurances* (avenue de la Gare 7, 1701 Fribourg) pour être en mesure de réparer les dommages relevant de sa responsabilité. Si vous avez subi un dommage, veuillez vous adresser au promoteur de l'étude.

13. Interlocuteurs

En cas de doute, de craintes ou de questions avant, pendant ou après l'étude, vous pouvez vous adresser à tout moment à l'un des interlocuteurs suivants:

Investigateurs :
Dr. rer. nat. Jan Ruffieux
Université de Fribourg
Section Médecine
Département des Neurosciences et Sciences du Mouvement
Bureau F440
Boulevard de Pérolles 90, 1700 Fribourg, Suisse
Email: jan.ruffieux@unifr.ch
Tél.: +41 26 300 72 62

Matteo Bugnon (doctorant)
Université de Fribourg
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UNIVERSITÉ DE FRIBOURG
UNIVERSITÄT FREIBURG

FACULTY OF SCIENCE AND MEDICINE
Department of neurosciences and movement sciences
Bd de Pérolles 90
1700 Fribourg

Déclaration de consentement

Déclaration de consentement écrite pour la participation à un projet de recherche
Veuillez lire attentivement ce formulaire. N'hésitez pas à poser des questions lorsque vous ne comprenez pas quelque chose ou que vous souhaitez avoir des précisions.

Numéro BASEC de l'étude (après soumission à la commission d'éthique compétente) :	
Titre de l'étude :	Apprentissage et consolidation d'une tâche motrice balistique.
Institution responsable (Promoteur avec adresse complète) :	Université de Fribourg Section Médecine Département des Neurosciences et Sciences du Mouvement Boulevard de Pérolles 90 1700 Fribourg Suisse
Lieu de réalisation de l'étude:	Université de Fribourg
Directeur / directrice de l'étude sur le site (nom et prénom en caractères d'imprimerie):	Prof. Dr. phil. Wolfgang Taube
Participant / participante (nom et prénom en caractères d'imprimerie) : Date de naissance :	☐ femme ☐ homme

- Je déclare avoir été informé, par l'investigateur responsable de cette étude soussigné, oralement et par écrit, des objectifs et du déroulement de l'étude ainsi que des effets présumés, des avantages, des inconvénients possibles et des risques éventuels.
- Je prends part à cette étude de façon volontaire et j'accepte le contenu de la feuille d'information qui m'a été remise sur l'étude précitée. J'ai eu suffisamment de temps pour prendre ma décision.
- J'ai reçu des réponses satisfaisantes aux questions que j'ai posées en relation avec ma participation à l'étude. Je conserve la feuille d'information et reçois une copie de ma déclaration de consentement écrite.
- J'accepte que les spécialistes compétents du promoteur de l'étude et de la Commission d'éthique compétente puissent consulter mes données brutes afin de procéder à des contrôles, à condition toutefois que la confidentialité de ces données soit strictement assurée.
- Je serai informé des découvertes ayant une incidence directe sur ma santé.

- Je peux, à tout moment et sans avoir à me justifier, révoquer mon consentement à participer à l'étude, sans que cela n'ait de répercussion négative. Les données médicales qui ont été recueillies jusque-là seront cependant analysées.
- Je suis informé que la responsabilité civile de l'institution couvre les dommages éventuels que je pourrais subir imputables au projet.
- Je suis conscient que les obligations mentionnées dans la feuille d'information destinée aux participant-e-s doivent être respectées pendant toute la durée de l'étude. La direction de l'étude peut m'en exclure à tout moment dans l'intérêt de ma santé.

Lieu, date	Nom et prénom du participant / de la participante (en caractères d'imprimerie) Signature du participant / de la participante

Attestation de l'investigateur:
Par la présente, j'atteste avoir expliqué au participant / à la participante la nature, l'importance et la portée de l'étude. Je déclare satisfaire à toutes les obligations en relation avec ce projet conformément au droit en vigueur. Si je devais prendre connaissance, à quelque moment que ce soit durant la réalisation du projet, d'éléments susceptibles d'influer sur le consentement du participant / de la participante à prendre part au projet, je m'engage à l'en informer immédiatement.

Lieu, date	Nom et prénom de l'investigateur assurant l'information aux participant-e-s (en caractères d'imprimerie) Signature de l'investigateur

Eligibility questionnaire

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1700 Fribourg

Questionnaire pour la participation à l'étude « *apprentissage et consolidation d'une tâche motrice balistique* »

Le présent questionnaire porte sur diverses questions personnelles qui nous permettront de déterminer si vous pouvez participer à l'étude. **Veuillez s'il vous plaît répondre aux questions de façon exacte**. Vos réponses seront **codées** et traitées de façon **strictement confidentielle**. **Aucune donnée ne sera transmise à des tiers**, et seules les personnes autorisées auront accès à vos réponses.

1) Souffrez-vous/ avez-vous souffert d'une maladie neurologique (exemples: **épilepsie**, Alzheimer,…) et/ ou de lésions cérébrales?

Non ☐ ⋮ Oui ☐

Si oui, laquelle/ lesquelles: _____

2) Souffrez-vous/ avez-vous souffert d'une maladie psychiatrique (exemples: dépression, trouble bipolaire,…)?

Non ☐ ⋮ Oui ☐

Si oui, laquelle/ lesquelles: _____

3) Souffrez-vous/ avez-vous souffert d'une autre maladie?

Non ☐ ⋮ Oui ☐

Si oui, laquelle/ lesquelles: _____

4) Possédez-vous des stimulateurs électriques dans votre corps (pacemakers, électrodes cérébraux, implants cochléaires,…)?

Non ☐ ⋮ Oui ☐

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5) Est-ce que l'un des membres de votre famille a déjà eu dans le passé ou présente actuellement des crises d'épilepsie?

Non ☐ Oui ☐

6) Avez-vous consommé de la drogue, autre que l'alcool, ou des médicaments (y compris les médicaments sans ordonnance) dans les 7 derniers jours?

Non ☐ Oui ☐

Si oui, veuillez nous indiquer de quelle(s) drogue(s)/ de quel(s) médicament(s) il s'agit, ainsi que le jour de la dernière prise: _____

_____

7) Avez-vous consommé de l'alcool dans les dernières 24 heures?

Non ☐ Oui ☐

8) Êtes-vous enceinte?

Non ☐ Oui ☐

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Par ma signature, j'atteste l'exactitude des réponses au présent questionnaire:

Lieu, date	Signature du participant:

Confirmation de l'investigateur:

Lieu, date	Nom et prénom de l'investigateur, en majuscules: Signature de l'investigateur: