Master thesis on Cognitive systems and interactive media

Universitat Pompeu Fabra

Determining the presence of musical rhythmic entrainment in healthy upper limb movements

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Dedication

To my parents, my brother, my supervisor Martina for being quite patient and willing to guide me throughout this thesis, and my friends from the CSIM program who taught me so much in such a short period of time.

Contents

Abstract

A stroke is a traumatizing event that triggers several impairments. Individuals who have withstood it may be disabled to the extend where basic actions in both the realms of fine and gross motor skills are an undertaking. Rehabilitation methods are aplenty, whether they are successful is an ongoing discussion that has ushered the development of novel protocols. Including ones that merge virtual reality and music therapy. In this research, the "Spheroids" motor rehabilitation protocol from the Rehabilitation Gaming System (RGS) was sonified to gauge its effectiveness in healthy individuals. If motor skills in this sample were to be increased, this should translate to patients with hemiparesis. Rhythmic entrainment was the focus of the thesis since anticipation and mental training of movements seem to be a key function in the motor system. Our results showed significance on the level of performance in the subjects who played the sonified version of the game. We concluded that while the developed sound cue may not have been solely responsible for the success in the experimental group, it does shed a light on how pivotal auditory stimuli are in motor skill learning.

Keywords: Entrainment; Rhythm; Virtual Reality; Timing; Neurological Music Therapy; non-specific virtual reality therapy; motor recovery; sonify; electroencephalogram (EEG); rehabilitation gaming system(RGS)

Chapter 1

Introduction

1.1 Problem Statement

Approaches to motor rehabilitation such as the Bobath technique and constraint-induced therapies (CIT) can be quite effective, since important learning principles ranging from verbal feedback, grading of functional task to ones of massed practice are incorporated resulting in a sharp uptick of hemiparetic arm use [Malcolm et al., 2009]. This, however, does not mean these methods suit every patient. In fact, individuals with severe hemiparesis cannot comply to a protocol such as CIT where their healthy arm is being restricted [Schneider et al., 2007]. Additionally, these systems seem to favor overcompensation strategies, since CIT does not appear to be bound by procedures that yield recovery of impairments or **true** neurological repair. Albeit, trials with animals have shown a level of plasticity that promoted protein 43 and synaptophysin; these results remain a debated topic, nonetheless [Kwakkel et al., 2015]. Moreover, the positive of effects of CIT on the Fugl-Meyer assessment scores are well documented within 3 months after stroke [Kwakkel et al., 2015]. Notwithstanding, these results are more predominant among patients with mild to moderate hemiparesis. Likewise, the effects of high dosage of CIT remain nebulous [Kwakkel et al., 2015], hence probably why alternative protocols continue to be explored.

Among additional forms of motor rehabilitation methods, music therapy remains a favored alternative due to its multidisciplinary aspects that address both physical and psychological limitations e.g. facilitating repetitive movements post-stroke and reduction of perceived exertion [Raghavan et al., 2016]. The recovery of movement can be facilitated by neurologic music therapy thanks to the **rhythmic entrainment of motor functions** [Thaut and McIntosh, 2014]. Furthermore, possible neural reorganization (improved activation of the motor cortex and better cortical connectivity) induced by music therapy seems to be an effect patients undergo after following protocols where motor skills are trained through MIDI-pianos and electronic drum pads [Altenmüller et al., 2009]. Unfortunately, similarly to CIT, some rehabilitation sessions seem to be lengthy and bound to patients with no severe hemiparesis [Altenmüller et al., 2009]. The difficulty of carrying instruments, properly handling them, and collecting information about the patient's performance may partly explain this hurdle.

Thankfully, the implementation of these forms of therapies has been expedited due to the rise of virtual and mixed reality technologies. In these environments gathering information about the patient's performance in the task is facilitated [Lehrer et al., 2011a]. Plus audio, visual, and sometimes haptic feedback can be provided to the subject. Simultaneously different forms of existing **task oriented** protocols can be recreated or improved upon through the interface. Whether one of these recovery methods is more effective than the other remains unclear, nevertheless [Lehrer et al., 2011a]. Regardless thereof, defining a clear task is key in upper arm rehabilitation [Lehrer et al., 2011b] and in some forms of virtual reality rehabilitation therapy that has been achieved with **virtual reality music therapy** [Malcolm et al., 2009, Adamovich et al., 2009, Bodak et al., 2014, Russo et al., 2005].

Rehabilitation of upper limbs in virtual environments can involve fine or gross motor skills, and even both depending on the protocol and impairment. A stroke may lead to hemiparesis of the hands, arms, or both limbs. One of the biggest challenges is how this partial paralysis is not static among patients, it may change by affecting more areas of the body and as such treatments should evolve based on the patient's needs [Raghavan et al., 2016]. As a result of this, rehabilitation protocols focus on recovering specific functions such as: reaching (gross motor skill), pronation/supination (fine motor skill), pointing/extension (fine motor skill), and grasping [Mousavi Hondori et al., 2013]. All of these are part of an existing spatial augmented reality systems that focuses on recovering the hand functions [Mousavi Hondori et al., 2013] to allow the patient to perform daily activities such as grasping a mug. Additional systems and environments ranging from a complex virtual reality piano simulator with hand devices providing haptic feedback [Adamovich et al., 2009] to a music glove [Friedman et al., 2011] where a guitar-hero like game is the task the patient should follow to recover finger extension as well as reaching showcase potential. These environments are prime examples where fine motor skills were the most important consideration in the design of the devices.

Rehabilitating the reaching movement of an arm is, however, necessary to perform daily activities as it is recovering fine motor skills [Malcolm et al., 2009]. Protocols such as rhythmic auditory-motor entrainment attempt to improve kinematic reaching in patients by addressing the trunk, elbow, and shoulder tasks on principles of rhythmic auditory stimulation (RAS) [Malcolm et al., 2009]. While the recovery of these movements seems to be debated, a reduction of compensatory strategies in patients suggests a higher likelihood of improved daily life functions [Malcolm et al., 2009]. RAS seems to be mostly effective with gait training and established protocols that rely more on rhythm rather than music e.g. BATRAC, nonetheless. Therefore why exploring other areas where music may yield rehabilitation benefits is encouraged [Schaefer, 2014].

It is noteworthy that the majority of these aforementioned treatments aim to aid the patient with fine motor skills in the hemiparetic upper limb, thus why the tools such as music gloves, pianos or MIDI keyboards have been developed. Concurrently, this unveils a shortage of mixed reality environments solely focused on gross motor skill rehabilitation. Although hand recovery is absolutely pivotal, bearing in mind the role of gross movements is key for a successful rehabilitation process [Malcolm et al., 2009]. This issue may stem from ill-defined music principles that are bound to systems striving to mimic musical instruments, instead of effectively merging existing neurorehabilitation protocols with concepts of neurological music therapy i.e. RAS. As such with this research, we decided to take a step back and gauge the efficacy of RAS without a high dependency on a musical instrument. Instead of developing another system, an existing non-specific VR scenario with gross motor tasks in mind was sonified to induce rhythmic entrainment in healthy subjects. Thereby if results were to be positive or negative, we could gauge the efficacy of RAS. Consequently, this research should yield an insight in:

1. Timing of the patients' movements and the impact of rhythmic cuing in a given gross motor task.
2. Efficacy of rhythmic entrainment in movements that are not inherently rhythmic.
3. Triggered behaviors during rhytmic entrainment.
4. Possible extensions for future virtual instruments and forms of music therapy that may involve the prediction systems in the brain.

1.2 State of the art

1.2.1 Motor recovery after stroke

Life expectancy among stroke survivors has increased in recent years and as such so has the need to development treatments for patients with different forms of impairment, ranging from moderate to severe hemiparesis [Albert and Kesselring, 2012]. Survivors can be impaired to a point where they may be unable to undertake activities of daily living such as picking up a cup or stretching their arm to reach a faraway object. In fact, from 70% to 88% of stroke survivors suffer from some degree of upper limb hemiparesis [Malcolm et al., 2009]. Although very early stroke rehabilitation yields higher functional outcomes in patients, stroke recovery continues being a challenge [Albert and Kesselring, 2012]. Functional rehabilitation consists of a relearning process where neural networks have been unsettled. Motor skill learning in healthy subjects and patients alike is split between **fast and slow learning** processes which are bound to one's ability to retain the new trained skill [Albert and Kesselring, 2012]. Amid the learning process, neural reorganization (or neuroplasticity) is seemingly an active underlying process that significantly improves with several training sessions [Albert and Kesselring, 2012].

Due to such findings in the rehabilitation field, traditional forms of therapy have been steadily improved. Task-oriented tasks hinging upon control training like Brunnstorm or Bobath have been revamped with the advent of technologies. Thereby enabling the development of treatments such as: **neurological music therapy** [Thaut et al., 2015], EMG-triggered neuromuscular electrical stimulation, robot interaction, and **virtual reality** [Albert and Kesselring, 2012]. An ongoing challenge even within this methods, however, is **extensive** training time with some taking up to 4 hours a day to recover the impaired limb, while other forms of therapy such as non-specific VR do not seem as effective as conventional therapy. [Albert and Kesselring, 2012]. With that said, the efficacy of training methods like virtual reality and neurological music therapy continues to be debated in the literature. In the case of the former the issue may not be that the novel methods are inefficient, rather they are relying on ill-defined principles [Maier et al., 2019]. Whereas the latter has shown that music rhythmic entrainment may be effective at recovering upper limb movements [Thaut and McIntosh, 2014].

1.2.2 Principles of motor recovery in VR

While the debate surrounding which principles yield high recovery remains, 11 have been identified as effective at enhancing neural plasticity [Maier et al., 2019]. Among them, the following 6 are predominant in scenarios in virtual reality rehabilitation systems that have yielded positive results [Cameirão et al., 2010].

1. **Massed practice:** number of repetition of movements is increased to improve their quality and retention.

2. **Task specific practice:** movements that are goal oriented, functionally meaningful and relevant for activities of daily living (ADL), i.e. learning is being optimized.

3. **Multisensory stimulation:** centered on restoring sensorimotor contingencies depending on the activities of the patient.

4. **Increasing difficulty:** use of the limb in the task is increased due to individualization of the training via difficulty levels.

5. **Explicit feedback:** knowledge about results is gathered to gauge which movements are better during training by analyzing data such as success rate and accuracy.

6. **Implicit feedback:** kinematic properties such as the limb's movement, its speed, and rotation can be visualized in the system. Thereby reducing the sensorimotor prediction error and promoting learning.

1.2.3 Principles of motor recovery in NMT

Neurological music therapy is not bound to exact principles rather mechanisms that are the foundations for rehabilitation techniques [Thaut et al., 2002]. 18 have been defined and they are utilized to address different disorders e.g. from aphasia to gait training and hemiparesis. In the field of upper motor recovery, it has been argued upper motor movements can be rhythmically cued to facilitate ADL [Thaut et al., 2015]. 2 specific techniques yield this level of **rhythmic entrainment**. These are the following:

1. **Rhythmic auditory stimulation:** used more commonly with movements that are intrinsically rhythmic, e.g. gait, but it has been implemented in protocols like the bilateral arm training with rhythmic auditory cueing (BATRAC) [Whitall et al., 2000].

2. **Pattern sensory enhancement:** dynamic musical patterns are used to cue movements that are not rhythmical by nature into functional movement patterns and sequences.

1.2.4 Music and the brain

Now that we have an overview of the principles behind neurological music therapy, it is key to understand basic concepts that enable it. Chief among them is performance, which involves 3 motor control functions: timing, sequencing, and spatial organization [Zatorre et al., 2007].

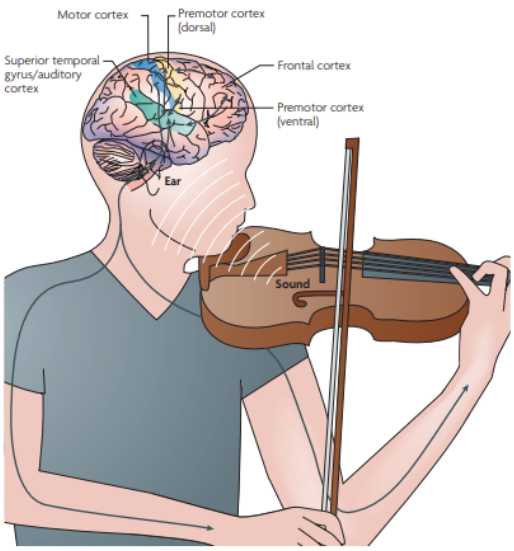

Figure 1: Auditory-motor interactions during musical performance [Zatorre et al., 2007].

Since output signals from premotor cortices may have an impact in the auditory cortex in the absence of sound, motor representations may be active even when the musician is not performing musical activities i.e. merely moving. In fact, a series of **timing systems** are in place due to the ubiquitous presence of *rhythm* in both music perception and performance.

Performing is, notwithstanding, a complex process that intertwines a bevy of areas in the brain depending on the motor timing. The basal ganglia the premotor cortex (PMC), and the supplementary motor area (SMA) seem to be involved in high-level control. On the other hand, the cerebellum seems to steer fine-grain correction of individual movements[Zatorre et al., 2007]. Additionally, as over-learning movements is part of music, the mirror neuron system works in conjunction with the auditory and motor interactions that are unfolding throughout the process [Zatorre et al., 2007, Johansson, 2012]. However, such claim remains contested due to the debate surrounding the existence of the mirror neuron system.

Consequently, it is not shocking to see structural changes in the brain in professional musicians ranging from greater grey-matter concentration in motor cortices, greater volume of auditory cortex, a larger anterior corpus callosum, and greater white matter coherence in the internal capsule [Zatorre et al., 2007]. Said skillset may be transferrable to learning in rehabilitaion [Johansson, 2012], albeit at a much lower rate. In short a level of neuroplasticity may be triggered by performing musical activities, which in turn would lead to recovery of motor skills.

1.2.5 Rhythm and Timing Systems

Voluntary movements have intervals of less that one second and regardless of musical ability, their timing can be consistently repeated. The temporal pattern mechanism seems to originate from different parts of the central nervous system. Namely, the central pattern generators in the spinal cord or in the motor cortex. This timing could also stem from changes in the activity of buildup cells, i.e. preparatory cells increasing their activity before performing a movement [Lewis and Miall, 2003]; albeit the cerebellum plays an important role in timing as well by supplying representations that guide the individual through the pattern. In other words, it is fundamental for pattern recognition of continuous predictable movements [Lewis and Miall, 2003, Ivry et al., 2002] that are habitual in motor rehabilitation. Therefore, relearning may be aided as retention could be arguably improved thanks to the subject being able to recognize the movement patterns.

Rhythm

Organization of rhythm in the brain follows through a subset of timing systems previously discussed. As one of the cornerstones of music, it is not necessarily bound to other elements such as harmonic progressions, melodic movements or structure. Although its definition is not consistent throughout the literature [Thaut et al., 2014], this research will adhere to the following framework of western music to understand what it entails:

1. A tactus or unit of time. That is to say a beat signaling the repetition of identical short duration periods [Thaut et al., 2014].
2. The frequency of said tactus
3. A music meter
4. Rhythmic patterns

Regardless of musical skill, when performing a rhythm pattern (even a simple one) medial, middle, and inferior frontal gyrus show activity linking rhythm to working memory. Moreover, spikes in the middle frontal gyrus, even with a debatable lack of impact on motor planning, may suggest that representing rhythms in a spatial format could be possible [Thaut et al., 2014].

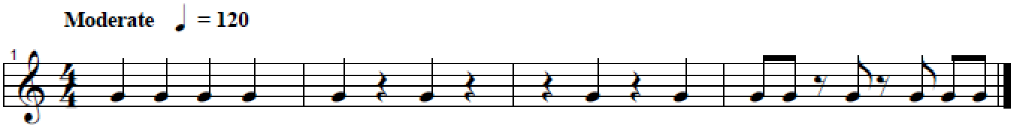

Figure 2: Four bars of basic rhythms in 4/4, the last bar includes syncopated ones that can be performed by beginners and non-musicians.

Rhythm entrainment

Rhythmic stimuli such as a metronome can guide arm and finger movements, which remain locked despite changes to the tempo that cannot be consciously perceived

[Thaut et al., 2015]. This phenomenon can be replicated with patients who have suffered a stroke since "the injured brain can indeed access rhythmic entrainment mechanisms." [Thaut et al., 2015]. By adhering to the bilateral arm training with rhythmic cuing (BATRAC) protocol[Whitall et al., 2000], patients can follow the rhythm to reach (and retrieve) actions while being cued with a metronome.

Advantages	**How are they triggered?**
Repetition	Motor system is conditioned to a beat.
Movements match sounds	Goals and expectations are set.
Implicit and explicit feedback	Audio and visual cues inform the patient

Table 1: Strengths of the BATRAC protocol [Whitall et al., 2000]

The presence of auditory-motor pathways that impact the excitability of motor neurons through reticulospinal connections underpin priming effect on the segmental motor system resulting from auditory inputs [Thaut and McIntosh, 2014]. The aforementioned effect could be therefore potentially be used (and in fact it has been used) as a timing effect of muscle activation patterns [Thaut and McIntosh, 2014].

Put it differently, motor relearning is not out of the patient's reach and can be achieved in less time than conventional therapy or other forms of rehabilitation such as CIMT [Whitall et al., 2000]. This normalization of hemiparetic arm movements can even be rapidly translated to daily activities [Malcolm et al., 2009]. Optimal motor routines during rehabilitation suggest that positive long-term effects may be more predominant, however thanks to the priming of movements. Mostly stemming from improvements on motor skill acquisition and consolidation [Thaut et al., 2002].

1.2.6 NMT in virtual reality systems

Despite the advantages of neurological music therapy, gathering kinematic data and the unwieldy nature of musical instruments remain steep challenges for patients with severe hemiparesis. Not to mention that some of the principles/mechanisms behind neurological music therapy may be ill-defined as it tends to be tethered to devices.

As a result of this, virtual reality systems implementing neurological music therapy techniques have become more predominant. Unfortunately, certain ones are designed with the expectation the patient is familiar with music, or in other cases, movements may not be operational enough for recovery [Lehrer et al., 2011a], therefore, interfering with the patient's implicit learning.

On the other hand, the immediate effect of percussion based systems (drum kits) where timing is key in tasks involving extension and extension exercises has been detected [Yoo, 2013]. Furthermore, the overall efficacy of certain systems on fine motor skills is, short-term, remarkable [Friedman et al., 2011, Mousavi Hondori et al., 2013, Adamovich et al., 2009]. Such systems strive to improve finger extension and fine motor skills by simulating a piano; or movements akin to ones used by a pianist [Bodak et al., 2014, Russo et al., 2005, Fischer et al., 2007, Regenbrecht et al., 2011].

When the principles utilized in the system are well defined, the effects can be more remarkable. The music glove expands upon principles of timing by including flexing of fingers that are necessary for daily activities such as holding a cup of tea. Visual feedback is incorporated into the system by informing the patient when they have accurately flexed their finger, but learning of the exact movements occurs a priori.

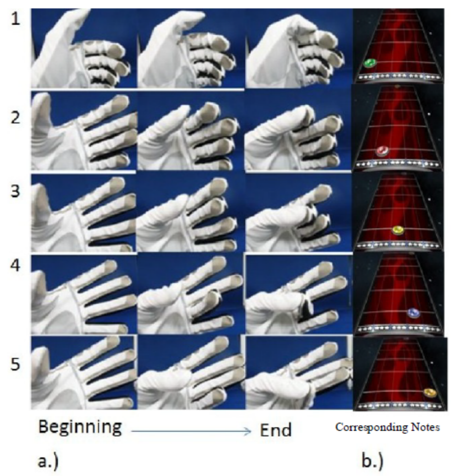

Figure 3: The five hand movements trained using MusicGlove [Friedman et al., 2011].

On the flip side, while Adamovich et al.'s virtual piano showcases a fascinating proof of concept (accurate haptic feedback per finger playing a key), it seems unwieldy for patients. In fact the authors have acknowledged that although improvements were not marginal during training sessions [Adamovich et al., 2009]. Concurrently systems that attempt different rehabilitation methods have employed electric drum pads to focus on both gross and fine motor skills [Schneider et al., 2010]. Exactly how motor skill principles are implemented in the training sessions remains unclear, however. Immediate effects should not be a benchmark, when learning over time is not being taken into account in the aforementioned systems.

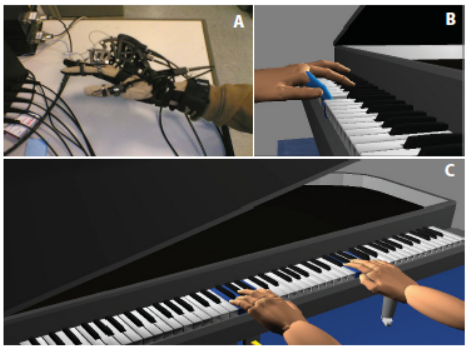

Figure 4: Virtual Piano Trainer [Adamovich et al., 2009].

It's pivotal to recall that not all feedback scenarios in virtual reality systems can effectively communicate information to the patient, despite how diverse the different forms of feedback may be [Lehrer et al., 2011b]. Additionally, excessive feedback may backfire as the subject may overly rely on it to perform well during the task [Lehrer et al., 2011a]. Rehabilitation systems should encourage understanding of the task to facilitate learning of the motor task while fostering independent detection [Lehrer et al., 2011a]. Optimizing amount of feedback should be part of the design as it is adapting the difficulty. This would allow for an individualization of learning of the motor task [Cameirão et al., 2010]. Therefore a neurological music therapy system that is not shackled by the issues hereto presented may be a better fit in motor recovery. Following the music glove example, adapting an ADL motion in a rehabilitation scenario while implementing principles of music therapy may bypass issues that systems like the virtual piano have faced.

1.2.7 Rehabilitation Gaming System

An existing rehabilitation framework that relies on the principles of motor recovery in VR section is the rehabilitation gaming system (RGS). It has yielded sustained improvements over a training period in the early stages after a stroke e.g. patients at "Hospital de L'Esperança" in Barcelona, Spain where it has been deployed [Cameirão et al., 2009]. Additionally, it could be argued that it simultaneously addresses the inherent issues of some protocols in music therapy, since it is not bound to a specific instrument or music task that may be overly esoteric for stroke patients and non-musicians. Moreover, the RGS lacks a "sonified" scenario or one that encourages rhythmic entrainment. By blending such principles from both motor recovery in VR and music therapy, a powerful rehabilitation tool may be devised to further improve existing recovery methods.

Figure 5: Basic setup of the RGS system [Cameirão et al., 2009].

One of the biggest advantages of the RGS is the protocols follow the previously defined principles. Training can be individualized as the difficulty is adaptable, it is task oriented, massed practice is part of said tasks, and forms of explicit as well as implicit feedback are present [Cameirão et al., 2010]. Furthermore, akin to mixed reality systems that rely on virtual music instruments, the RGS encourages for bimanual task oriented tasks in the environment to facilitate the reorganization of systems damaged by the stroke. To induce a stronger activation of sensory motor control areas, the system relies on a first person view where the limbs are clearly represented and they follow the patient's movement [Cameirão et al., 2010]. In other words, the RGS is exploiting the action execution and action observation paradigm to train specific motor skills via the systematic presentation of virtual limbs on the screen (visual feedback). The absence of such representation may not induce the same level of activation in the primary and secondary motor areas

[Cameirão et al., 2010].

New scenarios can be crafted in the system to cater to every user's needs. Even healthy users may become more proficient at complex tasks [Cameirão et al., 2010]. By extension, the feedback in the system may enhance cortical changes associated with motor learning and thus aiding the user to acquire new motor skills.

Chapter 2

Methods

2.1 Research question

As the literature has revealed, rhythmic entrainment may be a powerful tool in motor skill learning. Therefore, we ponder whether sonifying an established scenario in the RGS, namely "Spheroids", and adapting it to healthy participants may lead to an increase of motor skills.

2.2 Hypothesis

Due to the principles of rhythmic auditory stimulation (RAS), a music rhythm task oriented protocol in the rehabilitation gaming system (RGS) will increase the gross motor skills (uppper limb movement) of healthy young adults compared to ones who have not gone through rhythmic entrainment in a virtual environment or have not had any musical training whatsoever.

2.3 General Methodology Applied

The experiment was based on the "Spheroids" protocol from the RGS, wherein users must catch spheres to gain points. Spheres may spawn on the left or right (Figure 6.), encouraging the subject to train both upper limbs

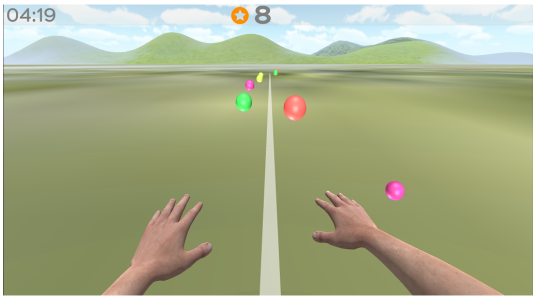

Figure 6: Spheroids: Custom version only relies on one limb

Throughout the game bonus spheres and bombs (false positives) may spawn. The spawning time of objects in-game occurs, however, during *sphere sequences*. Put it differently, different waves of spheres are generated during the training but these do not happen at the same time. Rather each spawns 10 spheres including bonus ones and sometimes false positives, thereafter a cool-off period occurs and then the next sphere wave is generated. All of the arm movements in the task involve horizontal unilateral arm movement in the x and z axes.

To sonify this protocol and avoid providing excessive feedback to the subject, various sound effects from the original game were removed and several pulses were added to incite rhythmic entrainment when spheres would come at the subject. The NMT principle that was employed in the RGS was the RAS since under it, variance in movement can be reduced, its speed may be increased, and the trajectory can be smoothed out [Thaut et al., 2002] when auditory-rhythmic cues are constraining the reaching movements of the hemiparetic arm [Malcolm et al., 2009]. By enhancing motor control, RAS is a principle that can be employed in the proposed task to improve the motor skills of unimpaired individuals.

Literature shows that music therapy tasks tend to hinge upon *standard instruments* such as keyboards or drum pads [Altenmüller et al., 2009]. However, protocols with unconventional "instruments" where rhythm bound tasks are part of the paradigm have shown potential to increase motor skills, e.g. Friedman et al.'s *Music Glove* [Friedman et al., 2011]. As such no instrument will be implemented in the spheroids protocol.

Finally an additional condition will be incorporated where the screen goes black during training. If subjects are entrained, they should then outperform the control group, especially when no visual feedback is present as the control group is not being rhythmically entrained whatsoever.

2.4 Design and development criteria

Learning occurs overtime, therefore the motor task was not performed only during one training session, rather 2 split in 2 different days. As such the spheroids protocol was modified for both training sessions accordingly. To ensure explicit and implicit feedback are part of the scenario, the RGS human limbs as well as kinematic data gathering system have remained untouched. Since rhythm entrainment will be gauged with an electroencephalogram (EEG) [Besle et al., 2009], the system was also modified to only be played with one limb. Therefore the EEG signal would not be further disturbed by other motions and additional movement artifacts would be hopefully bypassed. Simultaneously, the pulse chosen for the task in the experimental group is randomly selected in an array with 3 different sounds (guitar strum, piano melody, and a metronome beat)

2.5 Experimental design and setup

2.5.1 Experimental design

The experiment consists of two training sessions split in two different days. The participants will be split in two groups, an experimental and control group. The former will have the added condition of the sonified game, whereas the latter will not have any sonification whatsoever. Moreover, an added condition is introduced towards the end of training, namely the screen going black and subjects playing the game only with audio feedback. Each training session lasts 20 minutes with 5 minute breaks every 10 minutes.

2.5.2 Measurement tools

To gauge rhythmic entrainment, we did not solely hinge upon success rate or performance throughout the training, the wireless EEG cap Enobio 32 was used to measure entrainment in the brain. It was connected via an ad hoc network to a separate computer with a sampling rate of 500 Hz and the standard 10-20 system montage via the official software NIC2 - Neuroelectronics. The different channels were recorded with LabRecorder (official recording program that comes with the labstreaminglayer system for the collection of time series measurements). This ad hoc network was also linked to the main device where subjects played the sonified version "spheroids". The in-game events and arm movements (kinematic data) were linked to LabRecorder as well and the ad hoc network, then subsequently recorded during training.

2.5.3 Virtual Environment setup

Since the protocol Spheroids from the RGS was utilized, the Unity version for this project was 3.4, as such the custom made Spheroids was also built in Unity 3.4. The RGS has different tracking devices depending on the scenario. Spheroids' motion track is done with the Kinect sensor V2, ergo subjects have 6 degrees of freedom (DoF) per limb. Besides position, rotation may be tracked. However, since such action is not part of the game, it was not recorded with LabRecorder. Mapping of the arms is 1:1 thanks to trackers (Figure 7) the subject wears during the training.

Figure 7: Trackers placed on both limbs. The arms rest on the table before the game starts

2.5.4 Upper motor limb task

The custom spheroids motor task consists of catching as many spheres as possible before time runs out. Subjects participated in 2 sessions each one lasting 20 minutes in total with 5 minute breaks after 10 minutes of training. These cool-off periods were introduced for healthy participants since individuals during demo runs reported reported growing tired, which in turn could have influenced their performance in-game. Finally, as previously stated, during the last 5 minutes of the game during the last training session, the screen goes black.

Certain elements from spheroids were, nonetheless, kept intact. For instance, each sphere spawns between every 0.5 and 2.75 seconds. This is bound to the following formula "2.75f - 2.15f * adc" where the variable adc stands for the difficulty modulator value from the RGS. Such value changes based on the performance of the subject and it's carried out for any following training. Additionally, map dispersion respect to the middle line was not altered. Spheres may spawn 0.3 meters from the middle line or in a range from 0.2 meters to 0.6 meters from the middle line.

On the other hand, both speed and size of each spheroid were modified to increase the default difficulty. Since speed increases as a parabola, the default speed of 1.2 meters per second and 2.5 meters per second were increased to 8.5 meters per second and 9.2 meters per second respectively. Since the default radii of the spheroids was either 0.25 meters and 0.10 meters, only the highest value of 0.25 was reduced to 0.20.

More importantly, the motor task is cued by a **pulse** selected from an array with 3 sound files: guitar strum, piano melody, and a beat from a metronome. To ensure participants were not overly stimulated during training the following sound cues were removed: environmental music, the bonus sphere sound, and sound effects attached to the false positives (bombs). Hits, misses, and the sound effect that plays when a sphere wave is generated were not deleted but they were turned down.

The pulse does not play at any time during the game. Rather when the game starts, it is randomly selected from the array and the pitch is altered based on the difference between the position of the arm and the spheroid. The further away the arm is from the spheroid, the higher pitched the pulse will be. The closer it is, it will be lower. The pulse only plays once per spheroid to cue the subject where to place the arm or which position will be the most favorable to earn the highest amount of points. Naturally, the pulse does not play when false positives are generated since the in-game hit boxes detect is a bomb.

2.6 Procedures used to obtain data and results

2.6.1 Pre-experimental setup

This procedure took about 10 minutes per participant. Firstly, they had to fill out a consent form and the first part of filtering questionnaire where we gathered qualitative data and filtered out subjects who were not suitable for the experiment. Specifically the **exclusion criteria** were individuals who had suffered from a stroke or were physically impaired and professional musicians. The latter criterion was deemed crucial to avoid subjects who would greatly outperform the rest of the sample. The questionnaire included demographic data as well, such as gender, age, and subject's dominant arm.

Thereafter, a randomizer (randomizer.org) was used to place the subject in either the control or experimental group and select which arm would the participant use during both training sessions. Additionally, the subject's arms (Figure 8) were placed at the corners of the table to facilitate tracking. Due to the design of the game, the unused arm had to remain motionless on the table.

Henceforth, the subject had to put on the Enobio 32. This procedure took between 20 to 30 minutes per participant since dry electrodes had to be placed on the subject's scalp and they had to be connected to the Enobio's wireless communicator.

Figure 8: Subject's arms positioned to be tracked by the kinect.

2.6.2 Experimental procedure

Since entrainment is being gauged with EEG, it's important to record baselines to reduce noise per channel [Besle et al., 2009]. Thus, 6 minute baselines were recorded for every subject regardless of whether they were part of the experimental or control group. During the 3 first minutes participants had to remain with their eyes shut, after that they had to stare at the screen for another 3 minutes.

Following the recording of baselines, subjects would play the sonified version of Spheroids. On day 1, the control group would attempt to gather points by catching the spheres for 10 minutes followed by a 5 minute break and this was capped off by another 10 minutes of training. On day 2, the scenario for the control group remained the same, except in the last 5 minutes of training the visual feedback was removed.

On the other hand, the experimental group had the added condition of the **pulse** that was randomly selected after recording the baselines and before the sphere spawning coroutine would start. Training time for the experimental group on both days was the same as well as the condition of the screen boing black, except that the pulse remained playing when no visual feedback was provided.

2.6.3 Post-experimental procedure

After training was done on the second day, participants would finalize filling out the questionnaire. Final questions consisted on gauging their performance in the game, rhythmic skills, and whether the **pulse** was helpful during training.

Chapter 3

Results

3.1 Demographic Data

10 subjects partook in this experiment and were split in two groups: experimental and control. There were in total 7 women and 3 men who participated in this study with an average age of 27, a standard deviation of 6.03 and a median of 25. Although 50% of the subjects had to use their right hand and the other half the left, 8 participants were right-handed while 2 were left-handed.

3.2 Data analysis

Before juxtaposing the groups, normality for the gathered data in both control and experimental groups was tested using the Shapiro-Wilk test. Unsurprisingly the data was not normally distributed, perhaps as a result of the sample size. We used non-parametric tests to gauge the whether the data gathered was significant. Namely, Mann-Whitney to compare the experimental and control groups, and Wilcoxon to juxtapose the overall training during day 1 and 2. Since we have 4 groups in total (experimental group training session 1 and 2 and control group training session 1 and 2) and there are no two way mixed Anova, we used the Scheirer-Ray-Hare test (https://github.com/jpinzonc/Scheirer-Ray-Hare-Test) which is an extension of the one way Kruskal-Wallis when measures are affected by more than 1 factor.

Due to the number of conditions and amount of over testing, 2 different training sessions and 2 groups, the Bonferroni correction was taken into account. In this experiment that means that we needed a p value lower than 0.0125 (0.05/number of conditions) to have significant results. Although the small sample size proved to be an issue when testing success rate, this was not a hurdle when comparing speed and distance between populations as they had to be normalized.

Before delving into the results of the limb's speed during training, it is key to understand that due to the inherent design behind the game "Spheroids", higher speed and more area covered (distance) do not equate to entrainment or better performance. Subjects may rely on strategies where movements are slower to reach areas where spheres would spawn. Normalization of speed and distance covered during the experiment meant eliminating the cool-off periods as well as breaks during the experiment to effectively calculate the values. Otherwise, if the distance were to be calculated without said step, the data would not be significant ($P>.0125$).

3.2.1 Experimental Performance: Speed and Distance

Throughout the experiment, the success rates of both control and experimental groups were calculated by recording number of spheres hit per training session. Additionally, the x-position of the arms used during the experiment were stored to calculate both speed and distance covered during the motor task.

During session 1, the overall median of the distance covered was 35 centimeters and on day 2 said value was 26 centimeters (Figure 9). We have found that the difference between area covered in session 1 vs. session 2 is statistically significant ($P<.0125$).

Additionally we looked at the distance covered in the experimental (Figure 10) and control (Figure 11) groups separately. Both differences yielded statistical significant results ($P<.0125$).

We can see that the experimental group covered less area during training in both days compared to the control group; albeit one outlier is visible on the second day of training in the experimental group. Unfortunately, when checking for significance between the 4 datasets with the Kruskal-Wallis' Scheirer-Ray-Hare extension, significance was not able to be determined as a custom 2x2 Mixed Anova perhaps may be more suitable to gauging these results (Figure 12).

Similarly to the results gathered on distance covered, speed throughout training reveals that stagnation or slower movements yielded the better results. This is reflected in the overall difference of speed between session 1 and 2 (Figure 13.), as well as the speed during training sessions of the experimental group (Figure 14.)

Alas, even after normalization, these results were not significant with the Bonferroni correction ($P>.0125$). Even so, it is interesting to see that the group which better performed moved less than the control subjects.

3.2.2 Success rate

Although, according to the Shapiro-Wilk test the control group's success rate is normally distributed, this was not the case for the experimental group. Regardless thereof, the success rates between both groups greatly differ, with the experimental group having a median success rate of 54.76% whereas the control group had one of 30.7% (Figure 15). Such difference was found to be statistically significant ($P<.0125$).

3.2.3 EEG

Before pre-processing the data we plotted the raw signals of both groups. The baseline correction for both groups was processed as the mean of the signal gathered during the 6 minutes before the experiment started. Although the raw power spectra between groups seemed to be quite similar below the 40Hz frequency, the experimental group showed higher activity above the 40Hz threshold and below 50Hz (Figure 16), specifically on the frontal and right temporal lobes.

When removing artifacts such as eye movements, we could see that the auditory stimuli in the experimental group were affecting the occipital lobe; even when the main visual feedback was removed during training. On the other hand, under the same conditions, the occipital lobe in the control group did not show spikes in activity (Figure 17).

3.3 Graphs and plots

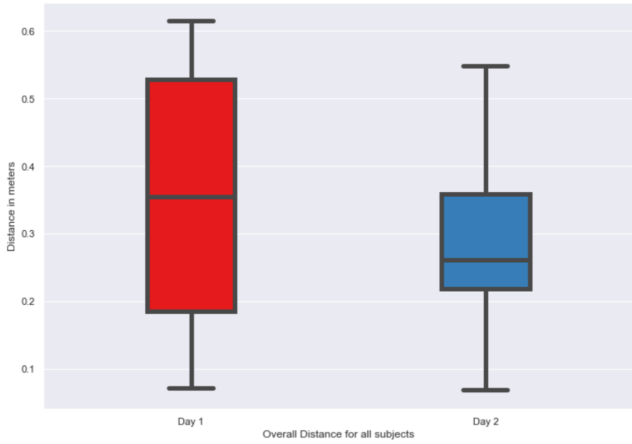

Figure 9: Overall distance covered in day 1 vs day 2

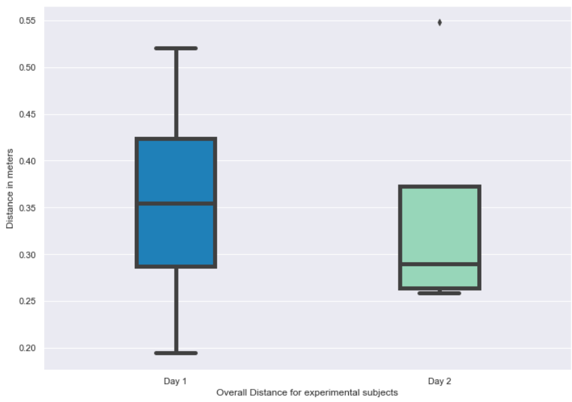

Figure 10: Experimental group distance covered in day 1 vs day 2

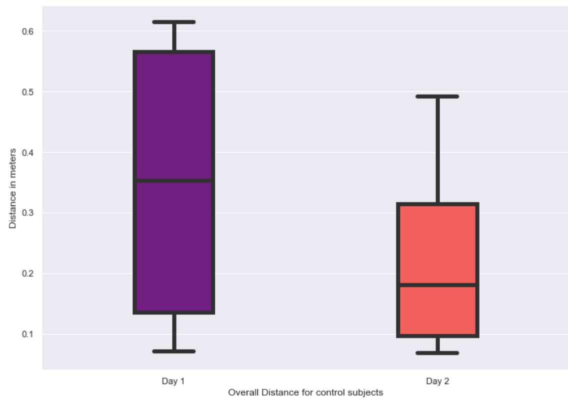

Figure 11: Control group distance covered in day 1 vs day 2

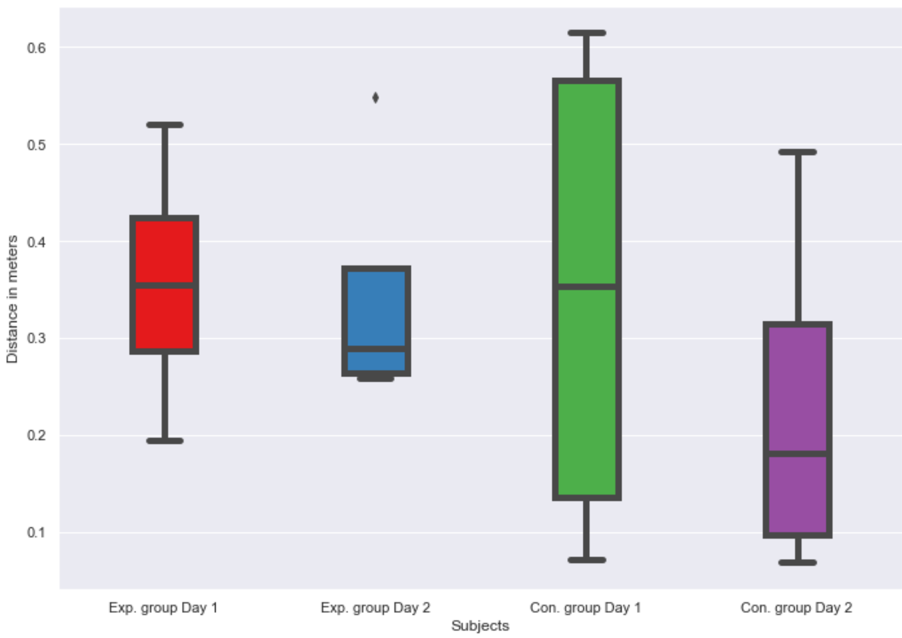

Figure 12: Distance covered between all groups

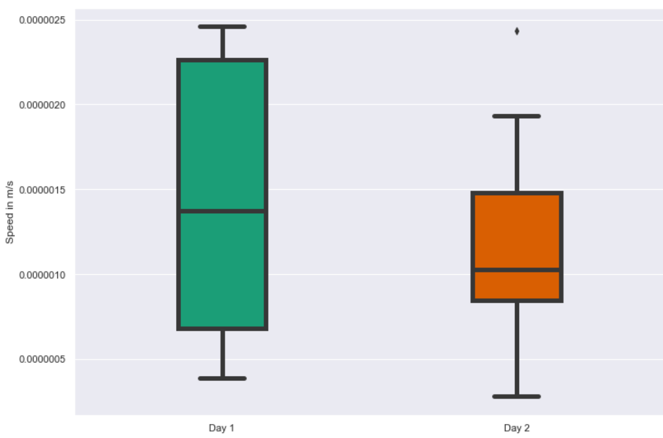

Figure 13: Overall speed in day 1 vs day 2

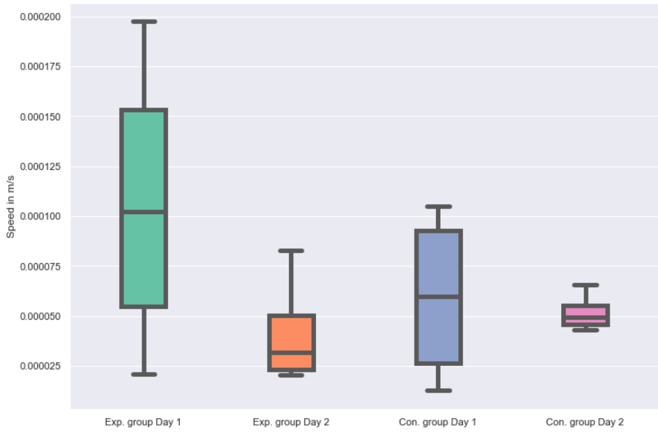

Figure 14: Speed during training across all groups

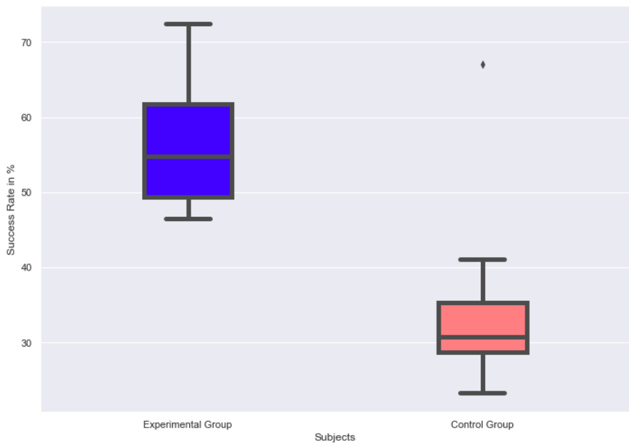

Figure 15: Success rate between groups

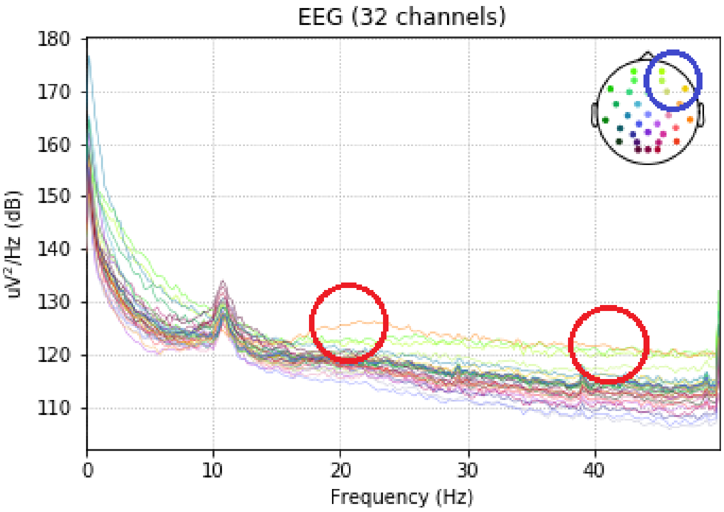

Figure 16: Spectra of activity. Right frontal channels show higher activity

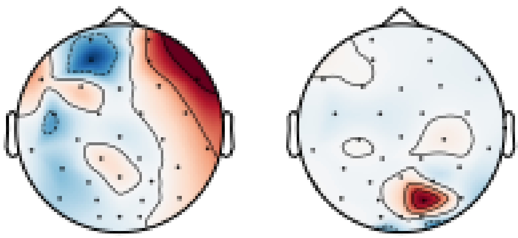

Figure 17: Activity in the occipital lobe during training (Control group)

Chapter 4

Discussion and Conclusions

The goal of this study was to merge principles of motor rehabilitation in virtual reality (task specific practice, multisensory stimulation, increasing difficulty, explicit and implicit feedback) with principles of neurological music therapy, namely rhythmic entrainment. As previously stated, the literature has claimed movements can be rhythmically guided by a pulse and as such participants whose actions are cued would perform better at motor tasks than subjects who would not. In other words, a level of **entrainment** should be visible in the brain during the task explaining the better performance of the experimental group. To achieve this goal, the virtual reality rehabilitation scenario **spheroids** from the rehabilitation gaming system was sonified and customized to be more challenging. The latter was an aspect carried over for both control and experimental groups since participants were healthy individuals.

To ensure whether learning was present during the task, movements over time during the training were compared. Specifically between the final sequence of spheres and the first. Recall that in the game "spheroids" different sequences of spheres are spawned throughout the game. Although performance during the first wave was similar between groups, in the last sequence, the experimental group displayed a higher success rate.

The results of the qualitative data may explain certain outliers (Figures 10, 12 and, 13). Subjects who claimed to have high level rhythmic skills and who have also partaken in VR experiences were part of the group with the outliers.

Even though, it may seem performance as well as the success rate corroborate our hypothesis, a challenge remains; whether the **pulse** was responsible for improving the prediction system before performing the motor activity. After removing artifacts, we could detect in the experimental group isolated activity in the central lobe (C3 and C4 channels). In fact, one of them showed simultaneous activity in the auditory system (T8) and the central lobe (Figure 18)

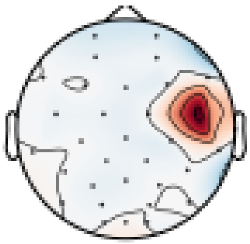

Figure 18: Activity in the central and right temporal lobes

When mapping the stimuli channel (events during the experiment) we get a different picture, notwithstanding. Auditory stimuli, from the pulse to the hit and missed sounds, were responsible for the results gathered.

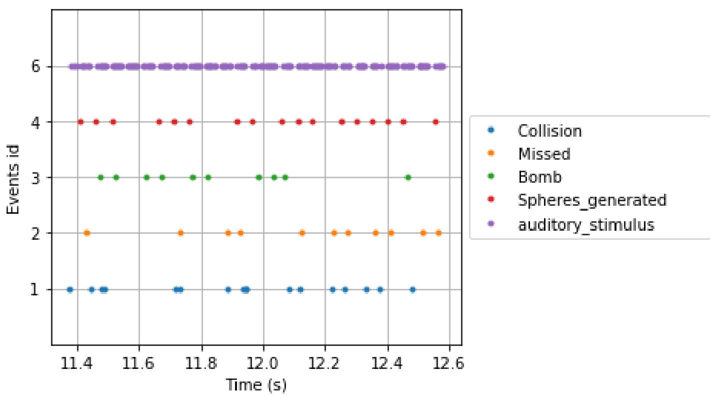

Figure 19: Events during a segment of the training (Exp. subject)

Recall that in the Spheroids game, the time between spawning of spheres was not customized. Although it is possible that our experiment supports our hypothesis, the results have may been modified by additional predictions the subjects made during training. Namely, timing between co-routines of spheres and spawning of said objects. Admittedly, we can see that said predictions when the screen went black may not be accurate following the spawning of a sphere (Figure 19.). It is worthwhile mentioning, nevertheless, how in intervals of 0.2 seconds, between 2 to 3 spheres are created regardless of the presence of the pulse (Figures 19 and 20.)

On the other hand (Figure 20.), the control group subjects shows a higher number of misses when no pulse is present. This correlates with the qualitative data where 100% of the subjects acknowledged the importance of audio cues when training.

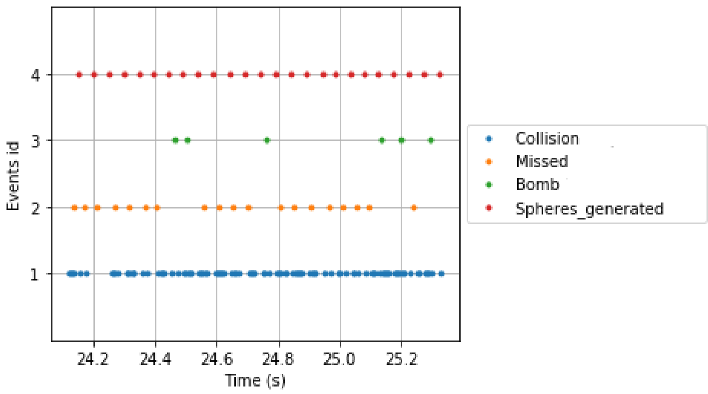

Figure 20: Events during a segment of the training (Control. subject)

Having said that, what further challenges the notion of whether the pulse was solely responsible is that the stimuli channel recorded the events of the pulse and hits in one array (Figure 19). This remained the main challenge throughout the study, pinpointing the stimuli in charge of the improved prediction system.

4.1 Validity of the results

We found significance when gauging area covered during the experiment as well as in the success rate. Through EEG we corroborated said data, however, the significance of the brain activity and of the speed of the limbs throughout the study remain contended.

4.2 Relevance with respect to state of the art

In the state of the art, the overly reliance on real and virtual musical instruments was discussed as a flaw in current NMT. Despite certain shortcomings, our study does underpin the notion of applying NMT mechanisms such as rhythmic entrainment without the need of an instrument. While it was stated that some principles in NMT may be ill-defined, under the correct principles of motor recovery, NMT and specifically rhythmic entrainment can be effective. At the very least in the form of several auditory stimuli.

4.3 Conclusions and future steps

Throughout this study, we have discussed the validity of rhythmic entrainment when training upper limb motor skills. We strove to argue that merging principles of NMT and non-specific virtual reality therapy would be the most accurate way to test this. In order to achieve this, the RGS protocol "Spheroids" was customized and sonified to adapt it to healthy participants. Besides the kinematic data gathered, we also recorded brain activity (EEG) throughout the experiment to gauge entrainment.

Although training with the condition of auditory stimuli yielded better results, fully measuring actual entrainment was not fully achieved. Looking at the event related potential components in the most active channels is a step that should be taken to further this research. The significant data does lend some credence to the interaction between the auditory cortex and motor system to predict when one should move a limb; even if said limb does not follow an inherently rhythmic pattern.

Additionally, while movements did heavily stagnate in the experimental group during the last minutes of training (displaying some learning), this does not fully reflect on the quality of the movement or whether they are functional. Of course the goal of the study was not to train movements to be more functional, but it is worth discussing. After all, this study could be a stepping stone in further developing forms of therapy for ADL. Besides, thanks to the success rate, accuracy of movements in a sonified form of therapy was gauged and it was significant, as expected.

Akin to systems relying on simple motor skills to learn[Mousavi Hondori et al., 2013], our system shows that less heavy-handed solutions may be more efficient in motor skill learning. No doubt virtual pianos with haptic feedback [Adamovich et al., 2009] are worth further developing, especially since under the right principles a VR system may yield a high degree of success [Maier et al., 2019]. Nevertheless, it is important to recall how severe the hemiparesis the patient is facing is and as such to develop systems accordingly.

Finally, it would be interesting to further sonify protocols in the RGS or develop separate ones. Not only with the goal of testing rhythm entrainment, but other NMT principles and mechanisms that could improve forms of therapy tackling disorders like aphasia. Regarding the current study, a replication should be pursued. Especially one where muscle activity can be recorded (electromyography). Employing EMG for a replication or in addition to EEG would better address the question of rhythmic entrainment and enable better future development of "sonified" virtual reality forms of therapy.

List of Figures

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