UNIVERSIDAD SAN FRANCISCO DE QUITO USFQ

Colegio de Ciencias Sociales y Humanidades

Spatial Music in Neurorehabilitation

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Psicología

Trabajo de fin de carrera presentado como requisito
para la obtención del título de
Licenciado en Psicología

Quito, 02 de Mayo de 2023

UNIVERSIDAD SAN FRANCISCO DE QUITO USFQ

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HOJA DE CALIFICACIÓN
DE TRABAJO DE FIN DE CARRERA

Spatial Music in Neurorehabilitation

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Quito, 02 de Mayo de 2023

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Lugar y fecha: Quito, 02 de Mayo del 2023

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RESUMEN

El ictus es la tercera causa de discapacidad y la segunda causa de muerte en todo el mundo. Los sobrevivientes muestran un mayor riesgo de sufrir un segundo accidente cerebrovascular y de desarrollar depresión y demencia (Johnson et al., 2016). La OMS informa que durante los últimos 40 años los países de ingresos bajos y medios, como Ecuador, muestran un aumento en la incidencia de accidentes cerebrovasculares y, por tanto, más sobrevivientes de accidentes cerebrovasculares con discapacidades cognitivas que necesitan (neuro) rehabilitación (Johnson et al., 2016). La negligencia espacial unilateral, resultado de daño cerebral unilateral, es la incapacidad de detectar, responder y orientarse hacia estímulos en el lado del espacio contralateral a la lesión cerebral (Schenke et al., 2021). Se ha demostrado que escuchar música con señalización espacial auditiva reduce significativamente la gravedad de la negligencia y es potencial complemento en su neurorrehabilitación (Kaufmann et al., 2022). Este estudio pretende desarrollar una estimulación cognitiva que mejore los síntomas de la negligencia a través de la música, que pueda ser utilizada en la etapa aguda y post-aguda de pacientes con accidente cerebrovascular y que pueda ser fácilmente aplicable en un entorno hospitalario o doméstico para la población ecuatoriana. Se desarrollarán dos pruebas auditivas experimentales y una estimulación cognitiva, la cuál deriva la música de un oído al otro. Primero se realizará una prueba piloto en personas sin negligencia hemiespacial para evaluar varios aspectos del ensayo clínico. En este último, los síntomas de los pacientes con ictus serán evaluados antes y después de la estimulación para medir el efecto de la misma. La estimulación cognitiva consiste en que los pacientes escuchen (a través de audífonos) y traten de seguir una deriva auditiva de izquierda a derecha implementada en su música favorita.

Palabras clave: negligencia espacial, estímulo auditivo, estimulación cognitiva, neurorrehabilitación basada en música.

ABSTRACT

Stroke is the third leading cause of disability and the second leading cause of death worldwide. Stroke survivors show higher risk in having a second stroke and developing (post stroke) depression and dementia (Johnson et al., 2016). The World Health Organization reports that during the last 40 years low and middle income countries, like Ecuador, show an increased number in stroke incidence and therefore a higher number of stroke survivors with cognitive impairments with needs of (neuro) rehabilitation (Johnson et al., 2016). Unilateral spatial neglect, from unilateral brain damage, is the inability to detect, respond to and orient towards stimuli on the side of space contralateral to the brain injury (Schenke et al., 2020). Furthermore, it's been shown that listening to music with auditory spatial cueing significantly reduces neglect severity and could be used as a supplement in neglect neurorehabilitation (Kaufmann et al., 2022). This study intends to develop a cognitive stimulation that can improve symptoms of neglect through music, that is suitable to be used in the acute and post-acute stage of stroke patients, and that can be easily applicable in a hospital setting or a domestic setting for the Ecuadorian population. Two experimental auditory tests and the mentioned cognitive stimulation, that drifts the music from one ear to the other one, will be developed. They will be tested in people without hemispatial neglect first for evaluating different aspects of the clinical trial. In the clinical trial, the stroke patients' symptoms will be assessed (with the line bisection test, the apple test and the clock test, besides the two experimental auditory tests made by the team) before and after the stimulation to measure its effect. This cognitive stimulation consists in the patient listening (through headphones) and trying to follow an auditory drift from right to left implemented into their preferred music.

Key words: spatial neglect, auditory cueing, cognitive stimulation, music-based neurorehabilitation

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Introducción

1. Introduction

1.1. Justification

Stroke is the third leading cause of disability and the second leading cause of death worldwide; moreover, stroke survivors show higher risk in having a second stroke and in developing (post stroke) depression and dementia (Johnson et al., 2016). The World Health organization reports that during the last 40 years low and middle income countries, like Ecuador, show increased stroke incidence and therefore a higher number of stroke survivors with cognitive impairments needing (neuro) rehabilitation (Johnson et al., 2016). In Ecuador, adequate neurorehabilitation is very limited. Most often, stroke survivors are stabilized in the hospital without receiving any specific neurorehabilitation and are discharged back home to their relatives, who do most of the care (and are not experienced or trained to work with the population suffering from such a complex condition) (Turgut, personal communication, December 12, 2022). This underlines the urgent need for a neurorehabilitation method that is easy to implement in the clinical routine, applicable from home, affordable and effective. Of all unilateral stroke survivors, 30% are estimated to present hemispatial neglect and show impairments in spatial attention after unilateral hemispheric damage (Esposito et al., 2021). Neglect is one syndrome affecting selective attention. A person with neglect perceives as if their complete world is shifted, most often resulting in ignoring any person or object on the side of space contralateral to the injury (Kerkhoff & Schenk, 2012). In their daily life, these patients will show difficulties completing simple tasks; very common examples of their impairments are putting on a t-shirt and just covering half of their body, eating only one half of the plate without realizing it, grooming only one side of their face and constantly bumping into walls and objects (Li & Malhotra, 2015). Even when receiving general neurorehabilitation, the outcome after leaving the hospital is significantly worse than in

stroke survivors without neglect (Kerkhoff & Schenk, 2012), so a specific neurorehabilitation is needed.

It's been shown that listening to music with auditory spatial cueing significantly reduces neglect severity and could be used as a supplement in neglect neurorehabilitation (Kaufmann et al., 2022). The cognitive stimulation proposed in this research is a cognitive stimulation that consists in a spatial drift in music, to be played through headphones. This movement comprises a drift from the functional side of attention to the one that suffers from neglect. Important features that make this neurorehabilitation software attractive for therapy and research are the following:

1. The music can be adjusted to the preference of the stroke survivor, which improves motivation and engagement to the product

2. Direction, presence and speed of the spatial drift can be adjusted easily

3. Priorly mentioned features enable a patient-oriented protocol based on the severity of the stroke survivor

This cognitive stimulation will have several potential benefits to the stroke patients using it. Music has a motivating, stress-reducing effect in clinical and everyday life settings, if the listener has control over the selection of the music played (Chanda & Levitin, 2013; Linnemann et al., 2015). As already proposed with methods that use visual cues, effective treatment should aim to be individually adjustable depending on the severity of spatial impairment. The goal of this method of neurorehabilitation is that the impairment reduces over time and therefore less cueing might be necessary to enable independent attention to the space (Turgut et al., 2018). To the teams' knowledge, no existing neurorehabilitation device that uses auditory spatial drift also includes an adjustment of direction, presence and speed.

Research has shown that treatment development in spatial impairments can be combined with existing treatment strategies and/or daily life activities (Kerkhoff & Schenk, 2012). The cognitive stimulation proposed in this research could be easily combined with existing visual or sensory stimulation methods (e.g. optokinetic drift or neck muscle vibration), physiotherapy or daily life activities (e.g. eating, reading, etc). Currently, there are different methods targeting an hemispheric balance using transcranial direct current stimulation (Tdcs), transcranial magnetic stimulation (TMS) and others (Kerkhoff & Schenk, 2012). However, the problem with neurorehabilitation devices utilizing current or magnetic stimulation is that they are not suitable for stroke survivors who have had damages to the skull or a craniectomy, therefore excluding a large population. This study's cognitive stimulation ideally will be a stimulation method that doesn't have any harming effects on cognition. This method is easy to implement in the clinical routine, but can also be effortlessly used from the patient's home. Moreover, because of its nature it would be quite accessible, benefiting a wide range of the target population.

1.2. Background Literature

Unilateral spatial neglect, a result from unilateral brain damage, is the inability to detect, respond to and orient towards stimuli on the side of space contralateral to the brain injury (Schenke et al., 2021). Addressing neglect is important during rehabilitation, as it's been associated with prolonged inpatient stays, reduced autonomy in daily activities and a reduced quality of life (Schenke et al., 2021).

Additionally, music therapy has been shown to reduce neglect severity and presenting auditory stimuli might improve hemispatial neglect at least temporarily, given that visual perception of neglect patients is modulated by the auditory clues' spatial position. It's also been found that using meaningful auditory cues could increase the stimulation effectiveness

(Schenke et al., 2021). While this type of stimulation has shown a reduction on egocentric neglect severity after repetitive auditory cueing stimulation in both severely and moderately impaired patients, further research is needed on dynamic auditory cueing (Schenke et al., 2021). Furthermore, it's been shown that listening to music with auditory spatial cueing significantly reduces neglect severity and could be used as a supplement in neglect neurorehabilitation (Kaufmann et al., 2022).

On the other hand, when investigating the effects of listening to classical music on neglect, it was found that there is an advantage of classical music over white noise and silence. This is an intervention based on bottom-up mechanisms for neglect that involve using sensory stimulation to improve visual attention on the neglect side (Tsai et al., 2013). Moreover, sounds have shown to be effective when reducing spatial neglect by increasing arousal (having auditory stimulation during or immediately before a spatial task) and improving mood (listening to preferred music improves spatial performance by having an increased positive effect and engaging the mesolimbic dopaminergic reward system) (Bernardi et al., 2015).

There is also prior research indicating that music-based stimulation for this type of disorder should be effective. Recovery from stroke-induced attention deficits has been shown through inter-hemispheric connectivity, which can be induced through listening to music (Bartolomeo, 2022). Bartolomeo (2022) suggests that connectivity patterns within and between the hemispheres are a major determinant of individual differences in recovery from attention and language deficits, inter-hemispheric connectivity is critical for shifting the role of the healthy hemisphere, from competition to cooperation with the lesioned hemisphere, and that listening to music can help reconnect brain regions isolated by the stroke, within and across the hemispheres. Listening to music should improve cognitive recovery and, at the

same time, increase values of neuroimaging indexes of brain connectivity. Finally, Turgut et al. (2018) have shown evidence that this type of adaptive cueing in a reading task improves neglect symptoms when applied in an intensive intervention of 3 weeks.

1.3 Objectives

General Objective:

Create and evaluate a type of cognitive stimulation that improves symptoms of hemispatial neglect through music, is suitable to be used in the acute and post-acute stage of stroke patients, and can be easily applicable in a hospital setting or a domestic setting for the Ecuadorian population.

Specific Objectives:

- Subjects' (stroke survivors') improvement of symptoms of spatial neglect by combination of spatial drift with music.
- Subjects' improvement in the line bisection test, clock test and apple test.
- Subjects' improvement in experimental auditory tests.

2. Methodology

The following study is under revision of the ethics committee.

2.1. Stimuli and experimental auditory tests development

Both the stimuli and the experimental auditory tests were recorded and developed in the digital audio workstation (or DAW) Pro Tools 12 by Ariel Alarcón, who has an undergraduate degree in Music Production.

2.1.1. First experimental auditory test

The first experimental auditory test (or Five Point Randomizer) consisted on a one minute track that contains several C4 piano notes that play every five seconds. These piano notes would be randomly panned (panning is the placement of the audio on the perceived sound field of the listener's headphones or speakers on an stereo or multichannel track) either complete left, complete right, medium left, medium right, or middle; in total, there were 5 possible positions the piano note would appear from (thus, the name of the experimental auditory test).

A lot of sounds were discussed and tested until finally a C4 piano note was chosen. The reason why has to do with both the simplicity and the familiarity of the C4 piano note. During testing, it was found that more complicated sounds rather obstructed the process, since it took attention away from performing the task correctly. A simple piano note is not distracting and the instrument used is, to some degree, familiar to most people. Lastly, the C4 note was chosen because of its frequency, given that older adults tend to have hearing problems at high frequencies (2 khz and up) (Salorio-Corbetto et al., 2017). So, a note with

rather middle-low frequencies (C4 frequency is of 261.6 Hz) is mostly in the clear; C4 or middle C (since on an standar 88-key piano, C4 would be the C in the middle) is a safe choice that ensures most people would be able to distinct the sound and where it's coming from.

After deciding that a C4 piano note would be the most appropriate sound for the first experimental auditory test, its development consisted in recording the note through MIDI in DAW Pro Tools 12. Once it was recorded in the length and velocity necessary, five channels were created and each was assigned a panning position correspondent to one of the five positions (complete left, complete right, medium left, medium right, or middle). To randomize, each position was given a number, and Research Randomized (https://www.randomizer.org/) was used to get a random set of numbers that would include all of the positions. Then, according to the numbers obtained, a note was implemented on the corresponding channel every 6 seconds. Lastly, the minute used from the session was bounced to mp3 and wav audio file formats.

The objective of the test is for the user to identify where the sound is coming from. Depending on where they hear the sound, they write down on a piece of paper where they hear it (right, middle or left).

2.1.2. Second experimental auditory test

The second experimental auditory test (or Sound Field experimental auditory test) consisted in a single note that plays in the same velocity without decreasing in volume from the complete right panning position of the right channel to the complete left panning position of the left channel. This note was obtained from Free Sound (https://freesound.org), a sound effect library with audio samples licensed under Creative Commons (a license that allows the free use of distribution of creative works under certain conditions). The reason a piano note

could not be used in this test is that any real or MIDI instrument will have either a decay or an increase in intensity as the note is being held.

Once the sound was chosen, it was implemented into a stereo track, where it underwent a panning automatization process that would steadily move the panning position of the channel from complete left to complete right in a time span of 20 seconds, giving the auditory effect of the sound moving or drifting from one side to the other. The time span of 20 seconds was based on Kaufman's (2022) study, in which the auditory cueing moved at a speed of 9 degrees per second (or 20 seconds from the complete right to the complete left). This study was also the foundation for the chosen time span in cognitive stimulation.

The objective of this test is for the user to identify where the auditory middle is. In this instance, the middle is the position where both the left and right channel are panned to the middle, creating a "mono" sound image (monophonic sound means there is only one channel instead of two, so there is no dimensional sound field and everything is perceived to be sounding in the exact front).

2.1.3. Cognitive Stimulation

For the stimulation, the more complicated part was undoubtedly the research. Since some benefits of the stimulation have to do with the patient listening to their preferred music, the sample of the stimulation had to include a set of songs recognizable and/or enjoyed by the elderly ecuadorian population (since, although the inclusion criteria for age comprises anyone older than 18 years old, patients that have suffered a stroke and display attentional problems are likely going to be of senior age). Even though for each patient there is going to be an effort from both the hospital and the team to find out the preferred music of the patient to use it in the cueing for the clinical trial, the study needed a sample cognitive stimulation of at least

20 minutes for piloting and backup in case utilizing the preferred music of the patient would not be possible.

Based on the authors' knowledge as a musical producer, several genres where discussed (focusing on genres instead of specific songs not only covered more ground, but made it more likely for patients to be familiar to some degree with the music on the stimulation), before doing a short informal survey among relatives to narrow down the genres to what most elderly ecuadorians would be acquainted with and/or enjoy. Finally, the genres chosen were pasillo, cumbia, salsa and bolero. A couple of songs (the most popular ones from 1960 to 1980) from each genre were selected to be included in the stimulation.

Once the music was chosen, each song was implemented into a stereo track, where it underwent a panning automatization that would steadily move the panning position of the channel from complete left to complete right in a time span of 20 seconds, giving the auditory effect of the sound moving or drifting from one side to the other. Once the song reached the complete left, it was automated back to its starting position, and the process repeated itself for as long as each song would last, for every song, for a total of 6 songs.

2.2. Pilot Study on Unaffected Population:

2.2.1 Study type

Experimental study

2.2.2. Pilot Study Design

To ensure that the auditory drift stimuli was appropriate before presenting them to students, a pilot study will be conducted on healthy people inside the USFQ community. Both the experimental auditory test and the cognitive stimulation, which drifts the music from one

ear to the other one, will be tested in this section. This part of the study aims to detect any problem with the intervention planned (if headphones and comfortable, the instructions are clear, the volume is appropriate, they are able to perceive the drift in the stimulation and the experimental auditory test, etc.) and implement the feedback before performing the cognitive stimulation on the clinical trial.

2.2.3. Definition of the Universe and details of the sample size calculation:

Since there isn't enough previous data to make a sample size calculation, it was instead based on previous literature. It is worth mentioning that, as this was not a trial on clinical population, there was a level of leniency in the calculation of the sample. Neither Schenke (2021) nor Kaufman (2022) had a healthy population group, so it was decided to use the historical control group of the study conducted by Schenke (2021) as a reference. The historical control group had 14 people, so this study will double that amount, benefiting from the availability of USFQ undergraduate students, which could represent a big portion of the subjects for this part of the study. The sample size of this part of the study will be of 20 to 30 people based on previous conducted study.

2.2.4. Inclusion criteria:

Patients must be at least 18 years old and in good health condition to participate in this section of the study. As priorly mentioned, this part of the study is not done in a clinical population, so there is no need to look for specific attributes in the subjects as long as they are healthy adults that can be awake during the intervention.

2.2.5. Exclusion criteria:

Stroke survivors of the right hemispheric lesion if impairment in spatial attention is shown and subjects with any auditory impairment or severe psychiatric symptoms will not be

able to participate in this study. The purpose of this piloting would not be achieved if subjects had the condition, as that would make them affected population. Also, there is a need for the feedback that the subjects will provide the study with to be in some measure accurate, which won't be possible if the subjects have hearing problems or severe psychiatric symptoms.

2.2.6. Variables to be analyzed during the investigation:

Since the purpose of this study is mainly to evaluate the aspects of the intervention, there will not be an effect in the symptomatology of the subject (since they will have no symptoms, otherwise they wouldn't have participated in this section of the study in the first place). Instead, the focus here will be put into detecting and evaluating potential issues that could occur due to oversight before the clinical trial.

2.2.7. Procedures:

The study will be explained in more detail at the research facility and Ariel Alarcón will make sure the participants understand it - either by asking them questions related to the stimulation or by asking them to repeat what the process consists of - before asking them to sign the informed consent document.

Between 20 and 30 subjects from the non-affected population, most likely students, will undergo two experimental auditory tests and a cognitive stimulation.

The first experimental auditory test consists of auditory cues (a piano note) that sounds on either the left or right side of the headphones randomly. The subject must determine where the sound cue is coming from. Since this part of the experiment is performed on a non-affected population, there should not be any mistake in their assessment of where the sound is coming from.

The second experimental auditory test consists of an auditory cue traveling from left to right. The subject is asked to assess when the sound is in the center of their soundfield or "in front" of the subject. When the sound is on what the subjects consider the middle, they will ask the experimenter to stop the moving cue. The level of neglect will be measured in relation to the azimuth position of the sound's panning at the moment of the stop (the angular measure of spherical coordinates systems; in this case, measurement of the panning in the spherical auditory field). Since this part of the experiment is performed on a non-affected population, the perceived middle should be fairly close to the actual middle.

Then, the cognitive stimulation will be presented to evaluate if they can also correctly and easily follow the movement of the music. All the feedback collected from this intervention will be implemented in the clinical trial with the affected population. For both the experimental auditory tests and the stimulation, the person responsible for the tasks and the recollection of data is Ariel Alarcón, supervised by Dr. Nergiz Turgut and Dr. Sol Garces.

2.3. Affected Population:

2.3.1. Study type

Experimental controlled study.

2.3.2. Study Design

After the feedback from the previous section of the study is implemented in the stimuli, the study will move on to the clinical trial. Here, stroke patients will be assessed before and after the stimulation to measure its effects. The exact duration of the experiment will be determined depending on the stay of the patient, but subjects will be receiving a minimum of 5 days of stimulation (one week) and a maximum of 10 days of stimulation (two weeks). The activity for them consists of trying to follow the drift.

2.3.1 Definition of the Universe and details of the sample size calculation:

The study oriented its sample size to previous literature. Kaufman (2022), in their spatial cueing in neglect study, had 9 subjects on the intervention group of her first experiment, and 12 subjects on her second experiment. Schenke had a similarly populated intervention group, with 11 subjects on the first experiments and 10 subjects on her second experiment. Based on this information, this study will have a sample size of 11 people.

2.3.4. Inclusion criteria

In order to participate in this section of the study, subjects must be unilateral stroke survivors with a large right hemispheric brain lesion, show impairment in spatial attention, in addition to having minimum 18 years old and being capable of being awake for at least 20 minutes during the stimulation.

2.3.5. Exclusion criteria:

There are several types of stroke survivors that will not be able to participate in this study. Stroke survivors with left hemispheric brain lesion, stroke survivors without impairment in spatial attention, stroke survivors with lesions on both hemispheres, stroke survivors previously diagnosed with dementia, stroke survivors with aphasia, stroke survivors with severe psychiatric symptoms, stroke survivors in minimal responsive state/coma, stroke survivors which develop hydrocephalus are not part of the study, since the listed circumstances make it so the condition they present (whereas this factors construct a more complicated clinical profile, or just a different one) is not the condition this stimulation is tailored to. Lastly, stroke survivors that fulfill the inclusion criteria but with attention/vigilance capacity lower than 20 min will not be able to participate in the study, since they can not undergo the cognitive stimulation.

2.3.6. Variables to be analyzed during the investigation:

When a stroke survivor is included, they receive an assessment at baseline including an evaluation of body posture, the Line Bisection Test, the Clock Test, the Apple Test, and the aforementioned experimental auditory test. After baseline testing is completed, the intervention group will receive a minimum of 5 days and a maximum of 10 of stimulation. Before the stroke survivor is discharged from the stroke unit, hospital staff (trained psychologist or medical doctor) will assess spatial attention using the same procedure as in Baseline.

2.3.7. Procedures:

The study will be explained in more detail in the hospital on the intervention day and Ariel Alarcón will make sure the participants understand it - either by asking them questions related to the stimulation or by asking them to repeat what the process consists of - before asking them to sign the informed consent document.

First, the subjects will be assessed using the mentioned assessments. Then, they will receive the stimulation, consisting of music that drifts from the right to the left. They will try to follow said drift to the best of their abilities. The exact duration of the experiment will be determined (it may vary depending on the stay of the patient), but subjects will be receiving a minimum of 5 days of treatment (one week) and a maximum of 10 days of treatment (two weeks). After said period, another assessment will be made. Since the sample size is small and the impairment is pretty serious, a control group wouldn't make much sense. Moreover, the study has a controlled condition to compare pre and post cognition assessment.

In the hospital, disinfectable over-ear headphones with disposable earpad covers are going to be used for hygienic reasons. To test the cognitive stimulation, the involvement of

hospitals treating severe right hemispheric lesions is needed. For this, the team will be working on the stroke unit of Hospital Eugenio Espejo. The person of contact is Felipe Romero, who will also communicate with the team if a patient fulfills the inclusion criteria and also wants to participate. The stimulation will be conducted in the subject's hospital room, putting effort in scheduling the procedure in a way that does not inconvenience the patient, as the intervention aims to be as less intrusive as possible. Also, possible collaborators are the hospital Bremen-Ost in Germany for data collection and University of Oldenburg for support in data analysis and with whom Nergiz Turgut has been working together for many years on various research projects. Ariel Alarcón is involved in a sampling process but another research assistant will be searched for assistance in this step.

2.4. Timetable

Table 1. Activity Timetable

Activity Timetable																	
ACTIVITY DESCRIPTION	January 2023	February 2023	March 2023	April 2023	May 2023	June 2023	July 2023	August 2023	September 2023	October 2023	November 2023	December 2023	January 2024	February 2024	March 2024	April 2024	May 2024
Preparation																	
Drafting and ethical approval																	
Creation of spatial audio drift																	
Healthy population feedback																	
Data sampling Healthy population feedback																	
Data analysis Feedback																	
Patient evaluation																	
Pilot patient																	
Data sampling Prototype																	
Data analysis																	
Thesis																	
Thesis creation																	
Alumni research assistance																	
Publication process																	
Manuscript creation																	
Revision process																	

Conclusiones

3. Discussion

3.1. Ecuador’s Situation

The expected results are an increase of hemispatial attention and a reduction of the severity of the symptoms of the subjects with neglect. If the effects are substantial, the stimulation could become a relevant form of treatment for the condition in Ecuador. This research is the first neurorehabilitation study that targets spatial impairments after right hemispheric stroke that uses auditory cueing in the country and, as such, if the results prove significant, there will be a lot of potential for future neurorehabilitation methods for people with this condition.

Besides the effectiveness of the stimulation (which can not be measured yet, while still on the “feedback from working population phase"), it would be comfortable and accessible to its users. These factors are quite relevant for the Ecuadorian culture; while stated earlier, most people left with spatial attention problems after a stroke are usually not given any type of cognitive stimulation and, after a couple of weeks, they are just sent home. While in their home, it will be their family who turn into their carers and, unfortunately, they are not suited to deal with a condition such as hemispatial neglect.

One of the problems for the family will be the complexity of the condition. The (standard) cognitive stimulation that is necessary to manage hemispatial neglect is not going to be present in the homes of the people affected by it. If the country's sanitary conditions do not allow for health professionals to be trained in neglect neurorehabilitation, there is even less prospect of the patient’s family to figure out (or even be aware of) what they could do to improve their loved one’s condition. This is the reason that the accessibility of this study’s

cognitive stimulation is so relevant. Any cognitive stimulation suitable to the context of Ecuador must be comfortable to operate by the patients and/or their carers in order to successfully reach the majority of the population.

Another important obstacle is anosognosia. For being a condition with such debilitating symptomatology, the effects of neglect are really difficult to explain to someone else. Additionally, hemispatial neglect is debatably harder to recognize within oneself; anosognosia, or the condition in which the patient is not aware of their neurological deficits, is quite prevalent among people with neglect (Grattan et al., 2017). Because it seems their limited attention cannot perceive the lack of perception on the affected side, they mostly do not recognize their neurological limitations, despite symptoms. Neglect patients will often not attribute abnormal behavior (such as complaining) to their hemispatial neglect. This, of course, will have a profound impact on their mood and irritability, since the ramifications of the condition in accompaniment to the overall confusion and frustration of not completely understanding their symptoms will often cause them to be ill tempered towards their carers.

Agnosognosia not only hinders rehabilitation, but makes it difficult to keep patients motivated in classical cue-based cognitive stimulations. That is why playing music the patient likes is so promising for this study's cognitive stimulation. As previously stated, listening to preferred music improves mood, increases arousal and has a positive effect in the mesolimbic dopaminergic reward system (Bernardi et al., 2015), which would make the stimulation have the advantage of more motivated, receptive and engaged patients, improving the overall effectiveness of the auditory drift cues.

Lastly, another important issue Ecuadorians face is that their medical attention is limited by money. Ecuador is a low income system where the state of the sanitary conditions are determined by the quality and accommodations that the public healthcare system can

provide, since most cannot afford expensive interventions in the private sector. In 2020, 74% of Ecuador's emergency cases were admitted in the public sector, while 5.2% of them were admitted in private non-profit organizations and only 20.4% of them were admitted in the paid private sector (INEC, 2020). As established earlier, the current practice of the public healthcare system to manage neglect is not doing anything about it, which is seldom the best strategy. Therefore, any cognitive stimulation that aims to aid Ecuadorians neglect patients must consider that the average patient will not be too keen in spending a lot of money for it, even in the case that they can afford it. That is why the study's cognitive stimulation affordability is relevant for the clinical picture of the country. Furthermore, if its effectiveness (should it be effective) catches the attention of public urgent care units, the fact that it is affordable would make the implementation of the cognitive stimulation in these hospitals an easier process.

3.2. Limitations

Limiting factors include the level of disposition and tiredness of the subjects at the time of the stimulation, since that could tamper its objective effects. As previously stated, motivation will be of paramount importance, since it has a significant effect in how accurately the subject tries to do the task for the stimulation, and their overall mood will have a salient effect on the outcome of the auditory spatial cueing. Thus, the betterment of symptoms will be closely related to how compelled the person is to undergo the cognitive stimulation. While music (especially preferred music) shows promise of improving both mood and motivation, it would be naive to solely rely on it to maintain their disposition (or lack thereof), especially since there are other factors (such the adequate or not volume of the headphones, the correct functioning of the stimulation, how long the setup takes, whether the instructions are confusing or clear, whether the subject is annoyed or irritated by having

people performing studies on them in their hospital room, etc.) that will definitely have an impact on the overall result.

This study's approach to minimize the impact of these limitations was to do a trial stimulation in Hospital Eugenio Espejo. Thanks to the collaboration of Felipe Romero, the team was able to go to the hospital to get familiarized with both the installations and the procedure. They also got the opportunity of doing a pilot experimental auditory test and cognitive stimulation on a patient that was staying on the stroke unit, but did not have hemispatial neglect nor hemispatial attentional problems. While the subjects on the clinical trial are likely to differ moderately in both capacity and disposition, the enactment of the procedure was incredibly useful to plan out the administration of the experimental auditory test and the cognitive stimulation in the clinical trial. While doing this trial session, multiple aspects of the limitations were taken into consideration. Prior to this visit, there was some concern of how eager to do the tasks the patients were going to be and how they were going to respond to strangers coming into their room to do experiments on them. As mentioned earlier, it was of the utmost importance to diminish as much as possible any effect a bad predisposition from them could have on the study. Luckily, the patient that participated in our test run lessened our concerns regarding this topic. They were really welcoming and interested in the project. According to Felipe, this will not be uncommon; when people get admitted into the hospital for stroke, they have to spend their entire day inside the hospital and visiting hours is only a fraction of the time they have to spend there. Therefore, they will spend a lot of their time inside their room alone. On that account, our trial's run subject behaved in a way that we can assume will be similar (in general terms, meaning the patient will probably not be in a bad mood, irritable or unmotivated in our account) to the patients that will undergo the auditory spatial cueing on the cognitive stimulation in the clinical trial.

Our trial's run subject provided the team with a lot of useful feedback; thanks to the information gathered in the session, the team could determine the appropriate default level of the headphones, track volume problems in both of the experimental auditory tests, fix some confusing explanations in the presentation of the assessments and informed consent, and got validation of the type of music chosen for the elderly population (the categories were cumbias, pasillos, boleros and salsa, all of which were enjoyed by the patient, who was already somewhat familiarized with all of the songs, going as far as to sing some).

Another limitation is that this cognitive stimulation would only yield results for egocentric hemispatial neglect, not for allocentric hemispatial neglect. The difference between the two of them is that people with egocentric neglect fail to perceive one side of space in reference to their own body midline, while people with allocentric neglect fail to perceive one side of space of an object in focus. Since the symptoms of allocentric neglect are not related to the attentional field of the person, this stimulation will not be suited for them, since the auditory cueing is designed to stimulate precisely that type of attention.

3.3. Next steps

During this paper's writing, there was a significant decrease in the hours dedicated to polishing the experimental auditory test and the cognitive stimulation. As soon as this paper is done, the revision of the auditory stimuli based on the feedback obtained in the trial-run visit will resume.

The immediate next step after getting approved by the Ethics Committee would be to start the piloting of the non-affected population, in the manner established in the 2.2. Non-Affected Population Methodology section. There is expected to be further refinement of the auditory cueing from the feedback obtained in the piloting.

After the approval of the ethics committee, the team will let Felipe know that from that point onwards he can contact it everytime someone who fits the description and wants to participate is available. Ideally, Felipe will let the team know about the preferred music of the patient on the initial call, so there will be enough time to implement it in the cognitive stimulation. Otherwise, the model cognitive stimulation will be used. The intervention will be performed as described in 2.3. Affected Population Methodology.

3.4. Future directions

The future directions foreseen are first and foremost the combining of the auditory cueing with other treatment methods, like mainstream visual cognitive stimulations. Schenke's (2021) studies provide strong evidence that there is a lot of potential in combining these two cueing types, since the visual perception of patients with neglect is modulated by the spatial position of auditory cues and it has been found that the use of meaningful auditory cues could increase the effectiveness of stimulation. Also, consider how Tsai (2013) findings show that the use of auditory stimulation based intervention (in that case, the passive hearing of classical music) improves visual attention, and how the study of Bernardi et al (2015) suggests that the hearing of preferred music also improves the patient's mood. Therefore, it would be only natural for the next step to integrate this method to other effective treatments. Besides the satisfactory results in the betterment of symptoms this study aims for, the scientific literature strongly suggests that the mere use of this stimulation, while performing other types of treatment, could significantly affect the outcome of each session, as patients would have improved attention and better mood while performing the tasks the intervention asks for.

For that reason, the next discussed addition to the cognitive stimulation would consist in a video that would mimic the sound of the current intervention to help the patients follow

the sound more accurately. The basic idea is that an object (i.e. a ball) would drift simultaneously along the sound of the auditory cueing, moving its position from right to left based on the azimuth of the auditory stimulation at that point in time. This could stimulate the visual element of the condition and potentially even help the patient follow the displacing sound more easily (when explaining sound panning to regular population, a technique often used is to utilize a visual cue to simulate the motion from the complete right azimuth position of the right channel to the complete left azimuth position of the left channel).

However, the next step for the intervention is to develop an app that lets the user perform the auditory cognitive stimulations for themselves or ones in their care. While the development part of the app is on hold until the project yields satisfactory results, a quick rundown of the elements the app developing would need includes a programer in charge of designing the app, a finance expert that could establish strategies for the stimulation to expand and be sustainable and an expert of distribution to reach rural areas of Ecuador. Since the app would ideally use a third-party library app (such as Spotify) to access the user's preferred songs, a legal expert is also necessary, since there is likely to be a lot of legal processes related to copyright.

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