Université de Montréal

# "Can Transcranial Magnetic Stimulation and Music Conjointly Influence the mood of the healthy population?" A Psychophysiological Approach

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*Ce mémoire intitulé*

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# Résumé

L'humeur, en tant qu'élément central dans notre perception du monde, englobe diverses émotions et affecte grandement le bien-être mental et physiologique. Une régulation efficace de l'humeur est vitale pour un fonctionnement quotidien normal et tout dérèglement peut mener à des troubles psychologiques majeurs comme la dépression. Au niveau cérébral, le système de récompense, en particulier le cortex préfrontal dorsolatéral gauche (CPFdl) et ses projections dopaminergiques, joue un rôle central dans la régulation de l'humeur et du plaisir. De nombreuses recherches montrent maintenant que l'écoute de la musique influence notre humeur, en agissant sur le système de récompense. En outre, la stimulation magnétique transcrânienne répétitive excitatrice (SMTr) ciblant le CPFdl gauche a donné des résultats prometteurs en modifiant l'humeur et l'activité du système de récompense, ainsi qu'en modulant le plaisir perçu et la motivation pendant l'écoute de la musique en augmentant l'excitabilité et la plasticité corticales. Cependant, les études existantes sur l'impact de la SMTr sur l'humeur des personnes en bonne santé aboutissent à des résultats contradictoires, et l'effet conjoint de la SMTr et de la musique sur l'humeur reste inexploré. Cette étude vise donc à déterminer si la SMTr excitatrice peut augmenter les effets de la musique sur l'humeur chez des volontaires sains. Plus précisément, nous souhaitons valider l'impact de la musique, de la SMTr et de leur application combinée sur l'humeur des participants.

Vingt-quatre participants ont suivi quatre sessions expérimentales, comprenant soit la SMTr seule, l'écoute de la musique seule, la SMTr associée à l'écoute de la musique, ou les conditions placebo/sham. L'humeur des participants a été évaluée à l'aide d'un questionnaire sur l'humeur et d'enregistrements de l'activité électrodermale (EDA) avant et après les stimuli. Les résultats ont révélé une amélioration significative de l'humeur générale et de l'humeur positive, ainsi qu'une diminution significative de l'humeur négative au cours de la séance de musique seule, ce qui indique l'efficacité de la musique en tant qu'intervention pour améliorer l'humeur. À l'inverse, la séance de SMTr seule a entraîné une diminution de l'humeur positive et une augmentation de l'humeur négative, ce qui suggère un effet négatif potentiel de la SMTr sur l'humeur. . Dans la session SMTr + musique, on a observé une tendance à l'amélioration de l'humeur, ce que nous

interprétons comme le fait que l'application de la SMTr sur le CPFdl gauche a entrainé une baisse de l'humeur, tandis que l'écoute de la musique contrecarrait cet effet en induisant une humeur positive et en réduisant l'humeur négative.En conclusion, les résultats de cette étude soulignent le potentiel de la musique en tant qu'intervention visant à améliorer l'humeur. En outre, les résultats suggèrent que la SMTr excitatrice ciblant le CPFdl gauche peut entraîner une baisse de l'humeur. Il est nécessaire de poursuivre les recherches dans ce domaine, notamment en explorant d'autres combinaisons de stimuli, telles que la SMTr excitatrice sur le CPFdl droit associée à la musique, afin de mieux comprendre les mécanismes sous-jacents et d'optimiser l'utilisation de ces interventions pour la régulation de l'humeur. Ces recherches supplémentaires permettront de mieux comprendre la modulation de l'humeur et d'améliorer l'efficacité des interventions dans ce domaine.

Mots-clés : humeur, système de récompense, cortex préfrontal dorsolatéral gauche, stimulation magnétique transcrânienne, activité électrodermale.

# Abstract

Mood, as a central element in our perception of the world, encompasses a variety of emotions and greatly affects mental and physiological well-being. Effective mood regulation is vital for normal daily functioning, and any disruption can lead to major psychological disorders such as depression. At the cerebral level, the reward system, in particular, the left dorsolateral prefrontal cortex (DLPFC) and its dopaminergic projections, plays a central role in regulating mood and pleasure. A large body of research now shows that listening to music influences our mood, by affecting the reward system. In addition, excitatory repetitive transcranial magnetic stimulation (rTMS) targeting the left DLPFC has shown promising results in altering mood and the reward system activity, as well as modulating perceived pleasure and motivation during music listening by increasing cortical excitability and plasticity. However, existing studies on the impact of rTMS on mood in healthy individuals yield conflicting results, and the joint effect of rTMS and music on mood remains unexplored. This study aims to determine whether excitatory rTMS can enhance the effects of music on mood in healthy volunteers. More specifically, we aim to validate the impact of music, rTMS, and their combined application on participants' mood.

Twenty-four participants completed four experimental sessions, comprising either rTMS alone, listening to music alone, rTMS + music, or placebo/sham conditions. Participants' mood was assessed using a mood questionnaire and electrodermal activity (EDA) recordings before and after the stimuli. Results revealed a significant improvement in overall mood and positive mood, as well as a significant decrease in negative mood during the music-only session, indicating the effectiveness of music as a mood-enhancing intervention. Conversely, the rTMS session alone resulted in a decrease in positive mood and an increase in negative mood, suggesting a potential negative effect of rTMS on mood. In rTMS + music session, there was a trend in mood improvement, which we interpret as meaning that applying rTMS to the left DLPFC resulted in a decrease in the mood while listening to music counteracted this effect by inducing positive mood and reducing negative mood. In conclusion, the results of this study underline the potential of music as a mood-enhancing intervention. In addition, the results suggest that excitatory rTMS

targeting the left DLPFC may lead to a decrease in mood. Further research in this area is necessary, including exploring alternative combinations of stimuli, such as excitatory rTMS on the right DLPFC in conjunction with music to better understand the underlying mechanisms and optimize the use of these interventions for mood regulation. This additional research will contribute to a more comprehensive understanding of mood modulation and enhance the effectiveness of interventions in this field.

**Keywords** : mood, reward system, left dorsolateral prefrontal cortex, transcranial magnetic stimulation, electrodermal activity.

# Table of Contents

# Liste des tableaux

# Liste des figures

# Liste des sigles et abréviations

aMT : active motor threshold

ANOVA : repeated measure analysis of variance

DLPFC : dorsolateral prefrontal cortex

EDA : electrodermal activity

EEG : electroencephalogram

HF-rTMS : high frequency repetitive transcranial magnetic stimulation

iTBS : intermittent theta burst stimulation

NAc : nucleus accumbens

rMT : resting motor threshold

rTMS : repetitive transcranial magnetic stimulation

SCL : skin conductance level

VTA: ventral tegmental area

*To all those whose hearts find resonance in the embrace of this universal language - music*

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# 1. Introduction

Mood as an enduring emotional state shapes our experiences by influencing how we perceive life, experience pleasure, and by modulating our mental and physical health, and behavior **(**Cohen et al., 1982; Ravindran et al., 2002; Chepenik et al., 2007; Young & Nusslock, 2016; Sekhon & Gupta, 2022). Moods changes are functional adaptations of the mood's system (Nettle & Bateson, 2012) and maintaining emotional well-being (Saarikallio & Erkkilä, 2007). "Mood regulation" refers to the various strategies and techniques employed to modify or sustain the intensity, duration, and frequency of both negative and positive moods (Parkinson et al., 1996; Cole et al., 2004; Eisenberg & Spinrad, 2004; Saarikallio & Erkkilä, 2007). Understanding the nature of mood and its regulation is crucial for improving mental health and well-being as the mood deregulations, for examples as observed in mood disorders causes significant distress in human beings (Nettle & Bateson, 2012). Pleasure and mood in humans are both linked to the activity in the brain's reward system, which involves, among others, the left dorsolateral prefrontal cortex (DLPFC) and its dopaminergic network (Strafella et al., 2001; Pogarell et al., 2007; Ko et al., 2008; Cho & Strafella, 2009**;** Mondino et al., 2015). Since the brain's reward system network and its dopamine signaling have a crucial role in mood regulation (Martin-Soelch et al., 2003; Radwan et al., 2018; Hasler, 2020), modulation of this system may lead to an effective mood modulation (Russo & Nestler, 2013; Martin-Soelc et al., 2003; Hasler, 2020).

One of the techniques used to modulate the reward system and modulate mood in clinical and research settings is neurostimulation such as repetitive transcranial magnetic stimulation (rTMS) (Strafella et al., 2001; Lam et al., 2008; schaller et al., 2011, Mas-Herrero et al., 2018). Repetitive transcranial magnetic stimulation is a non-invasive neuromodulation technique that uses a coil placed on the scalp to generate magnetic pulses that can penetrate the skull and induce electrical

currents to modulate functional activation or inhibition of a particular neural system and pathways (Kobayashi and Pascual-Leone, 2003; Krames et al., 2009). When it is targeted to the left DLPFC, it modulates the release of dopamine in crucial areas of the reward system (Strafella et al., 2001; Pogarell et al., 2007; Ko et al., 2008; Cho & Strafella, 2009; Haber & Knutson, 2010; Mas-herrero et al., 2018) and modulate mood (Pascual-Leone et al., 1996; George et al. 1996; Dearing, 1997; Schaller et al., 2011). Alternative methods of influencing the reward system and mood may involve auditory stimulation, such as using music. The capacity of music to activate the reward system has been well-established by previous studies (Pike, 1972; Sloboda & Juslin, 2001; Saarikallio & Erkkilä, 2007; Salimpoor et al., 2009) as it induces feelings of pleasure (Blood & Zatorre, 2001) and plays a role in mood regulation (Thayer et al., 1994; Juslin & Laukka, 2004; Saarikallio & Erkkilä, 2007; Chanda & Levitin, 2013).Consequently, music is also used as an intervention for mood regulation through its ability to evoke positive emotions, distract from negative emotions and generate feelings of pleasure. Importantly for this project, a recent study demonstrated that using excitatory rTMS over the left DLPFC following with music, significantly increased the perceived pleasure, psychophysiological indicators of emotional arousal, and the assigned monetary value attributed to music compared to sham stimulation (Mas-Herrero et al., 2018). These findings support the potential use of rTMS, to enhance the mood-regulating effects of music. By targeting the left DLPFC, which is involved in both mood regulation and reward processing, rTMS may amplify the pleasurable and mood regulating aspects of music listening consequently enhancing mood.

While studies have shown the influence of both music and rTMS on mood, there remains important inconsistencies in the results of rTMS studies on mood (Pascual-Leone et al., 1996; George et al. 1996; Baeken et al., 2008; Schaller et al., 2011). Additionally, there is a notable gap in the literature

regarding the combined effect of these two stimuli on enhancing mood. Therefore, this study aims to investigate the effect of music and rTMS, both independently and in conjunction, on the mood of participants with a particular focus on pleasure and mood improvement. The specific objective is to determine whether rTMS enhances the effects of music on the mood of healthy volunteers. By exploring the conjoint effect of these interventions, the study seeks to provide valuable insights into their combined potential for mood enhancement, contributing to a more comprehensive understanding of their effects on mood regulation. This also has important implications for developing interventions to enhance mood regulation and potentially alleviate symptoms associated with mood disorders.

### 1.1. Definition of Mood

Mood refers to a lasting and prevalent emotional state that is experienced internally and affects individuals' behavior and actions across various aspects of their life (Sekhon & Gupta, 2022). These prevailing psychological states can be temporary or habitual (Clark, 2005), encompass a range of emotions in response to daily life experiences, last for variable durations (from days to months), affecting various aspects of our lives, including our perception, mental and physical health, personal confidence, actions, goal-directed behaviors, reward processing and cognitive processes (Cohen et al., 1982; Ravindran et al., 2002; Clark, 2005; Lyubomirsky et al., 2005; Chepenik et al.,, 2007; ). Moods and emotions are distinct psychological phenomena with differing characteristics. According to Frijda (2000), moods are characterized by a more prolonged duration lasting for several hours to several days and is typified by a lower and more diffused intensity over time. In contrast, emotions are short-lived and transient psychophysiological events (Scherer, 2005). Moods play a fundamental role in shaping our existence by influencing our perception of the world and our encounters within it. They arise from our ongoing interactions with the

environment and can be influenced by a range of situational factors (Kiverstein et al., 2020). Moods can be triggered by a range of experiences, such as enjoying a pleasant conversation with an old friend or feeling frustrated by traffic when running late for work. These individual experiences can extend into prolonged states of positive or negative feelings, culminating in a specific mood state (Bliss-Moreau & Rudebeck, 2021) that subsequently impacts our actions and cognitive processes (Lane, 2007), such as feeling nervous during a public performance, or a job interview influences our thoughts and behaviors during those situations (Lane, 2007).

## 1.2. Mood Changes

One of the featured characteristics of moods is their instability. Indeed, mood changes over time are a normal function of moods' system to evoke a proper adaptive behavior (Nettle & Bateson, 2012). Moods can result from past positive or negative experiences, influencing a person's sensitivity to reacting to future positive or negative events in different contexts or time periods to give an insight about what is beneficial or harmful to our well-being (Nettle & Bateson, 2012). Gross (1998) suggests that the regulation of moods can be directed at different facets of emotions, including behavioral expression, subjective experience, or physiological responses (Saarikallio & Erkkilä, 2007). Importantly, this characteristic is of particular interest since sharp mood swings, chronic periods of any mood state and low mood may also be an indicator of mood disorders (Clark 2005; Hasler, 2020). These disorders are among the primary causes of disability on a global scale as they simultaneously affect one's emotions, energy, motivation, and losing the ability to experience pleasure, with direct impacts on the social and professional lives of patients (Rakofsky & Rapaport, 2018). One of the most prominent examples is major depressive disorder (Chepenik et al., 2007) which affects more than 264 million people worldwide (World Health Organization, 2021) and has an extremely prejudicial impact on an individual's social and professional life,

leading to reduced enjoyment of social activities and decreased work productivity, and even suicide (Chepenik et al., 2007; World Health Organization, 2021). Bipolar disorder is another mood disorder that is characterized by pronounced mood swings, encompassing episodes of both mania and depression (Merikangas et al., 2011; McIntyre et al., 2020). Mania, a central aspect of bipolar disorder, manifests as elevated or irritable mood coupled with increased energy and activity levels (McIntyre et al., 2020). Strategies for mood regulation for this disorder involve interventions aimed at stabilizing extreme mood episodes (Goodwin, 2003). Given these links, the ability to regulate mood has been proven to be crucial to improve one's life and mental well-being.

Moods are a biological phenomenon that appear to have a significant role in survival and reproduction, as it is highly conserved and widespread across different species (Nettle & Bateson, 2012). The brain reward system has been identified as a central regulator of mood, and throughout the process of evolution, this system has grown in relative size, suggesting that mood may be more important in humans than in other animals. Understanding the ancestral and present functions of mood is a critical area of research, as it may provide insights into how this essential biological mechanism has evolved over time and how it can be best harnessed to improve mental health and well-being (Hasler, 2020).

## 1.3. Reward System

The reward system is a complex neural network in the brain that is involved in our goal-directed behaviors, the anticipation of reward, processing and mediating the experience of pleasure and motivation, as well as positive emotional states (Bozarth, 1994; Berridge & Kringelbach, 2008; Nusslock & Alloy, 2017). The term "hedonic" comes from the Greek word "hēdonē," which means pleasure (Berridge & Kringelbach, 2015). It refers to anything related to pleasure or enjoyment,

whether it be sensory pleasure or higher-level pleasures such as cognitive and aesthetic experiences, or social interactions (Berridge & Kringelbach, 2015). The reward system is activated in response to certain stimuli or experiences that are perceived as rewarding or pleasurable (Koob, 1996; Elliott et al., 2000) and the reward process in the brain involves the association of these stimuli with desirable outcomes (Lewis et al., 2021).

According to Darwin's evolutionary theory (1872), affective responses, which includes emotions, were selected for their usefulness in aiding survival. Affective neuroscience supports this theory by positing that brain mechanisms of emotional reactions have evolved to mediate "survival functions," and can be observed across different species (LeDoux, 2012; Anderson & Adolphs, 2014; Berridge & Kringelbach, 2015). The development of pleasure-related reactions as a form of positive affect might have led the evolution of reward circuitry in mammalian brains, which was subject to the same selection pressures as any other evolutionary function (Haber & Knutson, 2010; Berridge & Kringelbach, 2015). Therefore, hedonic circuitry likely persisted throughout evolution because objective affective reactions provided significant benefits for survival (Kringelbach & Berridge, 2010; Panksepp, 2011; Anderson & Adolphs, 2014; Berridge & Kringelbach, 2015). This circuitry translates positive affective reactions or pleasure-related responses into conscious feelings of pleasure (Damasio & Carvalho, 2013; Berridge & Kringelbach, 2015).

This reward circuity was found in a pioneering study by Olds and Milner (1954). In their study, they discovered evidence of the links between reward and specific regions in the brain including tegmentum, septal area, cingulate gyrus and, subthalamus by creating a reinforcing effect using direct electrical stimulation. As pressing the lever by laboratory animals would lead to receiving a brief stimulation pulse to these regions, they would press a lever at high rates, over 6,000 times per hour, to receive it. This study identified for the first time an anatomical substrate related to

reward circuit and a specific behavior (Haber & Knutson 2010). Neuroimaging studies suggests now that the reward system of the brain involves several regions including ventral tegmental area (VTA), nucleus accumbens (NAc), amygdala, as well as prefrontal cortex such as portions of orbitofrontal, insula, and anterior cingulate cortices (Kelley & Berridge 2002; Hikosaka et al. 2008; Berridge & Kringelbach, 2015; Nusslock & Alloy 2017; Lewis et al., 2021). Clinical and animal research has accumulated substantial evidence that the functionality of this system is contingent on the mesocorticolimbic dopamine network as dopamine has a central position in mediating the reward value, processing of various stimuli and creating the pleasurable experiences such as in food, social interactions, substance abuse, and, as we will develop later, music (Hernandez & Hoebel, 1988; Bardo, 1998; Menon & Levitin, 2005; Braun Janzen et al., 2019; Lewis et al., 2021).

### 1.4. Mood and Reward System

The reward system and mood are closely interconnected as the reward system impacts mood modulation and mood can impact the reward processing and goal directed behaviors (Lyubomirsky et al., 2005; Russo & Nestler, 2013; Hasler, 2020).

Young and Nusslock (2016) established in a functional magnetic resonance imaging study the direct impact of positive mood on the reward-related neural activation. In this study, the authors induced positive mood by presenting 30 positive sentences combined with upbeat music. The results showed that the positive mood increased activity in brain regions that are involved in reward processing and goal-directed behavior (Young & Nusslock, 2016). The ability to seek out rewards and maintain a healthy balance between positive and negative affect (Coenen et al., 2011) is related to the communication between different brain regions within reward system including certain parts

of the striatum such as the NAc (Knutson et al., 2001; Ongur et al., 2003; Haber & Knutson, 2010; Young & Nusslock, 2016).

Dopamine signaling within the VTA, a component of the brain's reward system network, has been identified as playing a significant role in the regulation of mood (Radwan et al., 2018). Dopamine-producing neurons are primarily situated within three distinct brainstem nuclei including the retro-rubro field, substantia nigra pars compacta, and VTA (Cavalcanti et al., 2016; Radwan et al., 2018). There are two important neural pathways originating from the VTA. The mesocortical pathway extends from the VTA towards the frontal and temporal cortex, and the mesolimbic pathway projects from the VTA to various brain regions including the NAc, hippocampus, amygdala, and bed nucleus of the stria terminalis (Dunlop & Nemeroff, 2007; Radwan et al., 2018). These two pathways significantly contribute to the regulation of both mood and motivation within the brain (Radwan et al., 2018).

Berridge's (2003) study showed how the brain generates positive affective responses to pleasant sensations, such as the enjoyment of sweet tastes as the primary objective was to understand the brain mechanisms that give rise to "liking" the fundamental process that produces sensory pleasure and leads to positive affective reactions. Research indicates that the activity in a reward-related subcortical network of the brain, which includes specific areas of the NAc shell, ventral pallidum, and brainstem, is responsible for generating the feeling of "liking" and resulting positive affective reactions to sweet tastes (Berridge's 2003).

Similarly, studies have shown winning rewards, such as money, has been linked to an increase in mood in healthy control samples (Martin-Soelch et al., 2009; Kalebasi et al., 2015; Piccolo et al., 2019; Tandon et al., 2022). For example, Tandon and colleagues (2022) found a significant positive correlation between average mood ratings and average monetary reward in the healthy group. This

is concurrent with a positron emission tomography study that suggests there is an overlap between the neural mechanisms underlying reward processing and those underlying mood regulation including right amygdala and the orbitofrontal cortex. The response of the striatum, a crucial region for the reward processing, was correlated with changes in mood and the amount of reward. Also, the subjects experienced an improvement in their mood when they received the highest monetary reward (Martin-Soelc et al., 2003).

Experiencing normal pleasure and displeasure are substantial components of a human being's mental and psychological health (Berridge & Kringelbach, 2015). Affective neuroscience seeks to understand how the brain generates emotions, processes mood and affective states, including pleasure and displeasure, with the goal of developing more effective treatments for affective disorders such as anhedonia and mood disorders (Berridge & Kringelbach, 2015). Mood disorders like depression are distinguished by impairments in the processing of rewards and motivation, resulting in a diminished ability to perceive rewards effectively (Radwan et al., 2018). This is accompanied by a corresponding decrease in the drive to pursue hedonic goals (Radwan et al., 2018) and lead to pathological pleasure deprivation or an excessive level of displeasure (Berridge & Kringelbach, 2015). Anhedonia, the loss of the ability to experience pleasure (Ribot, 1896), is a core symptom of depression and is characterized by dysfunction in the reward system and altered experiencing and processing of rewards (Braun Janzen et al., 2019). In particular, a review that synthesized human and rodent studies proposed that depression is associated with a disruption in the balance of activity between excitatory cortical regions and subcortical reward-related structures, such as the NAc and amygdala. This imbalance in mood disorders can lead to an overactive response to negative stimuli and a blunted response to positive stimuli, which could contribute to the symptoms of depression (Russo & Nestler, 2013). This is supported by increasing

clinical, behavioral, and neurophysiological research that suggests that people with depression who experience anhedonia exhibit distinct responses to primary and secondary rewards compared to healthy individuals (Admon & Pizzagalli, 2015; Rizvi et al., 2018), specifically decreased levels of extraversion and reduced sensitivity to pleasure (Kazdin, 1989; Kotov et al.,2010; Nusslock &Alloy, 2017). As a result, the reward system has a crucial impact on mood, as disruptions in reward processing can contribute to the development and maintenance of mood disturbances (Nestler & Carlezon 2006; Nusslock & Alloy 2017), while positive experiences that activate the reward system can improve mood and provide a sense of well-being.

### 1.4.1. Role of Left DLPFC on Mood Modulationand Reward System

The prefrontal cortex, particularly its dorsal regions, has a significant role in the neural networks responsible for processing emotions and modulating mood (Spielberg et al., 2008; Mitchell, 2011; Nitsche et al., 2012; Remue et al., 2016). Additionally, fronto-striatal circuits of reward system, especially those involving the DLPFC and the dorsal striatum, play an important role in the anticipation and processing of rewards (Critchley et al., 2001; Knutson et al., 2001; Ito et al., 2002; O'Doherty et al., 2002; Wallis & Miller., 2003; Tsujimoto & Sawaguchi, 2005; Salimpoor et al., 2011; Mas-Herrero et al., 2018). Activation of the left DLPFC is linked with positive mood, mood upregulation and the processing of positive stimuli (Canli et al., 1998; Ochsner et al., 2004; Mondino et al., 2015; Mobius et al., 2017)

A meta-analysis comprising multiple neuroimaging studies investigating major depressive disorder has identified the DLPFC as a significant neural system involved in this disorder (Fitzgerald et al., 2008). Left DLPFC plays a crucial role in affective regulation, and depressed patients exhibit decreased activity in this region whereas recovery from depression and positive change of mood is linked with an increase in the activity of this region and deactivation of right

DLPFC can lead to the same results (Baxter et al., 1989; Mayberg et al., 2005; Mitchell & Loo, 2006; Fitzgerald et al., 2008).

There are many ways to modulatemood and the reward system, both through natural means and by using laboratory techniques, as listed by Parkinson et al. (1996), who identified over 200 different regulatory strategies. In this study, we use music as a potential behavior to regulate mood (Saarikallio & Erkkilä, 2007). Additionally, we aim to investigate the use of brain stimulation as a laboratory technique to modulate the reward system and regulate mood.

## 1.5. Mood Modulation Through Reward System Using Music and Neurostimulation

### 1.5.1. Effect of music on Mood: Modulating the Reward System

In evolution theory, pleasure is known for its crucial role in reproduction and survival using primary rewards like food or sex (Berridge & Kringelbach 2015). However, it appears that we can also experience pleasure through more aesthetic rewards like listening to music (Blood & Zatorre 2001) which is considered one of the top ten pleasurable experiences for us (Dubé & Le Bel, 2003). Music is an inseparable activity in our everyday life, and it has a long history in humankind life as it is often used intentionally on daily basis or research to produce pleasure (Blood & Zatorre 2001), induce emotion (Cavallaro et al., 2019), and regulate mood for example to decrease negative mood and increase the positive mood (Thayer et al., 1994; Juslin & Laukka 2004; Hewston et al., 2005; Saarikallio & Erkkila, 2007; Chanda & Levitin, 2013). Music possesses a profound ability to evoke emotions and modulate our emotional responses, contributing to its rewarding nature (Salimpoor et al., 2009). The rewarding experience of music is intertwined with the broader goal of mood regulation, aligning with the concept of hedonic motivation—the desire to pursuit pleasure and experience positive affect.Several studies have highlighted hedonic motivation as a major factor

in mood regulation (Zillmann 1988a, 1988b; Larsen, 2000a, 2000b; Tice & Bratlawsky, 2000; Tice & Wallace, 2000; Saarikallio & Erkkila, 2007).

Enhanced sympathetic autonomic nervous system activity is one of the physiological markers of emotional arousal (Ekman et al., 1983) and mood changes (Van der Zwaag & Westerink, 2009; Varies & Van der Zwaag, 2010). Numerous studies have demonstrated that emotional arousal plays a significant role in the pleasurable experiences people have with music (Salimpoor et al., 2009). These studies have utilized psychophysiological measures such as heart rate, respiration, muscle tension and skin conductance to investigate the physiological responses associated with such arousal and they generally agree that music can significantly and consistently influence these physiological markers and mood states (Blood & Zatorre, 2001; Menon &Levitin, 2005; Salimpoor et al., 2009; Zald & Zatorre, 2011). In addition, this strong emotional arousal and the pleasurable experiences associated with music has been demonstrated in brain networks responsible for processing emotion and reward. These networks include the cingulate cortex, orbitofrontal cortex, NAc, and amygdala (Blood & Zatorre, 2001; Menon & Levitin, 2005; Koelsch et al., 2006; Salimpoor et al.,2013, Salimpoor et al.,2015). In a study by Salimpoor and colleagues (2009), the authors provide evidence for a relationship between pleasure and emotional arousal induced by music using psychophysiological signals that are influenced by autonomic nervous system including electrodermal activity (EDA), heart rate, respiration rate and body temperature (Bradley & Lang 2000; Rickard, 2004). The study revealed that subjects have significantly higher EDA when they listen to music excerpts that they find pleasurable in comparison to neutral music excerpts. Electrodermal activity refers to alterations in the skin's electrical characteristics caused by the activity of sweat glands (Boucsein, 2012). It has been widely used in music and emotion studies and it is the best indicator of emotional responses and

experienced pleasure in music and other stimuli as it is not under subjects' conscious control and it is strongly influenced by changes in the autonomic nervous system (Khalfa et al., 2002; Rickard 2004; Grewe et al., 2007; Sequeira et al., 2009; Salimpoor et al.,2009). Rickard (2004) found that skin conductance could be used as a highly responsive measure to measure the intensity of affective responses triggered by musical excerpts. Changes in skin conductance were shown to accurately reflect the emotional impact of music on individuals (Zald & Zatorre, 2011). Also, our mood tends to fluctuate over time (Thayer, 1996), and these changes in mood are not only reflected in our mental and emotional states but also manifest in our autonomic nervous system (Van der Zwaag & Westerink, 2009; Varies & Van der Zwaag, 2010). Greco and colleagues (2014) found that individuals with bipolar disorder, a mood disorder characterized by extreme mood swings, exhibit distinct EDA patterns that vary depending on their current mood state. The inclusion of EDA in studies offers the advantage of being unobtrusive and easy to implement in our daily routines (Westerink et al., 2009; Varies & Van der Zwaag, 2010). This means that it can be used conveniently to monitor changes in mood and emotional arousal through autonomic nervous system activity in real-life situations without causing interference or discomfort to individuals. Therefore, the use of EDA as an assessment tool has the potential to provide valuable insights into mood fluctuations and emotional arousal.

Blood and Zatorre (2001) intentionally used subject-selected music pieces to induce intense pleasant emotional responses. They demonstrated that participants' experienced pleasure is in association with alterations of autonomic and other psychophysiological activities including heart rate, respiration, and muscle tension, as well as the co-occurrence of chills and changes in the pattern of blood flow in the brain reward circuit-related regions of the brain including the orbitofrontal cortex and subcortical regions including ventral striatum. Considering the role of

NAc, which is a major component of the ventral striatum, in reward, pleasure, motivation and emotional system (Pavuluri et al., 2017), this study implies that music may have the ability to activate comparable neural circuits similar to primary rewards (Zald & Zatorre, 2011). These results are congruent with a functional magnetic resonance imaging study in which researchers investigated the impact of listening to music on the reward system and affective processing (Menon & Levitin 2005). The effective and functional connectivity analyses demonstrated brain interactions between affective and autonomic systems as well as the impact of dopaminergic pathways in interposing the affective responses and positive emotions to music (Menon & Levitin 2005). Based on the scientific studies conducted thus far, we can conclude that emotional arousal evoked by pleasant music is closely associated with activation in reward neural system in the brain, as well as its dopaminergic projections. This relationship has been consistently observed across various studies and is supported by neuroimaging techniques and physiological measures that reveal pleasurable music increased activity in reward-related brain regions.

Having explored the physiological responses to music, our exploration now turns toward the psychological and behavioral dimensions. From the perspective of affective psychology, individuals often attempt to regulate or control their emotions and moods (Sloboda & Juslin, 2001). People often attempt to regulate their mood by using music to achieve the emotional state they desire.The mood regulating impact of listening to music has been recognized as a commonly employed strategy (Rippere, 1977; Parker & Brown, 1982; Silk et al., 2003; Thayer et al., 1994; Saarikallio & Erkkilä, 2007).Listening to music ranked as the second most effective method in decreasing a negative mood, increasing energy levels, and alleviating tension (Thayer et al., 1994; Saarikallio, 2008). For instance, people may listen to upbeat music to feel energized or listen to calming music to feel relaxed. Music's mood-inducing properties are also evident in various

cultural practices, where different types of music are paired with different activities to evoke certain emotions or moods (Gregory, 1997; Sloboda & Juslin, 2001). Music also serves as a means of expressing emotions and stabilizing mood, this explains its contribution in regulating emotional experiences. (Sloboda & Juslin, 2001). Pike's study (1972) is an example of a phenomenological analysis of emotional experience of music. In this study, participants who had no musical training listened to various pieces of music and were then asked to write down their emotional responses. The most frequently occurring factors were a feeling of pleasure, perception of stable moods, feeling of oneness with the music, perception of spontaneous and transient emotional states, and feeling of movement (Sloboda & Juslin, 2001). Another explanation for mood regulatory impact of music is its ability to serve as a distraction (Saarikallio & Erkkilä, 2007). According to Salovey and colleagues (1999), utilizing enjoyable activities to shift attention away from negative emotions and improve one's mood is recognized as an advanced and highly successful method of regulating moods (Saarikallio & Erkkilä, 2007) as people might use music to detach oneself from one's thoughts, emotions, and negative feelings (Sloboda, 1992; Behne, 1997; Schwartz & Fouts, 2003; Saarikallio & Erkkilä, 2007).

The use of music to regulate and maintain a mood has made its way to clinical settings. There is rising interest in music as a treatment for mood disorders studies including depression. Studies have indicated that listening to music or engaging in music therapy can have a positive impact on mood and alleviate symptoms of depression (Esfandiari &Mansouri, 2014; Verrusio et al., 2014; Leubner & Hinterberger, 2017). Braun Janzen and colleagues (2019) explored the impact of listening to music as a music-based intervention on depression symptoms including anhedonia. The results revealed significant alterations in measures of depression and related symptoms compared to baseline, including improvements in quality of life, and anhedonia. The results of this

study provide further support for previous evidence suggesting that music-based interventions have the potential to be an efficient treatment option for individuals with major depressive disorder (Maratos et al., 2008). A recent review of 28 studies involving 1810 participants revealed that music interventions were associated with a significant decrease in depression levels (Leubner & Hinterberger, 2017). Another randomized systematic review, reports evidence indicating that music therapy combined with other standard treatments including psychological therapies, and pharmacological therapies had a significant effect on reducing both clinician-rated and patient-reported depressive symptoms compared to other standard treatments alone. The results showed a large effect size favoring music therapy and standard treatments over only standard treatments for both clinician-rated depressive symptoms and patient-reported depressive symptoms. This reduction in depressive symptoms suggests that music therapy could be an effective treatment option for individuals with depression (Aalbers et al., 2017) and a mean to regulate the mood of healthy population (Sloboda & Juslin, 2001; Saarikallio & Erkkilä, 2007), along other ways of treatment such as neurostimulation (Levinson et al., 2010; George et al., 2010; McClintock et al., 2017; Li et al. 2018).

### 1.5.2. Effect of Neurostimulation on Reward System and Mood

#### 1.5.2.1. Transcranial Magnetic Stimulation (TMS)

Human brain activity can be modulated by non-invasive brain stimulation techniques including TMS. Transcranial Magnetic Stimulation coil generates magnetic fields to induce electrical currents in neurons aimed by the coil which leads to neural depolarization (Kobayashi & Pascual-Leone, 2003; Hallet, 2007; Krames et al., 2009). It is now largely used in the scientific community (Berlim, and Daskalakis, 2013; Berlim et al., 2014; Hui et al., 2019) as it helps to investigate the

specific functions of different regions of the brain and noninvasively modulate the brain neural activity (Remue et al., 2016; Mas-Herrero et al., 2018). A brief burst of neural activity that has been induced by a single TMS pulse can typically lead to short-lived acute impact on cortical activation for several hundred milliseconds (Allen et al., 2007). As this short-lasting single-pulse approach is usually used in exploring the function of the brain, repetitive TMS (rTMS) pulses have been shown to alter the neural activation that lasts after the stimulation period (Klomjai et al., 2015). This impact can be excitatory or inhibitory based on the stimulation duration and frequency used in the protocol (Pascual-Leone et al., 1998). Excitatory rTMS is a high-frequency stimulation (> 5 Hz) that generally leads to an increase in cortical excitability and plasticity and the induction of a form of plasticity (Klomjai et al., 2015).

A review on 61 studies discusses the efficacy of rTMS in modulating the cortical networks which can lead to performance enhancement and potency in healthy individuals and potential applications of rTMS in cognitive enhancement, including research into cortical function, rehabilitation therapy, and accelerated skill acquisition (Luber & Lisanby, 2014). The literature suggests that rTMS can potentiate and improve speed and accuracy in various tasks, including perceptual, motor, and executive processing (Luber & Lisanby, 2014).

While exploring new methods of applying rTMS to alter brain activity more effectively, researchers have shown that bursts of high-frequency theta stimulations can induce synaptic plasticity, similar to long-term potentiation. These findings have led to the development of patterned rTMS protocols called theta burst stimulation (TBS), which mimic the long-term potentiation induction paradigms observed in animal models (Larson et al., 1986; Capocchi et al., 1992; Huang et al., 2005). Theta burst stimulation closely imitates the natural theta rhythms of neuronal activity in the brain (Klomjai et al., 2015). Studies have shown TBS is comparable in

efficacy compared to simple rTMS classical parameters with more consistent results and a significant reduction of the duration of sessions (Hoogendam et al., 2010; Blumberger et al. 2018). Consequently, TBS is a promising avenue to modulate the cortical excitability of different brain areas which can lead to significant impacts on various brain functions. Recently, rTMS has been used in various studies to modulate the reward system and regulate the mood.

#### 1.5.2.2. rTMS on the Left DLPFC: Reward System and Mood Modulation

In behavioral, physiological, and neuroimaging studies, rTMS have been found to have a potential impact on the reward system and mood (Shajahan et al., in 2002; Barret et al., 2004; Li et al., 2014; Duprat et al., 2018). As mentioned previously, the DLPFC, linked to the fronto-striatal circuits of the reward system (O'Doherty et al., 2002; Wallis & Miller., 2003; Tsujimoto & Sawaguchi, 2005; Salimpoor et al., 2011; Mas-Herrero et al., 2018), has been a popular target region for rTMS as it has been implicated in a variety of cognitive and emotional processes, including mood modulation (Davidson & Irwin, 1999; Herrington et al., 2005). The studies have established the brain lateralization of affect representation, suggesting the different regions of the brain are specialized for processing positive or negative affect (Berridge & Kringelbach, 2015). Specifically, the left hemisphere of the prefrontal cortex is often associated with positive affect and higher subjective well-being (Davidson, 2004; Herrington et al., 2005; Price & Harmon-Jones, 2011; Kuhn & Gallinat, 2012; Lawrence et al., 2012; Berridge & Kringelbach 2015). When rTMS is targeted over the left DLPFC it alters the release of dopamine and the level of blood oxygenation in key regions of the reward system including the dorsal striatum since there is functional and structural connections that exist between these structures (Strafella et al., 2001; Pogarell et al., 2007; Ko, et al., 2008; Cho & Strafella, 2009; Haber & Knutson, 2010; Mas-herrero et al., 2018). Also, targeting rTMS on the left DLPFC leads to effective modulation of mood in healthy individuals (Schaller et

al.,2011) and those experiencing depression (Berlim et al., 2014; Kedzior et al., 2015). By increasing the connectivity between various brain circuits that are involved in the expression of affect, rTMS has been shown to modulate the activity of these circuits to regulate mood (Shajahan et al. in 2002; Barret et al., 2004). Two systematic reviews and meta-analyses have shown that HF-rTMS over the left DLPFC is effective in treating depression with a significant antidepressant effect observed compared to inactive sham rTMS (Ebmeier et al.,2006; Lam et al., 2008; Slotema et al., 2010; Berlim et al., 2014; Kedzior et al., 2015).

Studies have investigated the potential mood-modulating effects of rTMS on the DLPFC in healthy individuals. However, the literature reveals inconsistencies, posing challenges in reaching definitive conclusions regarding the impact of rTMS on mood in this population.. In a study by Schaller and colleagues (2011), it was demonstrated that applying HF-rTMS to the left DLPFC resulted in a significant decrease in the Beck Depression Inventory (Beck et al., 1961) score in healthy individuals who received HF-rTMS, compared to those who received sham rTMS. While there is a suggestion that either activating the left DLPFC or deactivating the right DLPFC could potentially yield favorable effects on mood and emotion among individuals with clinical depression (Mitchell & Loo, 2006; Schaller et al., 2011; Remue et al., 2016), there are studies suggesting that this lateralization might be contrary in healthy populations, as right DLPFC is likely to be responsible for positive mood and left DLPFC for negative mood (George et al. 1996; Pascual-Leone et al., 1996; Dearing, 1997). Pascual-Leone et al. (1996) observed an increase in anxiety and sadness levels, along with a decrease in happiness, as measured by a 5-item visual analog scale (VAS), following the application of 10 Hz rTMS over the left DLPFC. Likewise, George et al. (1996) discovered that participants reported a reduced happiness level following 5 Hz rTMS over the left DLPFC and a decreased sadness level after rTMS over the right DLPFC

(Mondino et al., 2015). In contrast to these investigations, some studies have reported a lack of significant mood alteration when employing HF rTMS over the DLPFC. The evaluation of mood using a 5-item VAS did not show modulation with 20 Hz over the left DLPFC (Mosimann et al., 2000). Similarly, no mood change was observed with 10 Hz over the left DLPFC, as assessed with both VAS and the Profile of Mood Scale (Baeken et al., 2006; Mondino et al., 2015)

The variations in findings across studies exploring the effects of HF rTMS over the left DLPFC on the mood of healthy individuals may be attributed to discrepancies in study protocols. These disparities encompass the presence or absence of a sham control, divergent rTMS parameters, variations in sample sizes, and distinctions in the coordinates targeted within the DLPFC.The inclusion of a sham (placebo) condition is crucial as it helps determine whether changes in performance can be attributed to the effects of rTMS on a particular brain area (Remue et al.,2016) and control the placebo effects.

Regarding the enhancing effect of rTMS, a recent study suggested applying excitatory TBS over the left DLPFC increases the perceived pleasure, emotional arousal such as EDA, and motivation measures (including amount of money participants spend on buying a particular music excerpt) during music listening. This study suggests that excitatory rTMS can enhance the neural circuit's sensitivity to music experience by increasing the excitation of fronto-striatal pathways (Mas-Herrero et al., 2018). In a mood induction study done by Mobius and colleagues (2017), they targeted the left DLPFC by HF-rTMS before presenting mood induction movie clips. This study showed a strong mood induction congruent with the emotions presented in the movie clips, suggesting use of HF-rTMS over the left DLPFC may potentiate the impact of emotional stimuli. This procedure may increase the likelihood of susceptibility to mood induction techniques in general for healthy young people (Mobius et al., 2017). These studies suggest that HF-rTMS on

the left DLPFC can potentiate the cortical sensitivity for the following stimulus, be it to induce the pleasure experience by music or the mood regulation by emotional movie clips.

Based on previous studies, it has been shown that mood can be influenced by music and HF rTMS independently. However, there is a lack of consensus regarding the impact of excitatory rTMS on the mood of healthy individuals. Additionally, there is no information available regarding the combined effects of music and neurostimulation on mood.

### 1.6. Current Study

This study aims to investigate how happy music and excitatory rTMS, either used separately or together, affect the mood of healthy volunteers. Specifically, we aim to determine the individual effects of happy music and excitatory rTMS on the left DLPFC on mood, as well as investigate whether excitatory rTMS can potentiate the mood-boosting effects of happy music. We hypothesize that both happy music and excitatory rTMS will individually improve the mood of participants. Furthermore, we hypothesize that the simultaneous application of these interventions will result in a synergistic effect, amplifying the overall impact on mood. This hypothesis is based on the idea that excitatory rTMS can increase cortical excitability, potentially strengthening the mood-boosting effects of music (Luber & Lisanby, 2014). Such potentiation would give us valuable information on the ability to regulate mood more efficiently and would open the door to potential therapeutic intervention when facing dysregulation of mood, such as apathy or anhedonia (Mas-Herrero et al. 2018) as observed in major depressive disorders.

Berridge et al (2003) suggest several different measurement approaches to study the pleasant events that trigger objective and subjective positive affective reactions. By subjective, we mean they are based on personal experience and perception, and objective, meaning they are based on

observable physiological reactions. The first approach is to measure subjective ratings of pleasure and mood changes, which involves asking individuals to report their experience in response to a stimulus (Berridge, 2003). This method can provide valuable insight into conscious pleasure experiences, evoke positive affective and mood changes, but since it is self-reported, it can be biased with factors like response bias. The second approach is to measure evoked physiological affective reactions to sensory pleasure, which involves observing or measuring changes in behavior or physiology in response to a pleasurable stimulus. This method can provide information about the immediate hedonic impact of sensory pleasure (Berridge, 2003). To address the limitations of any single measurement approach and take advantage of the strengths of these measures, in our study, we used both of these measurements.

At the physiological level, we recorded EDA and at the behavioral level, we assessed participants' overall mood state, negative mood and positive mood. The primary aim is to examine differences in the chosen measures between conditions and before/after each experimental session (sham, excitatory rTMS, sham rTMS+music, excitatory rTMS + music). Overall, the expectation is to see a progressively linear increase for all the chosen measures along with the four experimental sessions we had (sham, excitatory rTMS, sham rTMS+music, excitatory rTMS + music). More specifically, we hypothesized to observe an enhancement of mood in all conditions except for the sham session, with the highest increase in the rTMS+Music session The same pattern (increase) should be observed at the physiological level with EDA level as individuals show increased EDA when they experience pleasure and positive mood in response to stimuli.

# 2. Methods and Material

## 2.1. Participants and recruitment

A sample of 24 (Female= 19) healthy right-handed subjects aged between 18-35 years old (Mean Age=25.00, SD = 5.31), was recruited through online advertisements and posters using Facebook groups that were created for this purpose, Centre for Research on Brain, Language and Music and International Laboratory for Brain, Music and Sound Research websites and newsletters.

The exclusion criteria included experience of a specific contraindication for TMS (Rossi et al. 2009) (e.g., personal history of epilepsy or seizure), history of psychological disorders or a major unstable medical or neurological illness (e.g. uncontrolled diabetes or renal dysfunction), current or past (< 3 months) substance (excluding caffeine or nicotine) or alcohol abuse/dependency or currently smoking (including nicotine, recreational and/or medically prescribed cannabis), hearing impairment and being musician. Even if TMS is an extremely safe procedure, we also excluded pregnant, breastfeeding, or thinking of becoming pregnant women during study.

To confirm their eligibility, potential participants filled out an online screening questionnaire to acquire their demographic information and music training experiences, they completed a TMS safety and contraindication form, and filled out the Hospital Anxiety and Depression Scale online (Zigmond & Snaith 1983) to check their anxiety and depression factors. We excluded the individuals who had a score of > 8 in the anxiety and depression subscales (Rishi et al., 2017).

After the final recruitment, the eligible participants signed a written informed consent and the TMS safety questionnaire before their participation and sent it to us by email. All the forms and questionnaires in this study were in English or French based on participants' preferences. The study was approved by the Comité d'Ethique de la Recherche en Education et en Psychologie (CEREP) at the University of Montréal (CEREP-21-061-D). Also, participants signed another

informed consent form and the TMS safety questionnaire again upon their arrival to the laboratory in the first session. They were reimbursed with 125$ after the last session.

## 2.2. Stimuli

### 2.2.1. Music

Music preference is highly personal (Salimpoor et al. 2009; Hargreaves & North 2010) and music familiarity is a factor that influences our music preference (Peretz et al., 1998) and experienced pleasure (Witvliet & Vrana 2007; Daimi et al., 2020). Experimenter-selected music excerpts for a study without considering individual taste can create challenges in evoking strong and consistent emotions (Thaut & Davis 1993). The solution proposed by Zald and Zatorre (2011) is to use participant-selected music excerpts as they are aware what kind of music would produce intense emotional responses. In a study, the music chosen by the study participants was found to be more enjoyable and emotionally stimulating compared to neutral music (Blood & Zatorre, 2001). Therefore, prior to the experiment, participants were instructed to select twenty musical excerpts of their choice and send them to the experimenters. Specifically, they were asked to choose ten excerpts of sad music, and ten excerpts of happy music that they found pleasant (See Appendix B). To minimize the potential for participants to deduce the study's underlying hypothesis merely from the request for happy music, we instructed them to provide both happy and sad music selections, and both categories were incorporated into the study protocol. There were no limitations on the type of music that could be presented. This approach aimed to enhance the real-world relevance of our results and guarantee that any observed impacts were not influenced by a particular music genre (Salimpoor et al., 2009).

Importantly, to ensure that we were examining the impact of music on mood rather than memories associated with it, we specifically requested that participants choose music that was not associated with any specific life event, memory, or a specific period. This was done to ensure that the pleasurable or unpleasurable experience was solely attributed to the music itself and not related to any emotional memory (Salimpoor et al., 2009).

To select appropriate musical excerpts for our experiment, we needed two 15-minute happy and sad playlists. To ensure that we had a comprehensive understanding of the participants' music preferences, participants completed two questionnaires regarding their musical experiences and preference through a demographic questionnaire and the Music Preference Questionnaire (Nater et al., 2005) to have their complete musical profile in selecting the music excerpts. These questionnaires were sent to participants via LimeSurvey. The Music Preference Questionnaire consisted of eleven established categories of music as well as questions such as "What is your favorite music group?" and "How much does music make you feel chills?" In addition, we included six additional questions, such as whether they found sad or happy music enjoyable or whether they used music to improve their mood (see Appendix B). Using the information of these questionnaires, we created a customized playlist for each participant on Spotify, including both happy and sad music based on the protocol for each session. The musical stimuli were delivered via Bluetooth earbuds.

### 2.2.2. TMS

The TMS pulses were administered according to the application guidelines outlined by Rossi and colleagues (2008) on principles and procedures for use of TMS. We used TBS in two conditions: excitatory TBS protocol named intermittent TBS (iTBS) and sham condition. For iTBS protocol,

a series of 30 pulses (lasting 2 seconds) every 10 seconds for a total of 190 seconds, resulting in a total of 600 pulses was delivered (Huang et al., 2005) (See Figure 5). For intensity, we used 80% of Active Motor Threshold (aMT) of each participant (Huang et al., 2005). The process for establishing the aMT involved first determining resting motor threshold (rMT), defined as the minimum intensity required to evoke motor evoked potentials of around 50uV in 5 out of 10 trials. To assess the background contraction level, participants performed three maximal contractions of the index muscle, and the strength of the most robust contraction was recorded. Subsequently, we computed 10% of this maximal contraction, which served as the designated background contraction for participants to sustain throughout the procedure. Active Motor Threshold is defined as the lowest level of intensity that can elicit a motor evoked potential greater than 0.1 mV in at least 5 out of 10 attempts when the subject maintains a contraction of the left masseter muscle at around 10% of their maximum voluntary contraction (Ortu et al., 2008). For the sham condition, a coil identical to the real coil was placed exactly on the same target/anatomical location and in the same position, but without any active stimulation (Duprat et al. 2016). To locate each participant's left DLPFC, ensure stable coil positioning and accurate targeting of the left DLPFC, we used a Polaris camera to match participants' brains to standard MNI brain and the Brainsight neuronavigation system (Rogue Research Inc., Montreal). The used coordinates of left DLPFC were x = − 40, y = 32, and z = 30 (Strafella et al., 2001; Mass-herrero et al., 2018).

## 2.3. Measures

### 2.3.1. Physiological level: Electrodermal Activity (EDA)

To measure variations of activity in the autonomic system, we recorded EDA. This measure is a physiological measure of the electrical conductance of the skin, which is influenced by the activity

of sweat glands and reflects changes in sympathetic nervous system activity (Critchley & Nagai, 2013). Electrodermal activity data was recorded at a sampling rate of 1024 Hz using a constant voltage (0,5 V) coupler and 8-mm Ag/AgCI electrodes placed on the medial phalanx of the index and middle fingers of participants' non-dominant hand (Silvestrini & Gendolla 2007) via ActiView software (Biosemi) and digitized by an ActiveTwo AD-box (Biosemi) with 24-bit resolution. EDA signals contain two components including Skin Conductance Response and Skin Conductance Level (SCL) (Boucsein, 1992: Dawson et al., 2000). Skin conductance level is associated with the tonic discharging of the sympathetic nervous system (Cacioppo et al., 2007; Bosch et al., 2013) and reflects gradual fluctuations over time (Varies & Van der Zwaag, 2010). Studies have found that SCL is significantly higher when listeners find the music pleasurable compared to when it is neutral (Grewe et al., 2009; Salimpoor et al., 2009). Also, mood fluctuations are tonic and gradual (Varies & Van der Zwaag, 2010), therefore, we chose SCL component in our study.

In each session, we first recorded a baseline measurement period of 5 minutes before any stimuli and then 5 minutes recording after stimuli be it iTBS, music, or sham based on the sessions' protocol.

### 2.3.2. Behavioral level: Overall Mood State, Positive and Negative Mood Adjectives on VAS

We used positive mood adjectives, negative mood adjectives and an overall mood state question to measure mood variations. The participants were instructed to assess their current overall mood state, negative mood adjectives and positive mood adjectives using a 100-mm visual analogue scale (VAS; Hayes & Patterson, 1921). E-prime software (Psychology Software Tools, Pittsburgh, PA) was employed to present the scale and record their responses. Each session, participants

responded to these measures twice, once before any stimuli and once after stimuli based on the protocol.

We selected the positive and negative adjectives from the ones used in The Brief Mood Introspection Scale (BMIS; Mayer & Gaschke, 1988) to which we added two negative and two positive mood adjectives. The BMIS employs both positive and negative mood adjectives: Each mood is assessed using two "lively" and "happy" for Happiness, "loving" and "caring" for feeling of love, "calm" and "content" for Calm, "active" and "peppy" for Energetic, "gloomy" and "sad" for unhappy, "jittery" and "nervous" for Frightening/anxious, "grouchy" and "fed up" for Angry and, "tired" and "drowsy" for Exhausted. Notably, the first four moods (eight adjectives) are associated with positive adjectives, while the last four moods (eight adjectives) are characterized by negative adjectives. (Mayer & Gaschke, 1988; Pham, 2019). We added two additional adjectives to each mood category: "smiling" and "even-tempered" to the positive mood adjectives, and "serious" and "restless" to the negative mood adjectives. Participants assessed their current mood by responding to twenty mood adjectives through a Visual Analog Scale (VAS). The VAS comprised a horizontal line with endpoints marked as "definitely do not feel" and "definitely feel." Seated in front of a screen, participants used a mouse to indicate their current level of experience with each adjective by marking a point along the line.

Additionally, for the assessment of overall mood state, participants were to evaluate their current mood by responding to the question "Overall, at this moment, my mood is:" on the same VAS. The VAS featured endpoints labeled as "Not Pleasant" and "Very Pleasant."The use of VAS was motivated by its widespread use in previous studies examining the effects of rTMS on mood in healthy individuals (George et al., 1996; Dearing et al., 1997; Mosimann et al., 2000; Baeken et al., 2006, 2008), as well as its ability to capture instant changes in mood following stimulation

(Schaller et al., 2011). This procedure was set up so that participants could place their responses anywhere on a continuous line which eliminated the number of predefined categories of possible responses (Sung & Wu, 2018).

## 2.4. Research Design

The study followed a prospective, single-blind randomized sham-controlled trial design, where each participant was required to participate in five sessions. The first session was a preparation session, which involved determining the participant's aMT and locating their left DLPFC after asking them to fill out the consent form and TMS safety form again in person. The remaining four experimental sessions were designed to include 1) sham iTBS+ music, 2) only iTBS, 3) iTBS + music, and 4) sham. The order of the experimental sessions was randomized, and there was an interval of approximately one week between sessions (Huang, 2017). Each session was designed to appear the same to the participants and followed these steps:

### 2.4.1. Before the Stimuli: Pre-Test Data Collection

We installed the EDA electrodes at the start of each experimental session, while explaining the experiment to the participants in a standardized manner. After installing the electrodes, we asked the participants to sit comfortably on the experiment chair. Then, primary data was collected before the stimuli were presented. Participants filled out the VAS, and a 5-minute resting-state EDA was recorded while participants were instructed to stare at a cross in front of them and to avoid any major movements. We minimized the distraction in the experiment room to establish a baseline for the session. The pre-test data collection was carried out similarly at the beginning of all the experimental sessions.

### 2.4.2. Protocols of Experimental Sessions

We followed different protocols after pre-test data collection based on the experimental session. We adjusted sessions (see Figure 6) to ensure that all sessions were of similar duration and maintain the single-blind nature of the study. This was done by involving both stimulation and music in each session, ensuring that participants experienced a consistent procedure in all the sessions. To achieve this, if needed, we added an additional 5 minutes of EDA recording, played their sad music playlist, or delivered sham stimulation as per the protocol for each session. By doing so, we aimed to reduce any potential confounding factors that may have arisen due to differences in the length or content of the sessions, thus enabling us to assess the effects of the stimuli more accurately.

2.4.2.1. Only iTBS: Participants received the iTBS on the left DLPFC. After pre-test data collection, we instructed them to stay relaxed and avoid any major movement during the stimulation. Then, they underwent post-test measurements which involved recording a 5-minute EDA resting state and filling out the VAS. To maintain the similar protocol procedures, the session was then concluded by playing sad music for 15 minutes, followed by the recording of EDA for another 5 minutes.

2.4.2.2. Sham: This experimental condition was identical to the "Only iTBS" session, with the exception that the participant did not receive brain stimulation and instead, an inactive coil was used. Following this, post-test measurements (resting-state EDA for 5 minutes and VAS) were taken, and the session concluded with 15 minutes of sad music listening. Then, a 5-minute resting state EDA was recorded for standardization purposes.

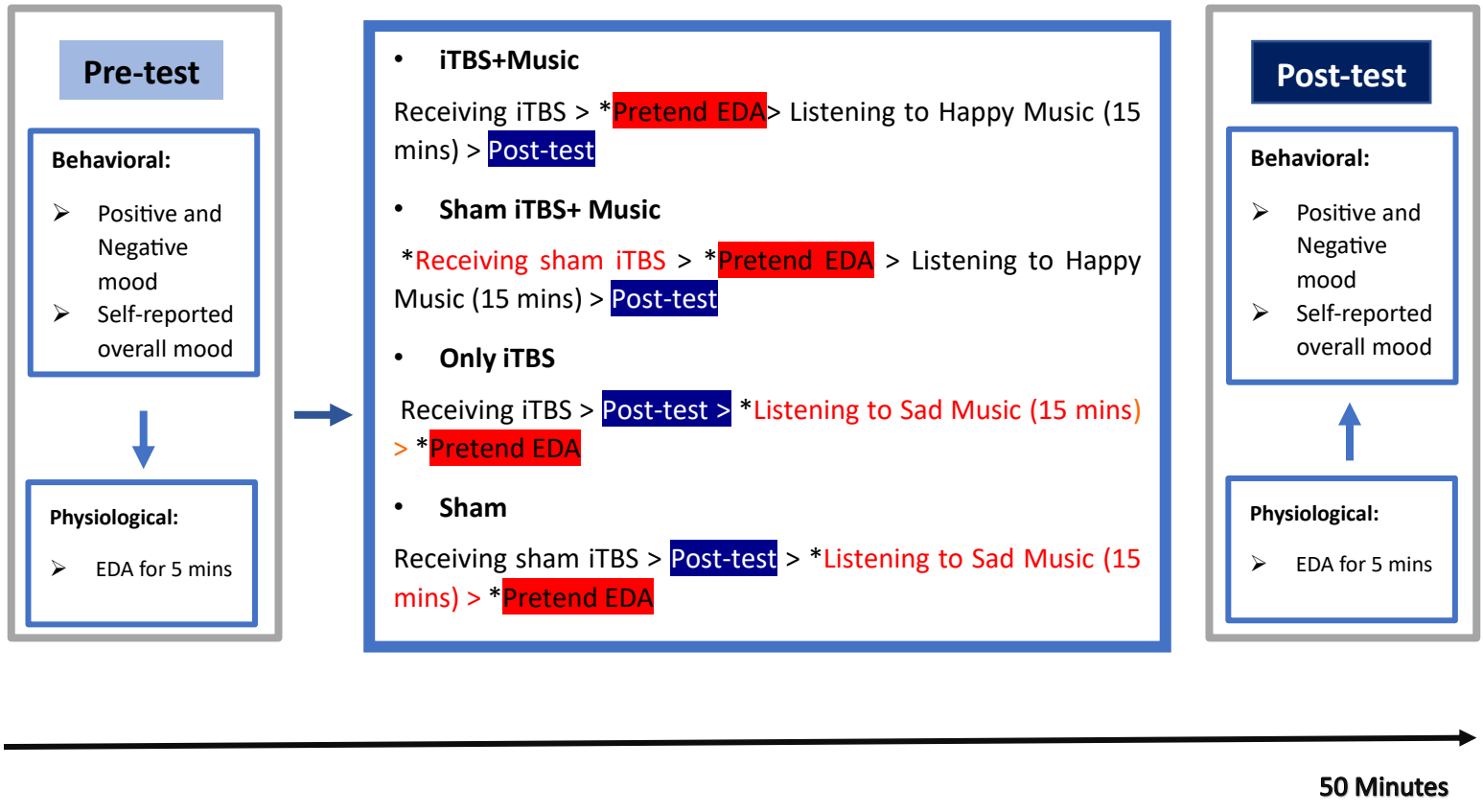
2.4.2.3. Sham iTBS and Music: For the "Sham iTBS+ Music" session, a sham stimulation was applied to the left DLPFC with no actual stimulation sent to the brain region after the pre-test data collection. Following this, EDA was recorded at rest for 5 minutes to maintain homogeneity across

all sessions, as previously stated. The participant then listened to happy music for 15 minutes, after which post-test measurements were taken.

2.4.2.4. iTBS + Music: In this experimental session, after pre-test data collection, the participants received iTBS on their left DLPFC. Following this, a 5-minute resting state EDA was recorded to ensure consistency across sessions. Next, the participant listened to happy music for 15 minutes. Afterwards, post-test measurements were taken.

At the end of the fifth session, we asked two blinding questions from the participants to assess if they were able to differentiate between the experimental sessions and to confirm the success of the blinding process. The questions included "Which session do you think was the main session?" and "Did you notice any difference in the protocols of experimental sessions."

**Figure 1.** Schematic Overview of Four Experimental Sessions Protocol



*Note.* **Pre-test**: The subject completes the mood questionnaire and self-reported mood state. EDA is recorded at rest for 5 min before all the experimental sessions**.** **Test: *iTBS + Music***: Stimulation of the left DLPFC. Then, resting state EDA activity is recorded for 5 min, then listening to happy music for 15 min. ***Music only***: A sham stimulation at the left DLPFC is applied and then resting state EDA is recorded for 5 min. Then, listening to happy music for 15 min. ***iTBS only***: Stimulation of the participant's left DLPFC. After that, the post-test measurements are performed and the session ends by listening to the sad music for 15 min, then the resting state EDA is recorded for 5 min. ***Sham***: experimental control condition, we apply sham stimulation with no inactive coil.Then, the post-test measurements are carried out to finish with 15 min of listening to the sad music and 5 min of resting EDA. **Post-test**: Recording EDA at rest for 5 min, then the subjects have to fill out the mood questionnaire and self-reported mood state.

## 2.5. Analysis

### 2.5.2 EDA Data Preparation

The EDA data were analyzed using the same procedures as those implemented in previous studies (Bosch et al., 2013). A low pass filter of 0.6 Hz was applied to eliminate noise and artifacts induced by motion. The EDA signal may exhibit a gradual decline over extended recording periods due to charge accumulation at the electrode-skin junction, leading to a linear reduction in conductance. Consequently, a detrend function (EEGLAB, Delorme & Makeig, 2004) was used to remove this drift in the EDA signal.

We analyzed the SCL data from the last two minutes of each EDA recording (Mori & Iwanaga 2013) and made four epochs of 30 seconds using PhysioData ToolBox (Sjak-Shie, 2022). Additionally, it is important to note that SCL can exhibit considerable variation both between different individuals and within the same individual across different experimental sessions (Cacioppo et al., 2007; Bosch et al., 2013). To take these differences into account, we calculated the potential range for each individual subject and subsequently normalized the subject's current value with respect to this range. To do so, the current SCL for a subject can be normalized with

respect to their personalized range by using the formula (SCL - SCLmin)/ (SCLmax - SCLmin), which requires identifying the minimum and maximum SCL for that subject. This normalization procedure serves to decrease data variability and improve the statistical power of analyses performed on the dataset (Lykken et al., 1966; Lykken & Venables, 1971; Bosch et al., 2013).

### 2.5.2. Statistical Analysis

In this study the independent variables were neurostimulation and music in different session protocols (Sham iTBS+Music, only iTBS, Music+iTBS, Sham) and the dependent variable is the data of our measures (Negative mood adjectives, Positive mood adjectives, Overall mood state, SCL).

Main analyses compared the measures before and after each experimental session. To do so, we used two factors within subject repeated measure analysis of variance (ANOVA) to statistically evaluate the difference between conditions for scores to Overall Mood State, BMIS, and SCL using SPSS Statistics (IBM Corp, New York, USA) version 28. If necessary, we applied the Greenhouse-Geisser correction to address potential violations of sphericity, and post hoc tests were conducted as required.

## 3. Results

### 3.1. Blinding Questions

Concerning the responses to blinding questions, fifteen participants indicated that they did not perceive any distinction in the protocol, while nine participants acknowledge a difference in the sensation between the sham and iTBS. Within this subgroup, two participants described the iTBS as notably uncomfortable, and one expressed discomfort with the sensation in their body while the

rest reported it mildly different. Notably, two participants opted to withdraw from the study due to finding the iTBS procedure painful in the first experimental session.

## 3.2. Behavioral level

### 3.2.1. Overall self-reported mood state

A two-factor within subject repeated measures ANOVA on the scores of the participants overall mood state indicated no significant main effects of experimental protocol ($F_{(2,56)=}1.153$, $p$=0.330) or measurement time ($F_{(1,23)=}0.078$, $p$=0.782). However, a significant interaction effect between experimental protocol and measurement time was observed ($F_{(2,46)}$=4.063, $p$=0.024).indicating there was a significant change in overall mood of participants depending on the sessions.

**Table 1.** Two-Way ANOVA on Overall Mood State

| Variable | df | F | p | Partial Eta Squared |
|---|---|---|---|---|
| Protocol | 2.470 | 1.153 | .330 | .048 |
| Pre-Post | 1 | .078 | .782 | .003 |
| Protocol×Pre-Post | 2.007 | 4.063 | .024* | .150 |

*Note.* This table demonstrates the results for the effects of measurement time and session type on overall mood state. 95% confidence interval of the mean are depicted.

Further analyses utilizing paired samples t-tests with Bonferroni correction revealed a significant increase in mood state for the Music session ($p$=.028) meaning happy music increases the overall mood of participants towards the pleasant. After the iTBS session, we observed a non-significant statistical trend toward a decrease in overall mood. Regarding iTBS+Music, and sham sessions, we did not find a significant alternation on the overall mood state of participants.

**Table 2.** Post-Hoc Test on Overall Mood State

| Variable | Mean (SD) | Mean(SD) | P (2-tailed) |
|---|---|---|---|
| | ***Pre*** | ***Post*** | |
| Sham iTBS+Music | 70.43(19.62) | 77.53(13.73) | .028* |
| Sham | 78.51(13.44) | 75.41(15.45) | .197 |
| iTBS | 74.85(19.09) | 70.54(20.36) | .075 |
| iTBS+Music | 76.55(19.13) | 78.98(14.77) | .535 |

*Note.* This table presents the results of the comparison of overall mood state scores with Bonferroni correction before and after the implementation of each protocol. The 95% confidence interval of the mean is depicted.

### 3.2.2. Positive Mood Adjectives

The analysis revealed significant effects of both protocol ($F_{(2,658)}$=6.552, $p$<.001) and measurement time ($F_{(1,239)}$=8.430, $p$=.004,) as well as an interaction between the two ($F_{(2,\ 693)}$ =21.242, $p$<.001).

**Table 3.** Two-Way ANOVA on Positive Mood Adjectives

| Variable | df | F | p | Partial Eta Squared |
|---|---|---|---|---|
| Protocol | 2.755 | 6.552 | <.001* | .027 |
| Pre-Post | 1 | 8.430 | .004* | .034 |
| Protocol×Pre-Post | 2.9.3 | 21.242 | <.001* | .082 |

*Note.* This table demonstrates the results for the effects of measurement time and session type on positive mood adjective modulations. 95% confidence interval of the mean are depicted.

Further post hoc comparison with Bonferroni correction revealed a significant increase in the evaluation of positive valence mood adjectives in the Music session ($p$<.001), meaning that happy music had increased the positive mood of participants. Additionally, there was a significant decrease in the positive mood of participants in both Sham ($p$<.001) and iTBS sessions ($p$<.001)

meaning participants had a lower positive mood afrer the sham and iTBS session. We could not observe a significant change of positive mood adjectives on iTBS+Music session ($p$=.935) suggesting the combination of these stimuli did not alter the positive mood.

**Table 4.** Post-Hoc Test on Positive Mood Adjectives

| Variable | Mean (SD) | Mean(SD) | P (2-tailed) |
|---|---|---|---|
| | ***Pre*** | ***Post*** | |
| Sham iTBS+Music | 64.55(23.84) | 69.67(19.84) | <.001* |
| Sham | 68.85(20.17) | 61.44(24.44) | <.001* |
| iTBS | 68.04(21.10) | 62.44(22.84) | <.001* |
| iTBS+Music | 69.90(20.53) | 70.01(20.31) | .935 |

*Note.* This table presents the results of the comparison of positive mood adjectives scores with Bonferroni correction before and after the implementation of each protocol. the 95% confidence interval of the mean is depicted.

### 3.2.3. Negative Mood Adjectives

The results indicated that measurement time did not have a significant effect on the dependent variable ($F_{(1,239)}$=1.298, $p$=0.256), while the experimental session did have a main effect ($F_{(2,693)}$=3.964, $p$=0.009). Additionally, an interaction effect between experimental session and measurement time was found ($F_{(2, 696)}$=4.465, $p$=0.004)

**Table 5.** Two-Way ANOVA on Negative Mood Adjectives

| Variable | df | F | p | Partial Eta Squared |
|---|---|---|---|---|
| Protocol | 2.901 | 3.964 | .009* | .016 |
| Pre-Post | 1 | 1.298 | .256 | .005 |
| Protocol×Pre-Post | 2.912 | 4.465 | .004* | .018 |

*Note.* This table demonstrates the results for the effects of measurement time and session type on negative mood adjectives. 95% confidence interval of the mean are depicted.

Paired-samples t-tests with Bonferroni correction revealed a significant decrease in negative mood adjectives in the sham iTBS+music session ($p$<.001) showing music decreased the negative mood in participants. The results on iTBS+Music ($p$=0.400), iTBS ($p$=0.690) and sham ($p$=0.187) sessions did not yield a statistically significant decrease or increase on the negative mood.

**Table 6.** Post-Hoc Test on Negative Mood Adjectives

| Variable | Mean (SD) | Mean(SD) | P (2-tailed) |
|---|---|---|---|
| | ***Pre*** | ***Post*** | |
| Sham iTBS+Music | 34.78(28.12) | 30.30(28.20) | <.001* |
| Sham | 31.05(27.34) | 32.66(27.86) | .187 |
| iTBS | 34.09(25.98) | 34.60(26.03) | .690 |
| iTBS+Music | 30.64(27.42) | 29.27(26.92) | .400 |

*Note.* This table presents the results of the comparison of negative mood adjectives scores with Bonferroni correction before and after the implementation of each protocol. the 95% confidence interval of the mean is depicted.

## 3.3. Physiological Data: SCL

A two-factor within-subject repeated measure ANOVA was conducted to assess the effects of experimental sessions and measurement time on SCL. The analysis, which used Greenhouse-Geisser correction, showed no significant differences between the various experimental sessions

($F_{(2,57)} = .724$, $p = .518$,) or measurement time ($F_{(1,23)} = 0.005$, $p = .945$). Moreover, no significant interaction effect between the two factors was observed ($F_{(2,51)} = 0.510$, $p = 0.625$).

**Table 7.** Two-Way ANOVA on SCL Data

| Variable | df | F | p | Partial Eta Squared |
|---|---|---|---|---|
| **SCL** | | | | |
| Protocol | 2.504 | .724 | .518 | .031 |
| Pre-Post | 1 | .005 | .945 | <.001 |
| Protocol×Pre-Post | 2.248 | .510 | .625 | .022 |

*Note.* This table demonstrates the results for the effects of measurement time and session type on SCL data. The95% confidence interval of the mean is depicted.

# 4.Discussion

Based on the existing literature, the present study aimed to investigate the conjoint and separate impact of iTBS on the left DLPFC and listening to happy music on the mood of a healthy population. The study revealed distinct variations in behavioral-level mood changes following different experimental protocols. These variations underscored the specific impact of each protocol on overall self-reported mood state, positive mood, and negative mood.

Specifically, the subjects experienced an improvement in their mood when they only listened to music as we observed on their overall mood and positive mood. In contrast, the negative mood of participants significantly decreased after listening to music. Interestingly, when participants received only iTBS on the left DLPFC, their positive mood showed a significant decrease, while there was a trend of decrease in the overall mood state.Furthermore, when combining iTBS on the left DLPFC with listening to happy music, we observed a non-signficant slight trend towards an increase in overall mood and positive mood, along with a decrease in negative mood.

Regarding the Sham session, our analysis revealed a statistically significant decrease in positive mood.

At the physiological level, we observed no changes regarding the different interventions, whether it be music, iTBS, or the combination of both.". These patterns are discussed below.

## 4.1. Effect of Music on Mood

The results from sham iTBS+ music protocol were congruent with our hypothesis and previous studies investigating the impact of music on mood regulation (Thayer et al. 1994; Saarikallio & Erkkilä 2007;). We incorporated three distinct mood change assessments, allowing us to

comprehensively capture various aspects of mood alterations. This approach accounts for overall mood changes and provides a nuanced examination of shifts in both negative and positive moods. We observed an increase in the overall mood state and positive mood after participants listened to their self-selected happy playlist. It appears that music is a highly versatile tool for regulating one's mood, with music having a particularly strong effect on mood improvement, consistently resulting in positive changes in mood when the musical activity was self-selected (Saarikallio & Erkkilä 2007). Gallup and Castelli (1989) conducted a study involving 1007 participants who were questioned about their strategies for alleviating feelings of depression. The findings indicated that 77% of the respondents preferred employing methods such as distraction and listening to music (Thoma et al., 2006). After listening to music, our participants showed a decrease in their negative mood. Consequently, Thayer et al. (1994) assert that music holds a dual function: it not only contributes to overall mood regulation but also proves efficacious in mitigating negative emotions, including the reduction of nervousness, tension and raising energy (Thoma et al., 2006). Music is effective in providing pleasure and changing mood because it has the capacity to evoke desired emotions and moods in individuals. (Gregory, 1997; Sloboda & Juslin, 2001). Van Goethem and Sloboda (2011) aimed to investigate which strategies are used in mood regulation using music. Music facilitates a comprehensive spectrum of mood regulation strategies, encompassing mechanisms such as distraction, introspection, and active coping (Van Goethem & Sloboda, 2011). The study showed that individuals used music to regulate a wide spectrum of affects such as transitioning from feelings of tiredness to a state of energy, experiencing shifts towards happiness, motivation, and tranquility (Van Goethem & Sloboda, 2011). Primarily, the aim of most of these regulatory efforts was to enhance positive affects and counteract negative ones (Van Goethem & Sloboda, 2011). In our study, we demonstrated the modulation of mood in both directions. Music

exhibited the capability to diminish negative mood and elevate positive mood, as well as enhancing the overall mood of participants. Music has the power to elicit strong emotional responses, whether it is excitement, happiness, sadness, or relaxation (Cavallaro et al., 2019). The experience of these emotions contributes to the pleasure we derive from listening to music (Salimpoor et al., 2009). The longing for positive feelings and the pursuit of pleasurable experiences is like hedonic motivation, which involves seeking pleasure and avoiding discomfort. Hedonic motivation is an important factor in regulating mood, as individuals actively engage in activities and seek out experiences that bring them joy and enhance their mood (Zillmann, 1988a, 1988b; Larsen, 2000a, 2000b; Tice & Bratlawsky, 2000; Tice & Wallace, 2000; Saarikallio & Erkkila, 2007). Music, with its ability to induce emotions and regulate mood, can be a means for individuals to fulfill their hedonic motivation and regulate their emotional state. It is a mean to express and release our emotions to stabilize our mood (Sloboda and Juslin, 2001; Saarikallio and Erkkilä, 2007) as it was shown that listening to music bring feeling of pleasure, perception of stable moods, feeling of oneness with the music, perception of spontaneous and transient emotional states (Pike, 1972; Sloboda and Juslin, 2001).

Contrary to our initial hypothesis, no noticeable changes in SCL were detected in our study in any of sessions be it sham iTBS+ music, only iTBS, or a combination of both In our study, the lack of significant effects on skin conductance raises considerations about the relationship between physiological and behavioral measures of mood. The observed absence of physiological changes does not necessarily negate the presence of mood effects, as demonstrated by significant alterations in behavioral measures. This discrepancy suggests that the behavioral manifestations of mood changes may not always align with the physiological response. The lack of discernible effects in SCL could be interpreted in two ways: either there is genuinely no effect, or there might be an

effect, but some aspects of our experimental procedures did not function as anticipated. As we cannot definitively identify the reason for the observed outcomes, we explain potential factors contributing to the absence of expected SCL changes in our study.

It seems plausible that the SCL measurement might be less sensitive to changes of mood compared to behavioral assessments, leading to the observed results in behavioral measures but not in SCL. This highlights the importance of considering multiple measures to comprehensively understand the impact of interventions on mood.

Also, skin conductance is recognized as a reflective indicator of mood and emotional responses to reward (Varies and Van der Zwaag, 2010). Studies highlight several factors that can impact the measurement of physiological response to interventions such as music. These factors can include anxiety from instrument "hook up," participant attention span and musical experience, physical and cognitive activity unrelated to the experiment, environmental temperature, emotions and stimulus type and intensity (Barden, 1996; Varies and Van der Zwaag, 2010). All these factors can affect the physiological response of the participant, leading to a wide range of results (Barden, 1996). Varies and Van der Zwaag (2010) proposed in evaluating the mood modulation with SCL, the existing methods to mitigate the effects of these processes are rudimentary.

For example, if a participant is distracted by cognitive activity unrelated to the experiment, this may also lead to an inconsistent physiological response. In this study, we used resting-state EDA measurement before and after our stimuli. Resting-state EDA can provide valuable insights into baseline levels of sympathetic nervous system activity; however, the use of resting-state EDA does not account for the cognitive processes that participants may undergo during recording (Barrett et al.,2004). When participants are at rest and not engaged in any specific task during EDA measurement, they may still be engaged in various cognitive processes that could influence their

sympathetic nervous system activity including daydreaming, worrying, or engaging in other forms of mental activity that could affect their EDA level. Since resting-state EDA measurement does not control for these potential cognitive processes, it is possible that the observed EDA patterns may reflect these cognitive processes rather than solely reflecting sympathetic nervous system activity. This could lead to difficulty in interpreting the EDA patterns and their relationship to the reward system and mood. Also, the timing of EDA measurement can have an impact on the results. As a single value, calculated by averaging responses over the entire stimulus, may not accurately reflect the second-by-second changes in the individual's subjective and physiological experiences (Salimpoor et al., 2009). Recording EDA after the stimulus has been presented may not capture the immediate effects of the stimulus on arousal, which may dissipate over time. To address this issue, we should continuously record both pleasure and physiological arousal in real-time (Salimpoor et al., 2009). Typically, studies that investigate the effects of music on emotional arousal, pleasure and mood using physiological measures like EDA, continuously record them during the presentation of the stimulus, to capture immediate changes in arousal (Barden, 1996; Krumhansl, 1997; Salimpoor et al., 2009; van den Bosch et al., 2013) and they use another component of EDA that is more sensitive to chills (Grewe et al., 2009; Salimpoor et al., 2009). By employing real-time recording of EDA signals during stimulus presentation, we would have mitigated the potential confounding influence of various cognitive processes engaged by the participants compared to the resting-state condition. This approach would have allowed us to capture the immediate and second-by-second effects of the stimuli on emotional arousal. The absence of real-time EDA recording in our study may have precluded the observation of these immediate changes however we were able to observe the mood modulation at the behavioral level.

Consequently, valuable insights into the transient and rapid effects of the stimuli on physiological arousal may have been missed.

While the valence (positive or negative) of music was checked in our study, we did not validate the intensity of pleasure experienced by participants. In previous studies that used EDA to measure pleasure, a validated procedure is to ask participants to rate their level of pleasure before and during the music listening session using a Likert scale (Salimpoor et al., 2009, 2011; Martinez-Molina et al., 2016; Mas-herrero et al., 2017). Additionally, before the main session, participants had the opportunity to evaluate the musical stimuli. This allowed researchers to capture their subjective experiences with the music excerpts before proceeding with the main study (Salimpoor et al., 2009). This approach would have ensured us that the "happy" playlists used in the study were genuinely enjoyable for each participant and elicited intense pleasure. In other words, it's important to not only consider the valence of music but also the intensity of pleasure it can elicit. It is possible that both the participants and the researchers did not select music excerpts that were sufficiently pleasant to elicit robust physiological arousal and emotional responses. This could have contributed to the lack of significant changes in SCL data.

## 4.2. Effect of Neurostimulation on Mood

Contrary to our hypothesis, iTBS on the left DLPFC did not improve mood or potentiate the impact of happy music on the mood of healthy population. The outcomes of studies examining the effects of rTMS targeting the left prefrontal cortex on the mood of healthy individuals do not align consistently and can be categorized into three distinct groups: 1) rTMS does not impact the mood, 2) rTMS decreases the mood and 3) rTMS increases the mood. The lack of consistency in the outcomes of these studies may arise from variations in factors such as the number of sessions

conducted, the quantity of participants involved, the specific rTMS parameters employed, the presence or absence of a sham control condition, variations in measurement techniques. A group of previous studies showed rTMS does not impact the mood state of healthy individuals (Mosimann et al., 2000; Grisaru et al., 2001; Padberg et al., 2001; Baeken et al., 2006, 2008; Baeken et al., 2014; Mondino et al., 2015; Moulier et al., 2016; Mobius et al., 2017). For example, in a study by Mosimann and colleagues (2000), there was not a significant increase in the mood 5-item VAS scale after 20 Hz HF-rTMS over the left DLPFC. The result was the same for 10 Hz HF-rTMS with Profile of Mood Scale and Positive and Negative Affect Schedule mood assessments on VAS (Baeken et al., 2006, 2008). In our study, when subjects underwent iTBS targeting the left DLPFC, there was a significant reduction in their positive mood and a trend towards a decline in their overall mood state. These findings agree with another group of studies showing that rTMS on the left DLPFC can decrease the mood of targeted population (Pascual-Leone et al., 1996; George et al. 1996; Dearing, 1997). It is possible that the left DLPFC is not the optimal target for iTBS to improve mood in healthy population. The right DLPFC may also play an important role in mood modulation, and that targeting this area with HF-rTMS may be more effective for certain individuals. Studies suggest that targeting the left DLFPC using HF-rTMS would cause negative mood such as sadness and decrease in positive mood such happiness compared to the effects of HF-rTMS on right DLPFC and the mood changes observed in healthy individuals following a HF-rTMS on left DLPFC are contrary to the mood changes witnessed in depressed patients (Pascual-Leone et al., 1996; George et al. 1996; Dearing, 1997; Padberg et al., 2001; Slotema et al., 2010; Berlim et al., 2014; Kedzior et al., 2015). This is congruent with a previous study by Pascual-Leone and colleagues (1996), suggesting that stimulating the left DLPFC with 10 Hz HF-rTMS resulted in higher levels of anxiety and sadness and lower levels of

happiness, as assessed by a 5-item VAS. Another study demonstrated the same result in lower levels of happiness by stimulating the left DLPFC with 5 Hz HF-rTMS while stimulating the right DLPFC with rTMS resulted in lower levels of sadness (George et al. 1996). Our results is a novel contribution to the existing literature since previous studies reporting similar results did not employ a sham-controlled condition However, Schaller and colleagues (2011) discovered that a nine-session course of HF-rTMS targeted the left DLPFC resulted in an improvement in mood, as measured by the Beck Depression Inventory among a healthy population. They did not observe the same effects using a 6-item VAS. The discrepancy between our findings and Schaller and colleagues (2011) may be attributed to several factors. One possible explanation is the difference in the number of stimulation sessions, as their study involved nine sessions of excitatory rTMS over the left DLPFC, whereas we only administered a single session. Additionally, the changes in mood were shown only on the Beck Depression Inventory whereas we used a VAS. Lastly, our sample size was smaller than theirs, which included 44 participants. It is possible that the sample size of our study was not large enough and the study may have been underpowered to detect significant improvement in mood. Future studies with larger sample sizes may be needed to fully explore the effects of iTBS on mood in healthy populations.

While iTBS is considered a non-invasive method, it may cause discomfort in some individuals. As previously highlighted, two participants withdrew from the experiment due to the pain associated with iTBS. Moreover, among the participants who completed the sessions, two individuals reported significant discomfort during iTBS, expressing sustained anxiety throughout the sessions. Additionally, seven participants observed a distinction in sensation between iTBS and sham sessions. Recognizing the potential of iTBS to induce discomfort or anxiety, these factors may have influenced participants' mood, potentially resulting in a decrease in their positive mood.

It is important to note that the optimal parameters for iTBS to induce changes in mood may differ between healthy individuals and those with mood disorders. The primary mood state of healthy individuals is generally more stable and does not fluctuate as much as that of individuals with depression (Bowen et al., 2017) and moods are influenced by both biological and environmental factors and include more subtle changes than emotional states. This means that even if rTMS is applied to the left DLPFC of healthy individuals, there is insufficient leeway for mood changes, and it is more difficult to observe significant mood changes after a single session of rTMS. Thus, understanding and addressing mood fluctuations may require a more comprehensive approach that considers a person's biological factors such as brain chemistry changes and genetics, life experiences such stress, and trauma and other influential variables that can have mor sustainable impact on the mood than immediate stimulus or even compensate the impact of experimental stimulus (George et al., 2009). In addition, in our study, we opted for an intensity of 80% of active motor threshold (aMT) for iTBS. It is plausible that employing alternative parameters and utilizing a more precise motor threshold measurement might have resulted in more optimal outcomes. Enhancing the precision of the motor threshold measurement can be achieved by increasing the number of positive motor evoked potentials to 10 out of 20 trials instead of 5 out of 10 trials (Rossini et al., 2015; Moulier et al., 2016). Using an intensity set at 80% of the resting motor threshold (rMT) instead of 80% of the aMT allows for higher stimulation power in iTBS (Bouaziz et al., 2021). This strategy has been adopted in certain studies to achieve stronger stimulation effects. Previous studies focused on iTBS for treating resistant depression, employed stimulation intensities at 120% and 90% of the rMT, respectively, and reported excellent tolerance (Blumberger et al., 2018; Cole et al., 2020; Bouaziz et al., 2021). Choosing rMT over aMT is crucial due to its potential influence on the aftereffects of iTBS. Using aMT may cause

spontaneous pre-activation of the target muscles, altering the subsequent effects of iTBS (Cole et al., 2020; Bouaziz et al., 2021). Opting for rMT helps mitigate such concerns as it represents the threshold without involving active muscle contraction. Implementing these methodological adjustments is likely to enhance the reproducibility of the study's findings. The brain's reactions to emotional stimuli can occur automatically and unconsciously, separate from the individual's ability to verbally express or report their emotional state (Baeken et al., 2008; Moulier et al.,2021). For instance, self-reported pleasure and mood state may be restricted to only those feelings that are consciously accessible and expressible, leading to the possibility of missing some positive affective reactions and mood changes that happen without conscious awareness (Zajonc, 1980; Zajonc, 2000; Berridge, 2003).

Observing the individual profiles of our participants, we noticed that we  responders and non-responders to the impact of iTBS on the left DLPFC. Multiple sessions of rTMS targeted at left DLPFC have been shown to increase cortical excitability and neuronal firing rates, resulting in an antidepressant effect. However, despite these positive effects, the clinical improvement achieved with rTMS is still limited even in clinical population, with low response rates and a small effect size (Lepping et al., 2014; Perera et al., 2016; Mutz et al.,2018; Zrenner et al., 2020). This means that even in clinical population, not all who receive rTMS will experience significant improvement in their symptoms. We should take into consideration that there is an individual differences in the inhibitory and excitatory impacts of rTMS and acknowledging this variability is crucial when interpreting the results of rTMS studies (Remue et al., 2016). We need to consider subgroups of individuals who respond better to rTMS compared to other groups as we have responders and non-responders to rTMS. Individual differences in baseline mood and susceptibility to the effects of rTMS may also play a role in the observed effects as needed rTMS sessions, duration, and

stimulation parameters to have a better impact may differ (Padberg et al., 2009; Loo et al., 2010; Baeken et al., 2014). The variability in response to rTMS targeting the left DLPFC suggests that certain stimulation coordinates may yield better results than others. Previous trials using a 5-cm rule to determine coil placement for DLPFC stimulation in depression treatment have shown inconsistent outcomes and often missed the intended target (George et al., 2000; Fregni et al.,2006; O'Reardon et al., 2007; Herbsman et al.,2009). In a study, researchers found that the effectiveness of rTMS treatment was associated with the precise location of stimulation, rather than the conventional categorical classification of the stimulated cortical region (Herbsman et al.,2009). The study observed a 5 mm difference in mean coordinates between responders (-46,23,49) and non-responders (-41,17,55) to rTMS treatment in three axes. While this difference may seem small in clinical terms, the study argues that within the context of the already small anatomical target, this disparity is significant and has a notable impact on treatment outcomes (Herbsman et al.,2009). Therefore, it is crucial to precisely place the coil in the prefrontal cortex region to achieve optimal TMS treatment and choose the optimal coordinates (Herbsman et al., 2009). A study by Fox and colleagues (2012) on the healthy population and patients with depression suggested the effectiveness of rTMS can vary among individuals due to differences in their brain connectivity patterns. By selecting stimulation targets in the left DLPFC based on each individual's specific connectivity to deeper limbic regions, such as the subgenual cingulate, it is anticipated that the treatment can be tailored to their unique neural circuitry (Fox et al.,2012; Moulier et al.,2016). It is possible that optimal left DLPFC target may be different from person to person which could explain the non-responders observed in this study. Another proposition to optimal rTMS result is oscillation synchronized with rTMS. Although HF-rTMS is typically considered to increase cortical excitability, its effects on synaptic plasticity and neuronal firing rates are more complex

than previously thought. High frequency rTMS has been shown to induce structural and functional changes in both excitatory and inhibitory synapses (Vlachos et al., 2012, Lenz et al.,2016). Studies in rats suggest that the timing of the ongoing oscillatory network activity can determine the type and strength of the synaptic plasticity induced by rTMS (Huerta & Lisman, 1993, 1995). Recent research has demonstrated that synchronizing rTMS pulses with the ongoing alpha rhythms detected by electroencephalogram (EEG) in the human sensorimotor cortex can lead to a differential modulation of cortical excitability. Specifically, repeated TMS pulses delivered during the high excitability state of the sensorimotor cortex, when alpha-rhythms reach their negative peak, can produce consistent and long-lasting increases in motor-evoked potentials. In contrast, triggering TMS at the low excitability state, when alpha-rhythms reach their positive peak, or at a random phase, does not affect motor-evoked potentials amplitudes. The findings suggest that rTMS must be synchronized with an individual's ongoing brain oscillations to effectively modify brain neural activity (Zrenner et al., 2018). Therefore, if the rTMS stimulation is not delivered at the right time in the ongoing oscillatory network activity, it may not induce the desired synaptic plasticity and, consequently, may not produce the intended clinical effects. Different brain connectivity and oscillation desynchronization are other possible explanation for the failure to modifying left DLPFC excitability with rTMS to potentiate the impact of music on the mood and inconsistency in the result of studies investigating the impact of TMS on the mood by targeting the DLPFC as researchers could successfully apply the alpha-synchronized TMS on the left DLPFC and demonstrate the changes in brain activity (Zrenner et al., 2020).

### 4.3. Conjoint Effect of Music and Neurostimulation

Regarding our findings, we were unable to demonstrate the enhancing effect of rTMS on the impact of music stimuli on the mood. One explanation for our different results can be our different

measurements and objectives. The research conducted by Mas-herrero and colleagues (2018) provided evidence that iTBS can enhance the responsiveness of neural circuits to music, particularly in terms of modulating pleasure (liking) and motivation (wanting) aspects. However, they could not find a direct impact on overall emotional arousal, as measured by EDA. This suggests that iTBS did not induce a general change in the participants' psychophysiology. In the same study, the authors aimed for wanting (purchasing the music excerpts) and liking (real-time rating of the experienced pleasure) variables of music stimuli while our measures were focused on mood changes and emotional arousal after the stimuli which provides crucial insights into the potential therapeutic impact of protocols on mood following each intervention. This disparity in the measurements, the timing of measurements and goals could explain the differences in the outcomes observed between the two studies.As Luber and Lisanby (2014) suggested in their review of 62 studies on the potentiation and performance enhancement impact of rTMS should be done immediately before the task or skill is performed to "prime" the relevant area of the brain for processing related to that task. This can explain our non-significant impact of rTMS on the impact of music since participants did not listen to music immediately after rTMS stimulation due to our EDA recording in between stimuli. One of the mechanisms through which rTMS enhances performance and potency, in addition to increasing the cortical excitability, is to be disrupting or inhibiting less essential parts of one or more functional brain networks that compete with a task, resulting in temporary reorganization of these networks (Luber & Lisanby, 2014). Such reorganization can occur on left/right axis (Hilgetag et al., 2001; Luber & Lisanby, 2014). As previously noted, our findings indicated an increase in positive mood and overall mood, coupled with a decrease in negative mood during the sham iTBS+music session. In the iTBS-only session, we observed a reduction in positive mood and a discernible trend toward decreased overall mood.

The outcomes of these two sessions may elucidate the non-significant improvement in mood observed in the iTBS + music session in which iTBS had decreased the positive mood and the overall mood state and music could compensate these negative changes to an extent. However, these compensatory changes were not sufficient to yield a statistically significant change comparable to the sham iTBS+music session.

Regarding SCL results, our study did not find any significant changes when participants were subjected to iTBS stimulation alone or a combination of music and iTBS. The same explanatory factors that accounted for the results in the music session can also be applied to the iTBS and iTBS+Music sessions. These factors include potential anxiety related to instrument setup, variations in participant attention span, engagement in activities unrelated to the experiment, fluctuations in environmental temperature, emotional states of participants, and the timing of EDA measurements. These variables may have influenced the outcomes in sessions, leading to the absence of significant changes in the measured parameters.

### 4.4. Strength and Limitations

In the present study, we demonstrated the positive impact of music on the mood of a healthy population. Furthermore, we explored the combined effects of iTBS and music as a potential intervention for clinical conditions such as depression and anhedonia. It is important to acknowledge several limitations of this study, which should be considered in future research.

Firstly, the study may have been underpowered to detect significant effects due to the choice of measurements and relatively small sample size number of sessions. Schaller and colleagues (2011) demonstrated the impact of TMS on the mood of forty-four healthy volunteers after nine sessions using Beck Depression Inventory. In contrast our study only involved a single session of iTBS and

a session of iTBS+ music with twenty-four participants. Mood regulation and its neural correlates can be complex processes that may require repeated sessions to produce significant and long-lasting effects. Future research could consider implementing a multi-session design with a bigger sample size to robust findings and increase the generalizability of the results.

Secondly, including EEG measures could provide objective data and a more comprehensive understanding of the effects of iTBS and music on mood regulation. EEG provides a non-invasive method for examining electrical brain activity recorded from the frontal cortex on both the left and right sides and can be an avenue to enhance our comprehension of the neurophysiological impacts of rTMS on emotional processing and mood regulation (Mobius et al.,2017)

Further, the study did not validate the level of induced pleasure by music stimuli before the study. Allowing participants to assess their subjective experiences with the music excerpts before the main study (Salimpoor et al., 2009) is to validate the authenticity of the "happy" playlists used in the research. This pre-evaluation approach would confirm that each participant genuinely would find the music selections enjoyable and that they elicited intense pleasure. By obtaining these individual ratings beforehand, researchers could have a more reliable basis for selecting music that would consistently evoke positive emotional responses in participants. This strategy enhances the internal validity of the study, ensuring that the chosen musical stimuli were aligned with the intended emotional experience for each participant.. Finally, this study only assessed the immediate effects of iTBS and music on mood. It would be valuable to investigate the duration of these effects and whether they persist beyond the immediate experimental session. Long-term follow-up assessments could provide insights into the sustainability of the observed mood changes as previously investigated in related studies (Moulier et al., 2021).

Addressing these limitations in future studies would enhance the understanding of the conjoint and separate impacts of iTBS and music on mood regulation and provide valuable insights into the underlying mechanisms and potential applications of these interventions.

## 4.5. Conclusion

In summary, the study contributes to the understanding of the effects of non-invasive brain stimulation techniques, such as iTBS, on mood of healthy population, and highlights the importance of considering other interventions, such as music therapy, in the design of experimental protocols. Our findings showed that the effects of the experimental protocol on mood changes differed depending on whether the experimental protocol components were used conjointly or separately. The sham iTBS+music session showed a significant improvement in mood state and positive mood and a significant decrease in negative mood. The iTBS-only session showed a significant decrease in positive mood and a slight decrease in overall mood sate, suggesting that iTBS on the left DLPFC may have a negative impact on mood. In the iTBS+music session, Non-significant small trends similar to the sham iTBS+ music session were observed, suggesting that iTBS on the left DLPFC may have decreased the mood while music have compensated it by inducing the positive mood and decreasing the negative mood.

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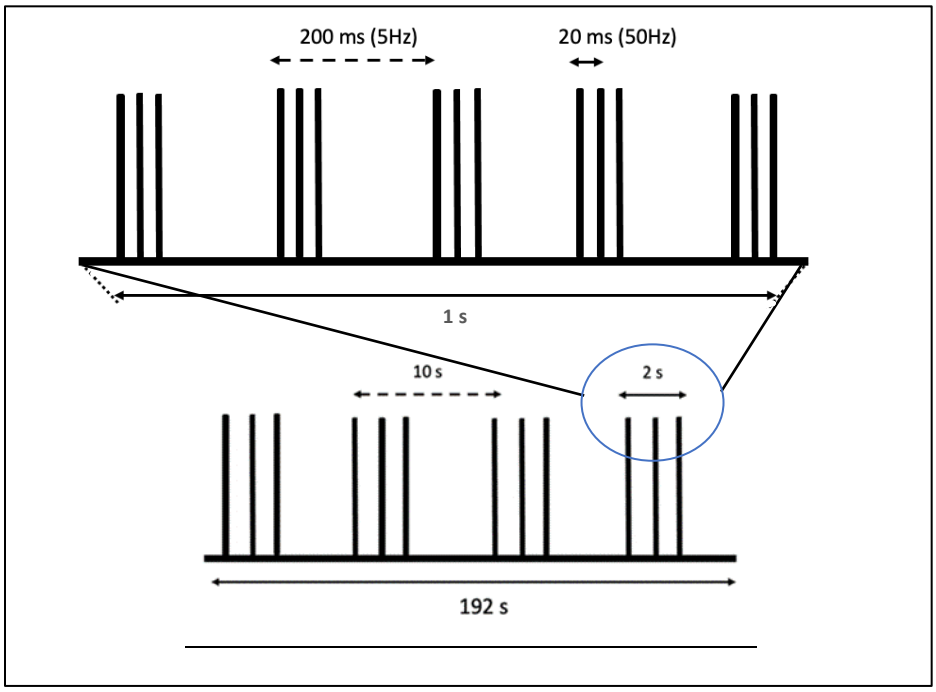
# Appendix A

**Figure 2.** Schematic of Theta Burst Stimulation and iTBS Condition.




*Note.* 3 pulses at 50 Hz, each repeated at 5 Hz. iTBS: 20 cycles of 2 s trains are applied, corresponding to 10 repeated bursts at 5 Hz and consisting of 3 pulses for a total of 600 pulses for 192 s. Each train of pulses will be followed by 8 s without stimulation.

**Figure 3.** Modulation of Self-reported Overall Mood State for Each Session

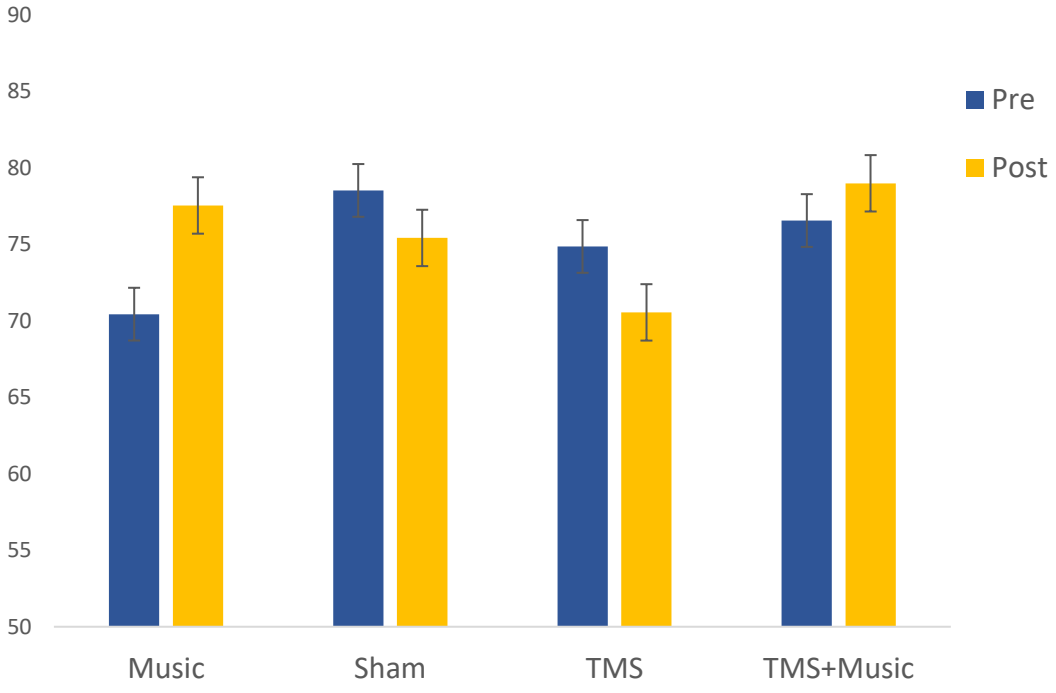



**Figure 4.**Modulation of Positive Mood Adjective for Each Session

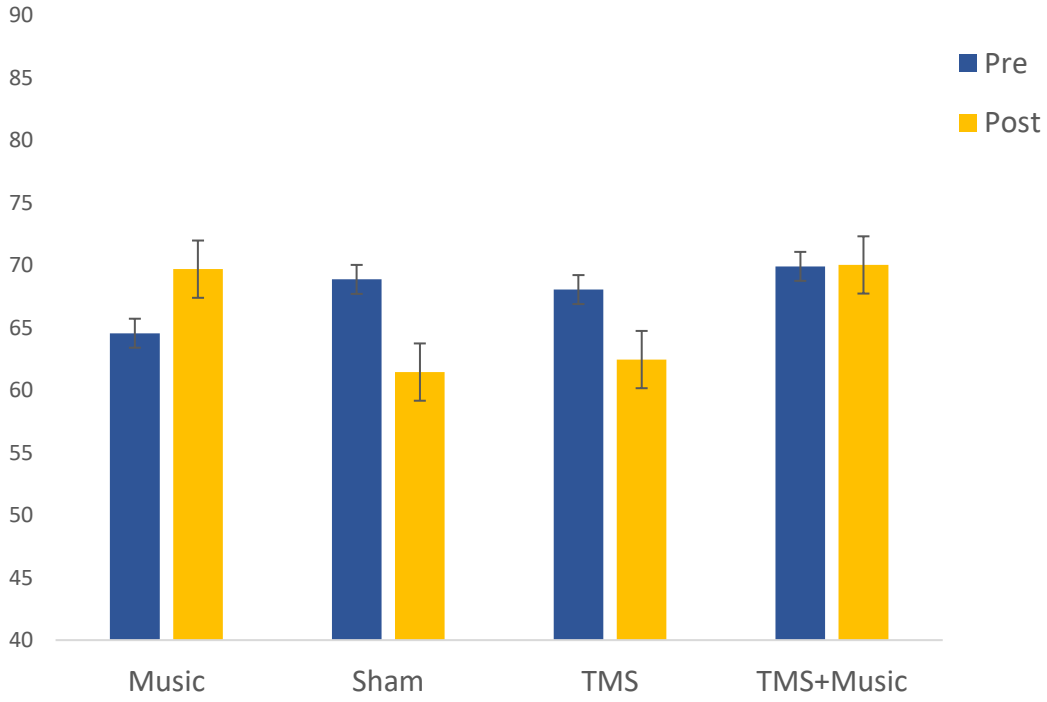


**Figure 5**.Modulation of Negative Mood Adjective for Each Session

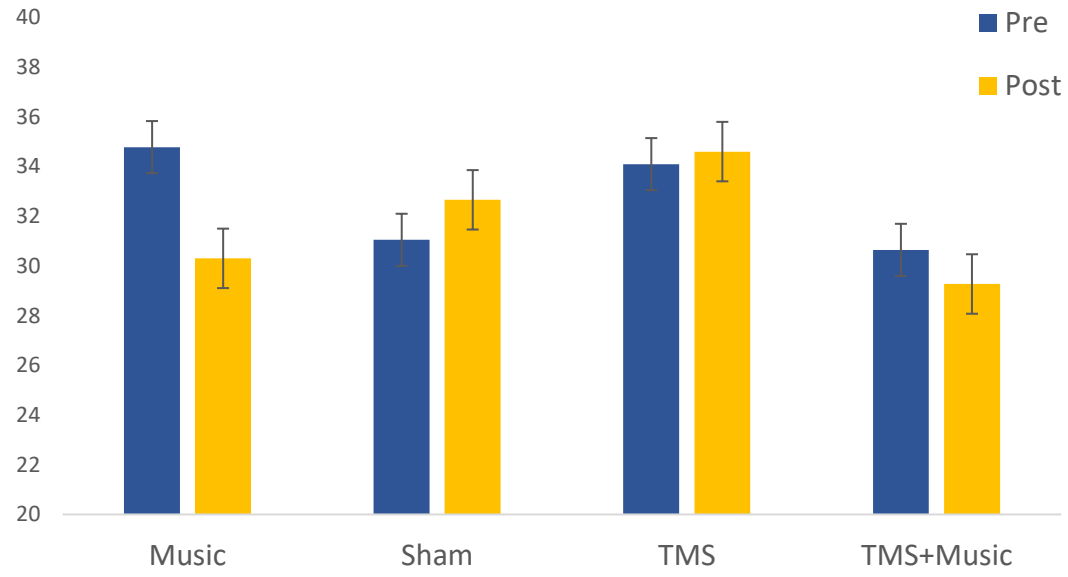
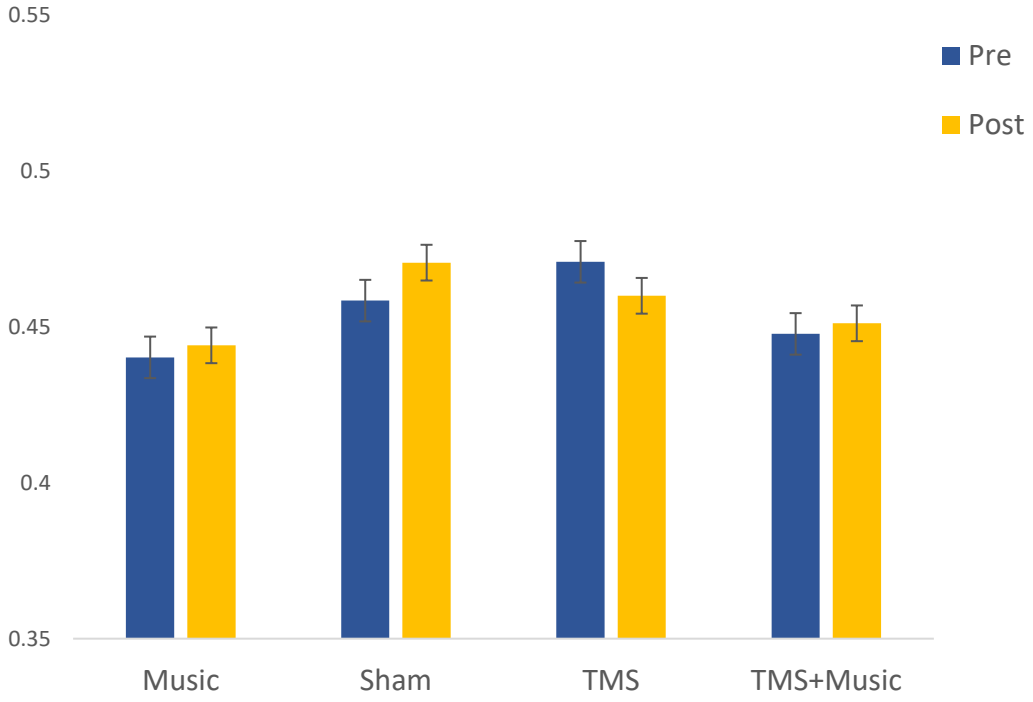



**Figure 6.**Modulation of Skin Conductance Level for Each Session



# Appendix B

**Table 8.** Happy and Pleasant Music Playlist

| | |
|---|---|
| African Queen by Blackface, 2Face | Les Colories by Alex Nevsky |
| Alexandrie Alexandra by Claude Francois | Levitating by Dua Lipa |
| Alien Blues by Vundabar | Liebe zu dritt by Provinz, MAJAN, JEREMIAS |
| All Around The World (La La La) by R3HAB, A Touch of Class | Look At Her Now by Selena Gomez |
| | Lover by Diljit Dosanjh |
| Babooshka by Kate Bush | Man Smart (Woman Smarter) by Harry Belafonte |
| Bad Habits by Ed Sheeran | Message in A Bottle by Taylor Swift |
| Bailamos by Enrique Iglesias | Mi Gente by J Balvin, Willy William |
| Bailando por Ahi by Juan Megan | Mujeriego by Ryan Castro |
| Bam Bam by Camila Cabello, Ed Sheeran | Nazi Joon by Shahram Kashani |
| Be My Yoko Ono by Barenaked Ladies, Michael Philip Wojewoda | Nerdy by PURPLE KISS |
| | No Lie by Sean Paul, Dua Lipa |
| Beautiful Monster by STAYC | No-No Song by Ringo Starr |
| Bei Mir Bist Du Schoen by The Hot Sardines | One Kiss by Calvin Harris, Dua Lipa |
| Bloody Valentine by Machine Gun Kelly | One Last Time by Christopher Jackson, Lin-Manual Miranda |
| Blue (Da Ba Dee) by Eiffel 65, Gabry Ponte | |
| Bones by Imagine Dragons | Paradise by MEDUZA, Dermot Kennedy |
| Bones by Imagine Dragons | Picture Perfect by The Regrettes |
| British Bombs by Declan McKenna | Play Hard by David Guetta, Ne-Yo, Akon |
| Cabin Fever by Jaden | Pompeii by Bastille |
| Chocolate by The 1975 | Quand je vois tes yeux by Dany Brillant |
| Come Around Me by Justin Bieber | Reseaux by Niska |
| Come On Eileen by Dexys Midnight Runners | Rolling in the Deep by Adele |
| Come Together by The Beatles | Rotab by Hassan Shamaizadeh |
| Come With Me Now by KONGOS | Roundtable Rival by Lindsey Stirling |
| Dance Monkey by Tones and I | Rubia Sol Morena Luna by Caramelos De Cianuro |
| Danza Kuduro by Don Omar, Lucenzo | Running Up That Hill by Kate Bush |
| Despacito by Luis Fonsi, Daddy Yankee | Safe and Sound by Capital Cities |
| Dokhtar Bandari by Shahram Kashani | Send Me On My Way by Rusted Root |
| Dragostea Din Tei by O-Zone | September by Earth, Wind and Fire |
| Easy Lover by Philip Bailey, Phil Colins | Shake It Off by Taylor Swift |
| Echame La Culpa by Luis Fonsi, Demi Lovato | She Wants Me Dead by CAZZETTE, AaronChupa, The high |
| El Donia Helwa by Nancy Ajram | |
| Electricity by Silk City, Dua Lipa, Diplo, Mark Ronson | Short Kings Anthem by Blackbear, Tiny Meat Gang |
| Farmer Refuted by Thayne Jasperson, Lin-Manual Miranda | Shower by Becky G |
| | Shut Up and Groove by HEIZE, DEAN |
| Firework by Katy Perry | Sparkling by CHUNG HA |
| Forget About the Joni by Eric Hutchinson | Stay by The Kid LAROI, Justin Bieber |
| Gentleman by Sasy | Still into You by Paramore |

| | |
|---|---|
| Get Around Town by Revolver | Striptease by Carwash |
| Ghost by Skip the Use | Stronger by The Score |
| Girls Like You by Maroon 5 | Sugar by Maroon 5 |
| Got My Mind Set On You by George Harrison | The Less I Know The Better by Tame Impala |
| Grans by Kane Brown | The Motto by Tiesto, Ava Max |
| Halghe Tala by Moein, Hayedeh, Shahram | Three Little Birds by Bob Marley, The Wailers |
| Heaven Falls/ Fall on Me by Surfaces | Thunder by Imagine Dragon |
| Hey Brother by Avicii | Too Funky by George Michael |
| Hypnotize U by N.E.R.D | Until I Found You by Stephen Sanchez |
| I wanna be your slave by Maneskin | Vacation by Dirty Heads |
| I'm an Albatraoz by AaronChupa | Visa Para un Sueno by Juan Luis Guerra 4.40 |
| It's a Beautiful Day by Michael Buble | Waka Waka by Shakira |
| ITIM by Shye | Wake Me Up by Avicii |
| Jimmy by Moriatry | Welcome To The Rock By Joel Hatch, 'Come From Away' Company |
| Joy by Bastille | |
| L'air de rien by Tete | You've Got The Love by Florence and The Machine |
| Last Christmas by Taylor Swift | |
| Last Night by Traveling Wilburys | |

*Note.* This table represents the happy and pleasant music excerpts that were submitted by participants, which were subsequently chosen to be included in the playlists utilized during the sessions.

# Primary Screening Questionnaire

**General Survey. Any information that can be linked to your identity will be used for administrative purpose. This information will not be transcribed in the datafiles. This form will remain confidential and away from your experimental data.**

Name: _____ Age: _____ Gender: _____

Email: _____

Do you wish to be contacted for future studies? (Circle) YES / NO

Are you right or left handed (When using a pen) ? Right-Handed / Left-Handed / Ambidextrous (Both)
Is your supporting foot the Right or the Left? Right / Left / No preference

What is your main language? _____

Which other language do you speak fluently? _____

If you currently have any auditory issues, please list them below (e.g.: otitis, hearing impairment, etc.):

_____

**I. <u>Formal musical training</u>:**

1. Have you ever taken any musical lesson? (All type of lessons included, such as elementary school music class)?

   (Circle) YES / NO

   * If **YES**, please fill section #2 and #3, if **NOT**, please fill section #4

2. Please, write which *instrument you've learned to play or what kind of singing training you have been following*, taking a different line for each instrument (or voice). "Individual lessons" refers to private lessons. "Group lessons" refers to group classes or schools lessons.

| Instrument/Voice | **Individual** lessons (How long?) | How old were you? | **Group** lessons (How long?) | How old were you? |
|---|---|---|---|---|
| 1) | | | | |
| 2) | | | | |
| 3) | | | | |
| 4) | | | | |

3. Please, write down any training you may have in *musical theory*:

| Type (for example, composition) | **Individual** lessons (How long?) | How old were you? | **Group** lessons (How long?) | How old were you? |
|---|---|---|---|---|
| 1) | | | | |
| 2) | | | | |
| 3) | | | | |

**II. <u>Non-formal musical training & participation to musical activities:</u>**

4. Do you have any self-educated musical instrument training, on your own or with a group (with any formal lesson with a teacher)?

| Instrument/Voice | **Individual** lessons (How long?) | How old were you? | **Group** lessons (How long?) | How old were you? |
|---|---|---|---|---|
| 1) | | | | |
| 2) | | | | |
| 3) | | | | |
| 4) | | | | |

5. If you once practiced music, are you still practicing (for example, as a spare-time, formal lessons, performances, etc…)?

(Circle) YES / NO

**If NO:** Since when did you stop (in years)? _____

**Si OUI:** Which instrument are you still playing? _____

Spare-time ( Write down **how many hours per month** and the **instrument**): _____

Formal lessons ( Write down **how many hours per month** and the **instrument**): _____

Non-professional performances ( Write down **how many hours per month** and the **instrument**): _____

Professional performances (paid)
( Write down **how many hours per month** and the **instrument**): _____

6. Do you consider yourself as a professional musician? (Circle) YES / NO

7. Do you listen to music in a regular way? (Circle) YES / NO

If YES, how many hours per day? _____

If YES, what type of music do you listen to (for example, classic, rock)?

_____

8. If you hear a musical note, can you *name* which note it is without using any other note as reference? YES / NO

## TMS Safety and Contraindication Form

Questionnaire to the participants : Transcranial magnetic stimulation

Date : _____ Participant number : _____

Have you ever :

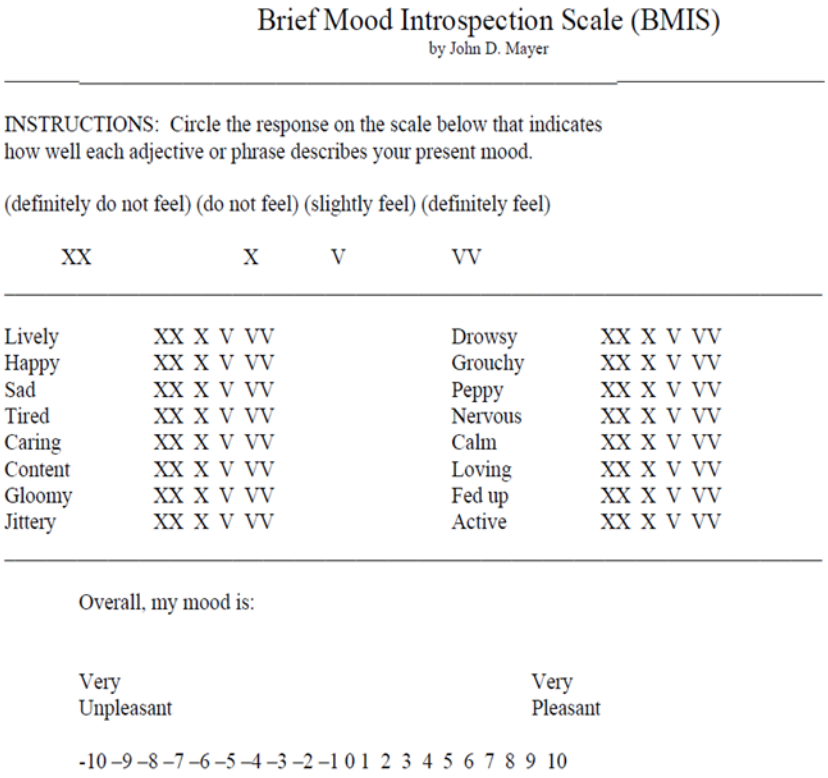
1. Suffered from an epileptic seizure? yes no
2. Had a loss of consciousness without explanation (fainting)? yes no
3. Suffered from a stroke (attack)? yes no
4. Had a severe head injury or a head trauma? yes no
5. Had a head surgery? yes no
6. Had a neurological disease or a brain condition? yes no
7. Had an accident or a disease that could have provoked a brain damage (lesion)? yes no
8. Do you suffer from regular or severe headache? yes no
9. Do you have any piece of metal in your head (except in the mouth) like metal plate, or surgical clips? yes no
10. Do you have any medical implants (pacemaker, cochlear implant)? yes no
11. Do you take any medication regularly? If yes, at the bottom of the questionnaire, please indicate which one? yes no
12. During the last 6 months, have you received cares for alcohol consumption or for other substances? yes no
13. Are you pregnant or there is any possibility of it? yes no
14. Do you have family members who suffer from epilepsy? yes no
15. Do you suffer from tinnitus? yes no
16. Have you ever participated in a study using the transcranial magnetic stimulation (TMS)? yes no
17. Have you ever had a unpleasant reaction because of the TMS? yes no
18. Do you want more explanations about TMS and its contraindications? yes no

If you answered yes at some questions above, please indicate details with the question number.

---

Participant signature: Experimenter signature:

## Brief Mood Introspection Scale (BMIS)



Brief Mood Introspection Scale (BMIS)
by John D. Mayer

INSTRUCTIONS: Circle the response on the scale below that indicates how well each adjective or phrase describes your present mood.

(definitely do not feel) (do not feel) (slightly feel) (definitely feel)

XX X V VV

| | | | |
|---|---|---|---|
| Lively | XX X V VV | Drowsy | XX X V VV |
| Happy | XX X V VV | Grouchy | XX X V VV |
| Sad | XX X V VV | Peppy | XX X V VV |
| Tired | XX X V VV | Nervous | XX X V VV |
| Caring | XX X V VV | Calm | XX X V VV |
| Content | XX X V VV | Loving | XX X V VV |
| Gloomy | XX X V VV | Fed up | XX X V VV |
| Jittery | XX X V VV | Active | XX X V VV |

Overall, my mood is:

Very Unpleasant — Very Pleasant

-10 –9 –8 –7 –6 –5 –4 –3 –2 –1 0 1 2 3 4 5 6 7 8 9 10

**Table 9.** List of Adjectives Utilized on the Visual Analog Scale (VAS):

| **Positive Valence Adjectives** | **Negative Valence Adjectives** |
|---|---|
| Heureux(se)/Happy | Triste/Sad |
| Bienveillant(e)/Caring | Mélancholique/Gloomy |
| Content(e)/Content | Fatigué(e)/Tired |
| Énergique/Peppy | Épuisé(e)/Drowsy |
| Calme/Calm | Nerveux(euse)/Nervous |
| Affectueux(euse)/Loving | Excité(e)/Jittery |
| Vif(vive)/Active | Grincheux(euse)/Grouchy |
| Dynamique/Lively | Agacé(e)/Fed up |
| Souriant(e)/Smiling | Sérieux(euse)/Serious |
| Tranquille/Even-tempered | Agité(e)/Restless |

## Hospital Anxiety and Depression Scale (HADS)

**Tick the box beside the reply that is closest to how you have been feeling in the past week.**
**Don't take too long over you replies: your immediate is best.**

| D | A | | D | A | |
|---|---|---|---|---|---|
| | | **I feel tense or 'wound up':** | | | **I feel as if I am slowed down:** |
| | 3 | Most of the time | 3 | | Nearly all the time |
| | 2 | A lot of the time | 2 | | Very often |
| | 1 | From time to time, occasionally | 1 | | Sometimes |
| | 0 | Not at all | 0 | | Not at all |
| | | | | | |
| | | **I still enjoy the things I used to enjoy:** | | | **I get a sort of frightened feeling like 'butterflies' in the stomach:** |
| 0 | | Definitely as much | | 0 | Not at all |
| 1 | | Not quite so much | | 1 | Occasionally |
| 2 | | Only a little | | 2 | Quite Often |
| 3 | | Hardly at all | | 3 | Very Often |
| | | | | | |
| | | **I get a sort of frightened feeling as if something awful is about to happen:** | | | **I have lost interest in my appearance:** |
| | 3 | Very definitely and quite badly | 3 | | Definitely |
| | 2 | Yes, but not too badly | 2 | | I don't take as much care as I should |
| | 1 | A little, but it doesn't worry me | 1 | | I may not take quite as much care |
| | 0 | Not at all | 0 | | I take just as much care as ever |
| | | | | | |
| | | **I can laugh and see the funny side of things:** | | | **I feel restless as I have to be on the move:** |
| 0 | | As much as I always could | | 3 | Very much indeed |
| 1 | | Not quite so much now | | 2 | Quite a lot |
| 2 | | Definitely not so much now | | 1 | Not very much |
| 3 | | Not at all | | 0 | Not at all |
| | | **Worrying thoughts go through my mind:** | | | **I look forward with enjoyment to things:** |
| | 3 | A great deal of the time | 0 | | As much as I ever did |
| | 2 | A lot of the time | 1 | | Rather less than I used to |
| | 1 | From time to time, but not too often | 2 | | Definitely less than I used to |
| | 0 | Only occasionally | 3 | | Hardly at all |
| | | | | | |
| | | **I feel cheerful:** | | | **I get sudden feelings of panic:** |
| 3 | | Not at all | | 3 | Very often indeed |
| 2 | | Not often | | 2 | Quite often |
| 1 | | Sometimes | | 1 | Not very often |
| 0 | | Most of the time | | 0 | Not at all |
| | | | | | |
| | | **I can sit at ease and feel relaxed:** | | | **I can enjoy a good book or radio or TV program:** |
| | 0 | Definitely | 0 | | Often |
| | 1 | Usually | 1 | | Sometimes |
| | 2 | Not Often | 2 | | Not often |
| | 3 | Not at all | 3 | | Very seldom |

Please check you have answered all the questions

# Music Preference Questionnaire (MPQ-R)

Name/Code: Date:

## Music Preference Questionnaire (MPQ-R)

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**Dear participant, the following questions refer to which music you like to listen to and in which situations you do so. We are aware that we cannot capture your taste in music comprehensively with this questionnaire, as we will doubtlessly have missed out some points that are important to you. However, we would like to ask you to go along with filling in these rough categories.**
**We hope you have fun filling in the questionnaire!**

1. Which of the indicated music styles do you prefer? Please mark your answer from 1 to 5 on the scale *for each music style*:

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Pop:<br>(E.g., "hit parade") | not at all | 1 | 2 | 3 | 4 | 5 | very much |
| Rock:<br>(E.g., Indie, Alternative) | not at all | 1 | 2 | 3 | 4 | 5 | very much |
| Hip Hop:<br>(E.g., Rap) | not at all | 1 | 2 | 3 | 4 | 5 | very much |
| Latin:<br>(E.g., Tango, Salsa) | not at all | 1 | 2 | 3 | 4 | 5 | very much |
| Soul/Funk:<br>(E.g., R'n'B) | not at all | 1 | 2 | 3 | 4 | 5 | very much |
| Hard Rock:<br>(E.g., Heavy Metal, Crossover) | not at all | 1 | 2 | 3 | 4 | 5 | very much |
| Electronic Music:<br>(E.g., Techno, House) | not at all | 1 | 2 | 3 | 4 | 5 | very much |
| New Age:<br>(E.g., Meditation Music) | not at all | 1 | 2 | 3 | 4 | 5 | very much |
| Folk Music:<br>(E.g., Country, Folk) | not at all | 1 | 2 | 3 | 4 | 5 | very much |
| Classical Music:<br>(E.g., Baroque, Romance, Opera) | not at all | 1 | 2 | 3 | 4 | 5 | very much |
| Jazz/Blues: | not at all | 1 | 2 | 3 | 4 | 5 | very much |
| Other: | | | | | | | |
| _____ | not at all | 1 | 2 | 3 | 4 | 5 | very much |
| _____ | not at all | 1 | 2 | 3 | 4 | 5 | very much |

2. Which is your favorite music/music group and what music style would you categorize it as (max. 3)?

   Favorite music/group:_____

   Music style:_____

3. How long do you listen to music on a typical day?

   _____ Hours. _____ Min.

4. For what purposes do you listen to music? Please mark your answer from 1 to 5 on the scale *for each purpose*:

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Relaxation: | never | 1 | 2 | 3 | 4 | 5 | very often |
| Activation: | never | 1 | 2 | 3 | 4 | 5 | very often |
| Distraction: | never | 1 | 2 | 3 | 4 | 5 | very often |
| To reduce aggression: | never | 1 | 2 | 3 | 4 | 5 | very often |
| To work better: | never | 1 | 2 | 3 | 4 | 5 | very often |
| To evoke certain feelings: | never | 1 | 2 | 3 | 4 | 5 | very often |
| To increase certain feelings: | never | 1 | 2 | 3 | 4 | 5 | very often |
| Against boredom: | never | 1 | 2 | 3 | 4 | 5 | very often |
| Against loneliness: | never | 1 | 2 | 3 | 4 | 5 | very often |
| Because of the music: | never | 1 | 2 | 3 | 4 | 5 | very often |
| Other purpose: | | | | | | | |
| _____ | never | 1 | 2 | 3 | 4 | 5 | very often |
| _____ | never | 1 | 2 | 3 | 4 | 5 | very often |

5. On what occasions or in which situations do you listen to music? Please mark your answer from 1 to 5 on the scale *for each option*:

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Disco/Club: | never | 1 | 2 | 3 | 4 | 5 | very often |
| Techno Party: | never | 1 | 2 | 3 | 4 | 5 | very often |
| Concerts (Rock/Pop): | never | 1 | 2 | 3 | 4 | 5 | very often |
| Concerts (Classical/Opera): | never | 1 | 2 | 3 | 4 | 5 | very often |
| As background activity when doing something else (e.g., sports, housework, on the move) | never | 1 | 2 | 3 | 4 | 5 | very often |
| When making music myself (e.g., singing) | never | 1 | 2 | 3 | 4 | 5 | very often |
| When I'm alone | never | 1 | 2 | 3 | 4 | 5 | very often |
| When I'm with friends | never | 1 | 2 | 3 | 4 | 5 | very often |
| Other situations/occasions | | | | | | | |
| _____ | never | 1 | 2 | 3 | 4 | 5 | very often |
| _____ | never | 1 | 2 | 3 | 4 | 5 | very often |

6. Do you *currently* actively make music? Please tick accordingly:

   - ○ no
   - ○ I play an instrument (which one and for how long?):_____
   - ○ I sing in a choir (for how long?):_____
   - ○ other:_____

7. Have you *previously* actively made music?

   - ○ no
   - ○ I played an instrument (which one and for how long?):_____

- I was in a choir (for how long?):_____
- other:_____

8. How important is music in your life? Please mark your answer from 1 to 5 on the scale:

Not at all important 1 2 3 4 5 very important

With the next question, we would like to find out how often and how strongly you experience so-called **chills**. Chills are physical reactions, a shudder or shiver, which spread from the head to the back and/or other parts of the body. These reactions occur in relation to many experiences, e.g. fear, fright or contemplation of art. However, we want to ask you limit your response only to chills that you experience **while listening to music**.

Please state how often you experience chills while listening to music:

not at all 1 2 3 4 5 almost always

If you experience chills, please indicate how intensive your experienced chills are:

hardly noticeable 1 2 3 4 5 overwhelmingly strong

## Additional Questions: (Responses: Yes/No):

- I can find sad music pleasant and enjoyable
- I can find happy music enjoyable and pleasant
- I use happy music to improve my mood
- I use sad music to improve my mood
- Sad music decreases my mood
- Which type of music do you listen to on a daily basis? (Sad/Happy)