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- in collaboration with SoundFocus, Oticon Medical, WS Audiology and Danish Sound Cluster

THE PAPER

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Summary

Evidence, challenges and perspectives for music interventions in health care

Preface

In 2014, Line Gebauer and Peter Vuust wrote a white paper describing the existing applications of music in health care, which has turned out to be relevant for a wide audience and health care professionals. Since then, many new applications have seen the light of day, and the existing literature on the subject has substantially developed in both quality and quantity. For the white paper to stay relevant, we have therefore decided to update it with the latest findings and progress in the field. Thus, in this edition, we have updated and reevaluated the sections on somatic and psychiatric disorders, and well-being of healthy individuals which were included in the 2014 white paper, with new evidence. Furthermore, this edition of the white paper includes the most recent research regarding the effect of music on important health issues such as chronic obstructive pulmonary disease (COPD), multiple sclerosis, dental procedures, pain management, ADHD, pregnancy and birth. Different in this edition is the way that we have classified the level of evidence within each topic. We have adopted the approach developed by Oxford Centre for Evidence-Based Medicine (OCEBM), which is a stringent way of assessing quality of evidence. We hope that this work can be used as a point of reference and as inspiration for using music as a supplementary intervention in health care.

Abstract

Music is rated to be among the top ten pleasures that people value the most in life, but music can do more than just lifting your spirit. A growing number of solid biomedical and psychological studies document the potential of music as a beneficial intervention in various health care settings. In this updated white paper, we describe the brain mechanisms through which music exerts these effects and review the evidence concerning music applications for a range of somatic and psychiatric disorders and for improving well-being in healthy individuals. In some fields, the quality and quantity of studies have reached a level allowing for systematic reviews of randomized controlled trials and meta-analyses of the effect. This development ensures a higher confidence in the results and a better understanding of the efficacy of using music in health care settings. The OCEBM classifies the evidence into five levels which is used throughout this paper. We find high quality evidence for an effect of music on anxiety during operations, dental procedures and for pain management. Similarly, we see systematic reviews documenting a beneficial effect of music for insomnia, stress reduction and for improving various aspects of exercise. In other fields like multiple sclerosis, cochlear implants and autism, we see promising findings, but fewer studies have been conducted and they are of more varying quality, also because of the inherent difficulties in conducting large scale randomized controlled trials in these populations. With this white paper, we hope to provide an overview of existing evidence that may facilitate applications of music and the development of novel technologies that can assist music intervention in the healthcare sector in Denmark as well as internationally.



Global Council on Brain Health (GCBH) presented a new report showing that music can improve brain health and promote well-being"

Introduction

The assumption that the environment is an essential part in the recovery from diseases has recently gained increased attention among health care professionals. Scientific findings showing that environmental sources, such as air quality, lightening, smell, music, art and architecture can improve recovery and well-being in clinical settings have led to new ways of thinking about the lay-out of health facilities. Particularly, music interventions have received extensive scientific interest. Since the publication of the first white paper, numerous initiatives have emerged focusing on the use of music in health care. A recent survey at Danish hospitals found that music initiatives was used in up to 75% of the responding departments (Jensen and Nielsen, 2019). Furthermore, a WHO health report recently synthesized the evidence on the role of the arts in improving health and well-being (Fancourt and Finn, 2019), and in 2020, the Global Council on Brain Health (GCBH) presented a new report showing that music can improve brain health and promote well-being (AARP, 2020). These initiatives reflect a growing evidence base supporting the potential of music interventions in health care settings.

When doing a literature search for scientific publications which include the word "music intervention", we found that 70 papers were published during the year of 2009, 227 papers in 2015, and a total of 753 scientific papers in 2021 (Figure 1). Thus, interest in integrating music into health care settings is blooming.

In this white paper we give an overview of the scientific literature available on music perception and music interventions. There is an excessive amount of studies on music interventions for somatic and psychiatric disorders and general well-being. A total of 4,140¹ papers were identified on the search term "music intervention". To limit the scope of this white paper to particularly promising fields, we have only included topics with the highest amount and quality of empirical evidence. For this update, we have focused on reviews summarizing the effects across multiple studies and evaluated the level of the evidence for each topic using the guidelines for treatment effects provided by the Oxford Centre for Evidence-Based Medicine.

The majority of studies included focuses on passive music listening of recorded musical pieces, either self-chosen or chosen by others. There are, no doubt, numerous well-conducted studies of music interventions with promising findings that are not included here. Therefore, we encourage the reader to use this white paper as an introduction to the possibilities that lie in using music interventions in the health care system, and to explore the growing number of scientific publications on this interesting topic. In this paper, we shall first give a short introduction to what music is followed by an account of brain processing of music. In the second part of the paper, we review the current evidence for the effect and use of music interventions in different somatic and psychiatric disorders and in general well-being. Lastly, we summarize the current state of research in music interventions and provide recommendations for future research and use of music in health care.

 $^{\rm 1}$ Output on the search term "music intervention" in the online scientific database Scopus.com on February 4, 2022.

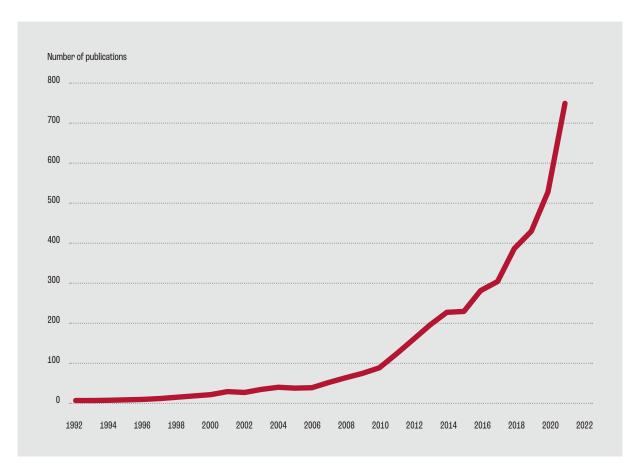


Figure 1: Scientific publications on "music intervention" per year since 1992

The number of publications per year on "music intervention" has increased dramatically. Publication statistics are extracted from the scientific database Scopus.com. A total of 4,140 publications were identified in the search conducted on February 4, 2022. "Though there is great diversity in musical styles and instruments across different countries and cultures, music is universally present in all known human societies and shows surprisingly many similarities across cultures"



MUSIC INTERVENTIONS IN HEALTH CARE · WHITE PAPER

\geq . The building blocks of music

It appears puzzling how seemingly meaningless changes in air pressure can create the strong emotions and significance we experience from listening to music. Yet, the virtue of music making can be tracked about 50,000 years back in time (Huron, 2001). Though there is great diversity in musical styles and instruments across different countries and cultures, music is universally present in all known human societies and shows surprisingly many similarities across cultures. As a consequence of music's universal presence,

many researchers have speculated about music's potential evolutionary utility. There is no firm evidence for the evolutionary value of having music, but researchers have found that musical structure taps into fundamental survival-related mechanisms of the human brain, which might explain why music is so widely present across cultures (Hauser and McDermott, 2003; Patel, 2010; Savage et al., 2021).



2 ↓ ⊥ How music works

Essentially, what makes music 'music', and not just a string of random sounds, is the structure. Just like language relies on grammatical rules for acquiring meaning, music relies on specific structures or syntax (*Patel, 2003; Vuust et al., 2022*). Some structural elements seem to be universally present across different cultures and musical traditions (*Drake and Bertrand, 2001*), whereas others are created by convention of a specific genre or culture (*Cross, 2003; Vuust et al., 2012*). The songwriter, Harlan Howard famously described country

"Music automatically creates certain (conscious or unconscious) expectations in the listener, and these are central for how music manages to create emotions, pleasure and meaning" music as "three chords and the truth", and at least illustratively speaking that pretty much goes for all music. Even though this obviously is a strong simplification, repetition is one of the most fundamental elements of music structure that seems to apply across cultures (*Huron, 2006*). This high level of repetition in music is what allows us, both as listeners and as performers, to learn the musical syntax - just like we spontaneously learn the language we hear as infants. Of course, music is not pure repetition, but variations, and sometimes even innovations, over existing themes.

One of the most studied relationships between statistical regularities of musical structure and brain responses is the tonal system of musical harmony, where EEG (electroencephalography) and MEG (magneto-encephalography) measures, such as the early right anterior negativity (often referred to as ERAN) and the mismatch negativity (MMN), are reliable markers for brain processing of chord sequence expectations in the brain (Garza Villarreal et al., 2011; Koelsch et al., 2001; Leino et al., 2007; Maess et al., 2001).

Musical structures are not fixed, but rely on statistical probabilities, so that some continuations are more likely (have a higher probability) than others given the immediate musical context (Gebauer et al., 2012). Just through listening to music we implicitly learn the statistical probabilities between different notes, which govern the musical structure in our culture (Loui et al., 2010; Saffran et al., 1999). Thus, music automatically creates certain (conscious or unconscious) expectations in the listener, and these are central for how music manages to create emotions, pleasure and meaning (Koelsch et al., 2019b; Vuust et al., 2009; Vuust et al., 2022). Indeed, for a piece of music to be perceived as pleasurable and interesting, it has to find the perfect balance between familiarity and novelty or in other words between repetition and variation.

2, **2** Emotions in music

When asked why they listen to music, people consistently answer that it is because it creates emotions and pleasure. Music emotions are sometimes described in terms of valence and arousal. Arousal describes whether a person is relaxed (low arousal) or alert and energized (high arousal). It covers both physiological activation, such as increased heart rate, blood pressure, respiration and perspiration, and psychological activation, such as alertness and attention. Music is particularly effective in regulating arousal and in inducing a range of different emotions including everyday emotions such as happiness, sadness, surprise and nostalgia, as well as emotions that are unique to music, such as for instance the sensation of swing or groove (Matthews et al., 2019; Matthews et al., 2020; Witek et al., 2014). One thing that is particularly interesting about music is that even emotions which are generally perceived to be negative, such as sadness or fear, can be experienced as extremely pleasurable (Brattico et al., 2016; Sachs et al., 2015).

How music is capable of creating such strong emotions and pleasure is, however, not a simple question to answer. Seven distinct mechanisms have been identified (*Juslin and Vastfjall, 2008*). These are:

(1) **Brain stem reflexes**, which are linked to very fundamental (universal) acoustic properties of the music. This can be compared to the orientation response and the increased arousal (increased alertness, heartbeat, blood pressure etc.) that we all experience when we hear a sudden, loud or dissonant sound. Brain stem reflexes are also central for rhythm perception and the sense of entrainment we feel when listening to a steady beat. Thus, brain stem reflexes are central for music's impact on arousal and can give rise to unpleasant reactions in responses to dissonant or loud/unpredictable music.

(2) **Evaluative conditioning** is when a piece of music becomes associated with an emotion solely because they repeatedly have occurred together in time. So, for instance when kids really like the tune from the Friday evening cartoon it might be because the tune has become associated with having candy.

(3) **Emotional contagion**, which is mirroring the emotional expression of music. In general, emotional expressions in music share several psychoacoustic features with speech (Bowling et al., 2010). As an example, both music and speech, which is low-pitched, slow and have a low sound level are likely to be perceived as sad.

(4) Some music might arouse **visual images**, which creates emotions.

(5) Music might be linked to **episodic memories**. You might for instance experience strong emotions every time you hear the melody you heard when you and your husband first meet.

(6) Cognitive appraisal can be an important part of music listening. You might mentally analyze a piece of music and appreciate its experimental nature or compare it to other versions of the same piece, and this might create a special sort of aesthetic pleasure.

(7) Finally, **musical expectancy** is by many believed to be the most fundamental mechanism behind musical pleasure (*Vuust and Frith, 2008*). Musical anticipation is assumed to create pleasure by establishing, fulfilling or disappointing the anticipatory structures formed in the listener (*Huron, 2006; Meyer, 1956; Narmour, 1991; Vuust and Frith, 2008*).

Mismatch between the musical structure and the listener's expectations have been associated with strong emotions, laughter, awe and music-induced chills (Huron, 2006; Sloboda, 1991). The emotional impact of music is essential for why so many people across the globe use substantial amounts of their time to listen to music. While several universal patterns have been identified, large cultural variations and individual differences exist in the way we perceive music. When thinking about music applications it is relevant to consider whether the effect one is hoping to create is associated with universal, cultural or individual aspect of music. This is central for designing effective products and for modifying existing music products to new markets.

"While several universal patterns have been identified, large cultural variations and individual differences exist in the way we perceive music."

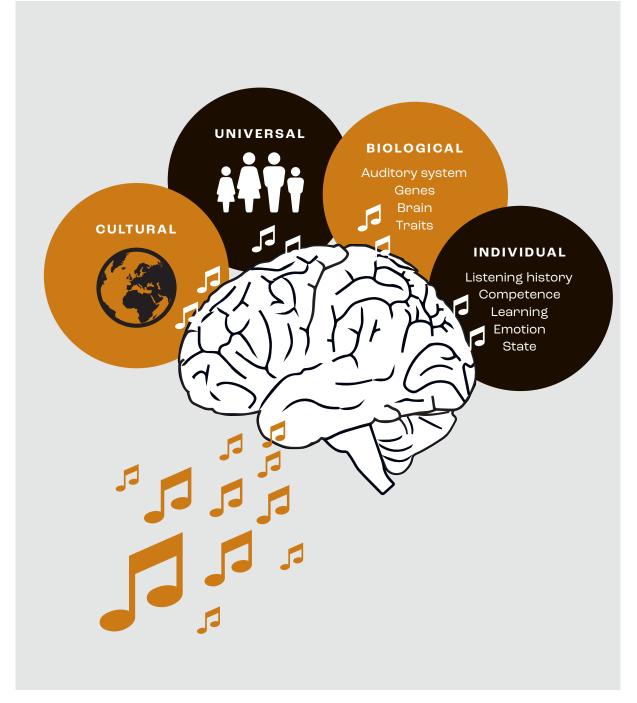


Figure 2: Universal, cultural, individual and biological influences on music perception

When we listen to music, the brain is constantly trying to predict the musical structure based on universal, cultural and individual rules. Thus, when evaluating the effect of music interventions it is necessary to consider whether the intervention is aimed at features that are universal, depend on musical enculturation or rely on individual and maybe even situational factors.

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2 , **3 Universal aspects of music**

There exist numerous universals in the way music is used and in the structure of music (Brown and Jordania, 2013; Jacoby et al., 2019; Mehr et al., 2019). Across cultures music is used for social and religious gatherings, and instrumental music is often combined with singing. People across the world also dance or move to music, and music coordinates and emotionally unites people. Parents sing lullabies for their newborns, and music making is very often one of the earliest activities that infants engage in (Trehub, 2003). Interestingly, research shows that babies respond with relaxation even to unfamiliar lullabies from different cultures, suggesting that lullabies share universal characteristics that infants may be predisposed to respond to (Bainbridge et al., 2020; Trainor, 1996).

In relation to the structure of music, the use of discrete pitches, musical scales, melodic modes (rules for pitch combination) and transposable pitch sequences seem to guide music making cross-culturally (Brown and Jordania, 2013). Across cultures the same musical modulations are used to intensify the emotional expressions. It has for instance been shown that native Africans who have never been exposed to western music can correctly identify happy, sad and fearful expressions in western music (Fritz et al., 2009). In general, music with a high tempo, high pitch or strong dissonance increases arousal and make us more alert and energetic, while music with a slow tempo, low pitch and low intensity will make us calm down (Bernardi et al., 2009; Bernardi et al., 2006). So, for relaxation, we will typically pick slow music with low-pitched instruments, such as a cello or low voices, while upbeat music in a high pitch might be better suited for cleaning or other energetic activities. These effects on arousal fit well with the universal design of our auditory system, which automatically extracts regularities and responds to unforeseen changes in our auditory environment. Overall, studies have found that there is a strong link between the music characteristics and the behavioral context in which the music is used. For example, people

across the globe can correctly identify unfamiliar songs used for dance, healing, lullabies or love songs in small-scale societies (*Mehr et al., 2018*). Interestingly, the use of music therapeutically also seems to be extremely common both across cultures and back in time (*Brown & Jordania, 2013*).

> "In general, music with a high tempo, high pitch or strong dissonance increases arousal and make us more alert and energetic, while music with a slow tempo, low pitch and low intensity will make us calm down"



2,4

Cultural aspects of music

By listening to music from tribes in Africa, who has had very little contact with Western music, for just a few seconds, it becomes apparent that, despite the musical universals described above, large cultural differences exist in musical styles such as is also the case for language. Musical syntax and modes are different. It has been suggested that the rhythmic patterns of languages are mirrored in the rhythmic patterns of the national musical tradition (*Patel and Daniele, 2003; Patel et al., 2006*).



The musical culture that we grow up in and is affected by throughout life has a large effect on the way we perceive music and on our musical taste. Our musical expectations are highly dependent on the statistical regularities we have learned through all the music that we have listened to in the radio, been singing in school, danced to with our first true love, or been playing in the garage (Haumann et al., 2018). When we listen to music from foreign cultures it is readily apparent that this music violates many of the expectations we have learned throughout our musical upbringing. Initially, it can be difficult to decode foreign music. It all sounds the same, because our brain is not prepared to pick up the regularities and variations of this particular musical style. Before we can really appreciate foreign musical styles, we have to learn the underlying statistical structure. When selecting music for a specific intervention, it is therefore crucial to consider the cultural background of the patient, because it might be stressful for people to be forced to listen to music from a cultural tradition that they are not familiar with.

"The musical culture that we grow up in and is affected by throughout life has a large effect on the way we perceive music and on our musical taste."

2, **5 Individual aspects of music**

In addition to variations in musical taste and genre across different cultures, there are also large individual variations within cultures, so that people listen to different kinds of music depending on their personality, social affiliation and age. Certain styles of music are commonly associated with specific values or personality types, and studies from social psychology have shown that we believe that musical taste/preference tells us a lot about another person (Rentfrow and Gosling, 2007). People who score high on the personality trait 'openness to experience' listen to a variety of musical styles outside of mainstream pop music (Dollinger, 1993). Jazz listeners are generally more extrovert, whereas rock and punk music is listened to by rebellious and high sensation seeking personalities (Dollinger, 1993; Hansen and Hansen, 1991; Litle and Zuckerman, 1986; Weisskirch and Murphy, 2004). Similar associations between personality and musical preference are also found in professional musicians, where rhythmic/rock/ band musicians score higher on sensation seeking than classical musicians and experience less stage fright (Vuust et al., 2010). Indeed, belonging to a specific musical sub-culture creates identity and a sense of belonging in a larger social group. This strong identification with a specific genre of music is most dominant in adolescence, where it is a central element in creating a stable identity (North and Hargreaves, 1999). Consequently, the music we listen to during our youth often remains our favorite tunes throughout life. There is, however, a tendency for people to be more inclined to listen to classical music as they grow older (Franek 2008).

Another individual factor that greatly influences music perception is musical training and competence. Years of musical training change the sensitivity of the auditory system. For instance, musical expectations differ between musicians schooled in different musical genres (jazz vs. rock/band musicians vs. classical musicians, (*Vuust et al., 2012*). Thus, the unique impact of the specific musical environment that we grow up in has tremendous impact on how



"The music we listen to during our youth often remains our favorite tunes throughout life"

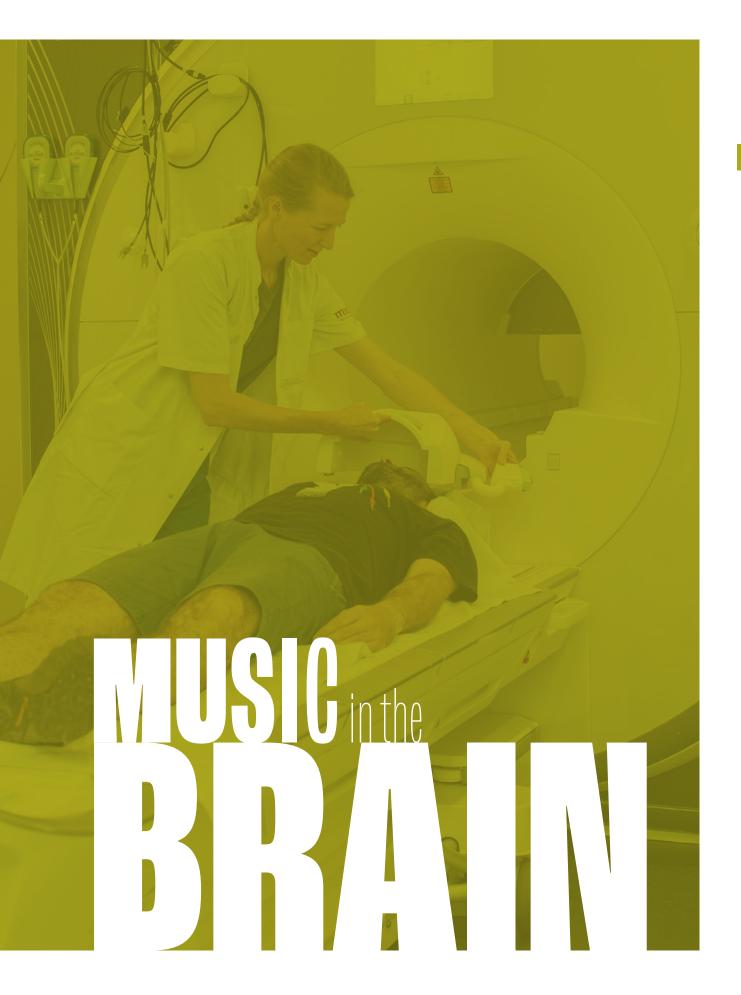
we respond to music and what music we enjoy listening to.

Most people have clear musical preferences about which genre they prefer to listen to, based on their familiarity with that specific style of music. Indeed, most people have probably had a song or melody that they heard over and over



again. Familiarity seems to be very important for our appreciation of music, and it is consistently found that people experience familiar music as more pleasurable than unfamiliar music (*Pereira et al., 2011*). Yet, the degree of familiarity that makes a musical piece appreciated has an optimum, so after hearing the same song too many times we become bored with it, and the music that was previously experienced as highly pleasurable starts to annoy us (*Berlyne*, 1971; *Green et al.*, 2012; Orr *and Ohlsson*, 2005). This is because we learn the musical structure of the particular piece of music too well, and it no longer has the perfect balance between familiarity and novelty.





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Music in the Brain

Whether you prefer to listen to Bob Dylan or Nirvana, music affects you both psychologically and physiologically. Some effects are inherently due to the music itself, while other mechanisms are more closely dependent on extra-musical effects, such as distraction or learned associations, where music might just be one type of stimulation that could provide this effect. Music has a remarkable ability to affect a wealth of distinct brain regions specialized for auditory processing, rhythm and motor coordination, arousal regulation, emotions and pleasure, and cognitive processing (Figure 3). Accordingly, there is an overwhelming literature showing a strong influence by music making on neural plasticity over both short and long term (Chakravarty and Vuust, 2009; Gaser and Schlaug, 2003; Seppänen et al., 2012; Wan and Schlaug, 2010). Likewise, music influences the neurochemical balance of the central and peripheral nervous system (Chanda and Levitin, 2013), and affects bodily and emotional arousal (Rickard, 2004).

The mechanisms through which music exerts its health beneficial effects can coarsely be defined into five mechanisms: auditory, rhythm and motor, arousal, emotion and pleasure, and cognition.

It should, however, be emphasized that though the brain can be divided into auditory, rhythm/motor, emotion and cognition regions for illustrative purposes, such clear borders do not exist in the real, living, human brain. The brain is a complex dynamical system, consisting of around 85,000,000,000 neurons. Each neuron has up to 10,000 synaptic connections with other neurons, resulting in a total of around 60 trillion connections that passes information around in the brain. The assumption that specific information remains in a restricted area of the brain is not true. Rather, neuroimaging research shows that the brain communicates across regions in intricate networks (Bassett and Sporns, 2017; Cabral et al., 2017; Deco and Kringelbach, 2014). Music, and all aspects of music, is processed all across the brain. What is true, however, is that the described brain regions have a higher specialization

for specific information. So, not surprisingly, the auditory cortex indeed has a higher specialization for processing sound that other parts of the brain - but this does not mean that sound is only processed in the auditory cortices.

> "The mechanisms through which music exerts its health beneficial effects can coarsely be defined into five mechanisms: auditory, rhythm and motor, arousal, emotion and pleasure, and cognition."

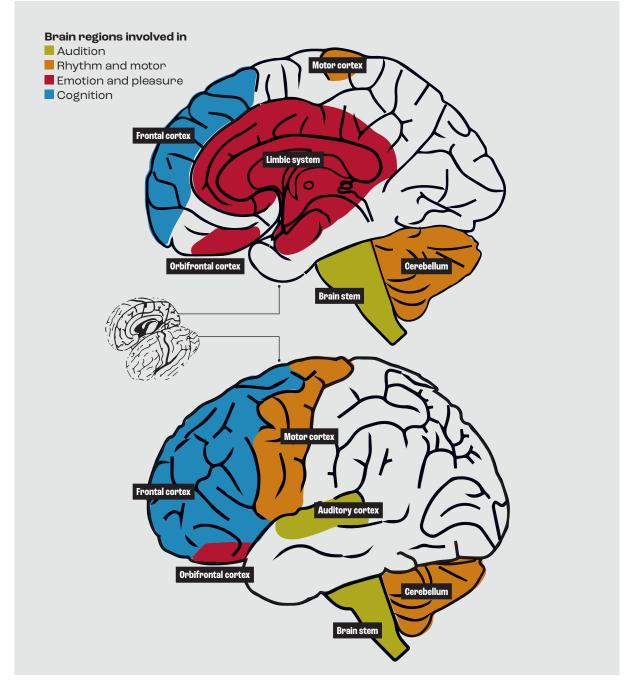


Figure 3: Brain regions involved in music perception

Brain regions involved in audition, rhythm and motor, emotion and pleasure, and cognition. Auditory cortex and the brain stem are involved in audition. Cerebellum and motor cortex are central for rhythm and motor effects of music, but also brainstem and midbrain regions are implicated. Orbitofrontal cortex, and limbic and paralimbic brain regions are fundamental for emotional processing of music, while pre-frontal regions are associated with the cognitive evaluation of music. 23

∃ ⊥ The Auditory System

The most apparent property of music is that it consists of a sound signal, which is picked up by the brain. As such, music is simply changes in air pressure, which travels through the ear canal and reaches the basilar membrane in the cochlea (Figure 4). The oscillations of the basilar membrane are then determined by the frequencies that the music is composed of - high pitches with a short wavelength make the membrane oscillate close to the entrance of the cochlea, while lower frequencies with long wavelengths creates oscillations deeper into the cochlea. In the cochlea, the oscillation of the basilar membrane is translated into neural signals by hair cells. Two kinds of hair cells are present on the basilar membrane. Inner hair cells that transmit the

movements of the basilar membrane to neural signals, and outer hair cells that help amplify soft sounds and improve frequency selectivity. The signal from the inner hair cells is transmitted via the auditory nerve to auditory parts of the **brain stem**, relay structures in the midbrain, and to primary and secondary auditory cortices in the temporal lobe (Figure 3 and 4). The brain stem processes low-level elements of the music, such as localization of the sound in the surroundings based on which of the ears the sound reaches first. The tonotopic organization of the basilar membrane also governs neural processing of sound in the primary auditory cortex, so that different frequencies are processed by different neuron populations. While language typically is

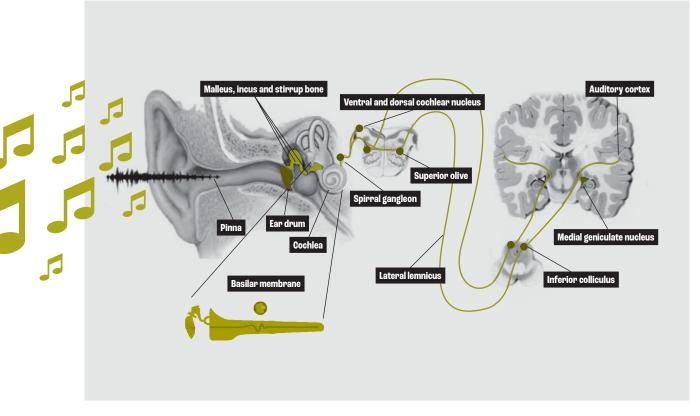


Figure 4: The auditory system

Sound pathways to the brain: Sound creates oscillations in the cochlea, which is transferred into electric nerve impulses and processed at different levels in the brain. Basic auditory processing, such as location of the sound, happens in the brain stem before the nerve impulse reaches the auditory cortex.

processed in auditory regions of the brain's left hemisphere, music is generally more right-lateralized in the brain (*Zatorre et al., 2002*). Thus, the right auditory cortex is primarily concerned with pitch, harmony and melody processing and will for instance 'tell' us if a tune is out of pitch. The auditory stimulation that music provides is central for creating neural changes in auditory brain regions, which can be utilized in patients suffering from tinnitus or people with cochlear implants.

B 2 **Rhythm and Motor systems**

A unique property of music is its ability to translate into motor action. Humans of all ages move spontaneously to music by tapping their feet, bobbing their heads or dance. Surprisingly, rhythm perception and enjoyment of rhythm seem to be a feature that is unique to the human species. Besides, making us want to move, rhythm and tempo in music very often mirror other human periodicities such as breathing, heartbeat, walking or running (Karageorghis and Terry, 2008), and seem to synchronize physiological responses between people (Olsson et al., 2013). Interestingly, studies have found spontaneous entrainment of neural activity to steady beats (Nozaradan, 2014), and this mechanism may underlie the potential of music to facilitate audio-motor coupling.

The rhythmic structure of music is primarily processed in the **brain stem**, cerebellum and motor regions. Besides being one of the early regions in the auditory pathways, the brain stem is essential in processing rhythm and involved in regulating physiological responses such as heart rate, pulse, blood pressure, temperature, skin conduction and muscle tension. Thus, it seems that the rhythmic components of music are of particular importance for its effect on arousal regulation, including changes in heart rate, pulse, blood pressure and respiration (*Bernardi et al.*, 2009; *Bernardi et al.*, 2006).

All parts of the body are represented in the motor cortex. For instance, the hand area of the motor cortex is activated by hand movements and so on, but when listening to music, parts of the motor cortex is activated even when people lie fixated in a scanner unable to move (Chen et al., 2008; Meister et al., 2004). The cerebellum is primarily involved in balance and muscle coordination, but it seems cerebellum is also important for keeping rhythm (Danielsen et al., 2014; Penhune et al., 1998). As such, large brain networks involving both audio and motor areas are involved in music perception, and in particular, music production requires very precise fine tuning of motor skills and auditory feedback loops (Keller et al., 2014; Zatorre et al., 2007) (Figure 5).

"A unique property of music is its ability to translate into motor action. Humans of all ages move spontaneously to music by tapping their feet, bobbing their heads or dance."

Also, rhythm influences the release of neurotransmitters involved in pleasure, namely dopamine (in the **limbic system**), and in arousal regulation, particularly cortisol. The arousal dimension of music is closely linked to both rhythm/motor and emotion/pleasure (*Gomez and Danuser, 2007*). As such, music which reduces arousal can be experienced as relaxing and may reduce negative emotions such as anxiety, while music with more rhythmic complexity can be experien-

ced as energizing and may create strong positive emotions. In a series of studies, it has been found that music with medium rhythmic complexity elicits more pleasure and desire to move to the music compared to low or high complexity rhythms (Matthews et al., 2019; Vuust and Witek, 2014; Witek et al., 2014). These studies suggest that there is a sweet spot with optimal sensation of groove, and this is also reflected in engagement of motor and reward networks in the brain (Matthews et al., 2020).

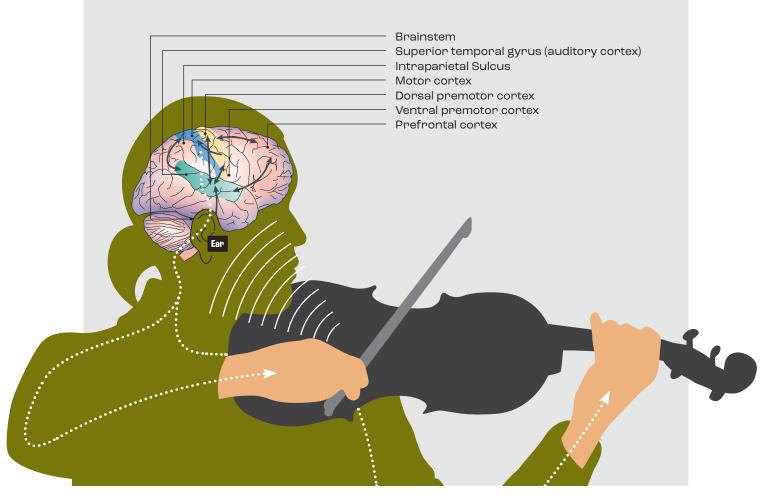


Figure 5: Auditory feedback loops in music production

Music production involves very precise fine tuning of motor skills to produce the desired sound. The produced sound is processed by the auditory system, and it feeds back information to the motor areas to continuously adjust the sound. This process reflects the interwoven nature of music perception and production. Adapted from Zatorre, Chen & Penhune (2007) with permission from the authors.

3,3

Emotion and pleasure

In addition to auditory and rhythmic stimulation, music also creates strong emotions in the listener. The brain structures that mediate music perception and pleasure are thought to be anatomically and functionally separated (Peretz, 2010). The emotional content of music activates limbic and paralimbic brain regions and the brain's reward system (Koelsch, 2020). These structures include amygdala, anterior hippocampus, ventral striatum, nucleus accumbens, anterior cingulate cortex and orbitofrontal cortex. These brain structures also respond when observing emotional expressions from faces, visual scenes or voices (Adolphs, 2001). Particularly amygdala, an almond-shaped nucleus in the limbic system, is central to emotion processing. The amygdala was

"The emotional content of music activates limbic and paralimbic brain regions and the brain's reward system" originally believed to be involved in fear processing only (Davis, 1992), but more recent investigations have shown that the amygdala is equally important in processing of positive emotions and rewards (Baxter and Murray, 2002). For music, the view of amygdala has changed from primary involvement in scary, sad or fearful music. Now, amygdala activation has been found in both fearful and pleasant responses to music, and this may relate to the emerging view of amygdala as a structure important for emotional coordination, a "conductor of the emotion orchestra in the brain" (Koelsch, 2020). The anterior hippocampal formation is densely connected with the amygdala and also located in the limbic system. Together with amygdala, these structures form a network important for emotion processing and particularly for identifying dissonance (Koelsch, 2010). Hippocampus is particularly implicated in memory and learning, as well as novelty and expectedness (Koelsch, 2010). As previously described, memories and learned associations might create strong emotions when listening to music (Juslin and Vastfjall, 2008). In addition, the hippocampus is probably critically involved in the observed preference for familiar over unfamiliar music. However, the hippocampal activation does not seem to be related to memory processes alone, but also emotional processes per se. It has been suggested that hippocampus may be particularly associated with attachment-related emotions and social bonding promoted by music (Koelsch, 2020).

Pleasant music has been found to activate the brain's reward system (Blood and Zatorre, 2001; Brown et al., 2004; Koelsch et al., 2006; Mitterschiffthaler et al., 2007; Osuch et al., 2009; Suzuki, 2009). The reward system includes regions of the limbic system and consists of the **ventral tegmental area**, **nucleus accumbens** and **orbitofrontal cortex** (Berridge and Kringelbach, 2008). In addition to limbic and paralimbic brain regions music also activates parts of the orbitofrontal cortex, where the match between the listener's expectations and the actual musical structure is evaluated (Gebauer et al., 2012; Salimpoor et al., 2013).

Cognition

In addition to the basic auditory properties and emotional impact of music, music listening is often also accompanied by involuntary thoughts, such as episodic memories or associations, or voluntary higher-order cognition such as intellectual appreciation/evaluation of a particularly challenging piece of music. These cognitive functions are primarily associated with regions in the **prefrontal cortex** that are the primary brain areas for executive functions, attention and evaluative processing. Furthermore, music might provide a source for distraction by directing attention towards the music (Dickson and Schubert, 2019; Garza Villarreal et al., 2012), and the nature of the music we listen to can influence the content of our thoughts during mind wandering (Koelsch et al., 2019a). Music is also closely linked with our memory systems, and specific music pieces can often trigger memories of important events from across the lifespan (Jakubowski and Ghosh, 2021). Some studies suggest that musical memory may rely on distinct brain networks since memory for music can be preserved in cases where other memory functions are impaired and vice versa (Jacobsen ${\it et}$ al., 2015).

"Music is also closely linked with our memory systems, and specific music pieces can often trigger memories of important events from across the lifespan"

Brain plasticity

All activities we engage in affect the way our brain is wired, and the evidence for musical activities as inducer of neural changes in the brain has been mounting significantly during the latest decades (Altenmüller and Schlaug, 2015; Dalla Bella, 2016). There are various techniques with which researchers are able to measure the thickness of the human cortex, one is the so-called voxel-based morphometry (VBM), with which it is possible to measure the amount of grey matter, containing the cell bodies of the neurons, in various areas of the brain. By using this method, it has been shown that musicians possessing absolute pitch, the ability to name a tone without the aid of reference tones, are equipped with relatively more grey matter in the Planum Temporale, an auditory area on the dorsal temporal lobe of the left hemisphere, than musicians or non-musicians not possessing absolute pitch (Dohn et al., 2015). By comparing the cortices of twenty professional musicians with the cortices of twenty amateur pianists' and forty non-musicians, researchers also found enlargement of the cortex in pre-motor, motor and sensori-motor cortices, areas likely related to coding from score to music, as well as enlargement in left inferior gyrus, an area considered as a language area by some researchers (Gaser and Schlaug, 2003). Other studies have shown that string players' motor cortex have a larger representation of the left than the right hand, which is not surprising considering the specialized performance of string players' left hand, compared to the right. It is also known that the number of hours musicians practice per day correlates with the absolute and relative size of the cerebellum (responsible for fine-motor skills) compared to the rest of the brain (Hutchinson et al., 2003). In other words, practicing music stimulates and preserves areas essential to music and language. So even though the issue of how to interpret thickness of the cortex is under debate, it appears that daily music practicing leads to structural changes in areas of the brain related to motor, auditory activity, and probably also certain areas essential to language. Musical training involves a rich sensory-motor and multi-modal experience that can shape both brain structure and function (*Dalla Bella*, 2016). These changes can be seen when comparing musicians and non-musicians, but they are also evident in children undergoing music training. In a longitudinal study, researchers found a faster maturation of auditory brain processing as measured with EEG in a group of children attending a musical play school for two years compared to children who attended only shortly (*Putkinen et al., 2019*). These results show that even informal music group activities in children can shape brain function and enhance the development of neural sound discrimination.

B , **C** The impact of music on neurochemistry

The widespread brain processing involved in musical activities is coupled with release of a range of neurochemicals, which are of large importance to the health benefits of music listening. One of the neurotransmitters that have received most research interest in music studies is dopamine. **Dopamine** is involved in two central functions: rhythm and anticipation/pleasure.

Musical pleasure involves the brain's reward system, and dopamine is a key neurotransmitter within these structures. The dopaminergic reward system has consistently been associated with the pleasure experienced from a range of physiological and psychological rewards, from the pleasure of sex and gambling, to the taste of

"All activities we engage in affect the way our brain is wired, and the evidence for musical activities as inducer of neural changes in the brain has been mounting significantly during the latest decades"



"Music can affect cortisol levels in both healthy participants and patient groups reflecting reduced stress responses"

chocolate or the pleasure of a good laugh (Berridge and Robinson, 1998; Frijda, 2010; Georgiadis and Kringelbach, 2012; Kalivas and Volkow, 2005; Knutson and Cooper, 2005; Kringelbach et al., 2012; Mobbs et al., 2003; Morgan et al., 2002; Pfaus, 2009; Robbins and Everitt, 1996). In a brain imaging study in healthy participants, it was found that the intensity of pleasurable music induced chills correlated with activity in the brain's reward circuitry, including the areas high in dopamine receptors (Blood and Zatorre, 2001; Salimpoor et al., 2013). Another study demonstrated a causal role of dopamine in musical pleasure using a pharmacological design. In this study, healthy participants were administered one of three drugs: a dopamine precursor enhancing the level of available dopamine (levodopa), a dopamine antagonist limiting the level of available dopamine (risperidone) or a placebo pill (lactose), before listening to self-selected and researcher-selected music excerpts. The findings showed that the two active drugs led to opposite effects. Measures of musical pleasure were increased in the levodopa sessions, whereas risperidone led to reduced musical pleasure (Ferreri et al., 2019). This suggest that the level of dopamine can modulate the degree of pleasurable responses to music.

Dopamine interacts with other neurotransmitters in the brain - of special interest here is oxytocin and the opioid system. Particularly, oxytocin projections from the amygdala and nucleus accumbens display strong interactions with the dopamine system. Oxytocin is a neurohormone, and has colloquially been dubbed the 'cuddle hormone' or 'love drug', because of its role in reproduction and social bonding. It has been suggested that the capacity to engage in temporally matched interactions, such as music, is associated with the release of oxytocin (Feldman, 2007), and indeed it has been shown that oxytocin can improve precision in interpersonal synchronization (Gebauer et al., 2016). Correspondingly, music is highly efficient in synchronizing movements (Repp, 2005), emotions (Huron, 2006; Juslin and Vastfjall, 2008) and even physiological responses, such as heart rate and blood pressure between

people (Olsson et al., 2013). Temporally-matched interactions are central for music-making, which is pleasurable, motivating and creates social bonds between people who play or listen to music together. Indeed, singing in groups (Grape et al., 2002) and passive music listening (Nilsson, 2009b) lead to an increase in peripheral oxytocin. This might explain why music is so commonly used in social situations, and why we experience a strong sense of community when singing together or being at a large concert, hinting at a possible survival value of musical activities.

Opioids are the body's natural painkillers and are released during music listening (Chanda and Levitin, 2013; Stefano et al., 2004). Opioids might on one hand be central for the calm and relaxation that we can experience from certain music, but at the other hand opioids also seem to be responsible for the strong emotions or pleasure that we experience from music listening. One study found that when the effect of opiates was blocked, people did not experience chills when listening to music (Goldstein, 1980). Thus, opioid activity might be central for the pleasurable responses/experience of music and has been speculated to underlie the analgetic effect of music (Lunde et al., 2019). Yet, a study testing this hypothesis did not find evidence for a role of the endogenous opioid system in the analgesic effect of music (Lunde et al., 2022). Using a pharmacological design, participants listened to either music, nature sounds or noise while being exposed to thermal pain in three separate sessions. In one session, they received the drug naltrexone that blocked the opioid system, and at the other sessions they received a dopamine antagonist or an inactive agent. The results showed no changes in pain ratings with any of the pharmacological manipulations. The only factor that could predict perceived pain was the participants' expectations for pain relief (Lunde et al., 2022). Naturally, this study warrants further investigations to better understand the pathways through which music can alleviate pain.

Finally, music affects the so-called **HPA axis** (hypothalamic-pituitary-adrenal). The HPA axis

is a major part of the neurochemical system that regulates a number of body functions, such as the immune system, arousal and stress, attention, mood and emotion. It is a sensitive system, controlling the release of several hormones and affecting both the central and peripheral nervous system. The HPA axis also controls the hormone cortisol, which is crucial for sleep/wakening cycles, arousal and stress reactions. Various studies have found impact of music on cortisol levels in different experimental and clinical settings (Finn and Fancourt, 2018). In one experimental study, healthy participants underwent a stressful task while cortisol levels were regularly monitored. The results showed that participants listening to relaxation music had a smaller increase in cortisol during the stress task than participants without music (Khalfa et al., 2003). Another study measured cortisol levels in surgery patients under regional anesthesia. Patients were randomized to listen to either instrumental music or a non-music auditory control condition including nature sounds. The results showed that participants in the music group had lower cortisol levels compared to those in the control group (Koelsch et al., 2011). These results indicate that music can affect cortisol levels in both healthy participants and patient groups reflecting reduced stress responses. Overall, the effect of music on neurochemistry is closely linked to the general effect on arousal and contributes to both the relaxing and energizing properties of music.

Bodily responses to music

The autonomic nervous system plays a key role in the regulation of arousal as reflected in measures of heart rate, blood pressure, respiration and perspiration. In many cases, music can modify these physiological measures, which has importance for the use of music for promoting health including the effect of music on both sports and stress reduction.

Cardiac activity is the most common measure in studies investigating bodily responses to music, and several studies have found that music can affect heart rate and heart rate variability in both healthy and patient populations (Koelsch and Jäncke, 2015). Some of the features that have been investigated is the role of tempo and music intensity. Generally, the findings show that a fast musical tempo has a stimulating effect on autonomic nervous activity, whereas slow tempo can facilitate a relaxation response (de Witte et al., 2019; Wright et al., 2022). For example, one study matched the music tempo to the individual heart rate of the participants in one condition, and then in a second condition, participants listened to the same music with tempo increased or decreased by 15%, 30% or 45%. The results showed that the activating effect of listening to ambient instrumental music was modulated by the music tempo as reflected in slower heart rate with lower tempi (van Dyck et al., 2017). Still, the findings on the impact of tempo are mixed, and this may relate to various definitions of what constitutes fast and slow music (Wright et al., 2022). Furthermore, some experimental studies with healthy participants may find a floor effect since it can be difficult to reduce e.g. heart rate below the resting baseline. In contrast, effects of music on heart rate are more consistent in clinical studies where people experience higher levels of stress (de Witte et al., 2019). Entrainment has often been mentioned as a mechanism that would enable the synchronization of bodily rhythms to the beat of the music, but so far, there is no direct evidence for entrainment of physiological measures such as heart rate and respiration to music (Koelsch and Jäncke, 2015).









MUSIC INTERVENTIONS IN HEALTH CARE · WHITE PAPER

How can music be used in health care?

Music impacts our auditory environment, affective states (mood, pleasure, emotions), behavior (movement, social behavior), cognition (distraction, focus and concentration) and physiology (heartbeat, blood pressure, cortisol, oxytocin, dopamine, opioids), and these effects of music can be utilized to improve patient care. When evaluating the utility/applicability of music interventions, it is relevant to consider the following: 1) whether the music intervention is active (dancing, playing, singing or music therapy) or passive (listening to/watching a performance), 2) whether it is a live performance or a recorded piece, 3) whether the music is self-chosen or chosen by health care professionals, music therapists or others. Some studies use a combined selection procedure where patients/participants are offered a choice between a number of predefined playlists selected by professionals (Robb et al., 2011). In the below reviewed studies, we have primarily focused on passive music listening of a

recorded musical piece, either self-chosen or chosen by others, here labeled music intervention (note that studies investigating the effect of traditional music therapy, involving intervention by a specialized music therapist, are not widely included in this review).

Looking at music interventions for somatic and psychiatric disorders and general wellbeing, there are an excessive amount of studies available. It is thus a considerable challenge to summarize it succinctly, owing to the wide range of research questions and methodologies that have been employed. Therefore, we have aimed to include the fields of research which have been most extensively studied, and where the quality of the studies meets scientific standards. We here aim to draw general conclusions based upon a critical appraisal of multiple experimental studies that nonetheless apply different experimental designs, musical stimuli and measures and address a multitude of different questions.

"Music impacts our auditory environment, affective states (mood, pleasure, emotions), behavior (movement, social behavior), cognition (distraction, focus and concentration) and physiology (heartbeat, blood pressure, cortisol, oxytocin, dopamine, opioids), and these effects of music can be utilized to improve patient care."

		INTE	RVENTIO		NISMS		
	Audition Cognition Rhythm/Motor Arousal Emotion Level of evidence						
Somatic disorders							
Operations						Level 1	
Cancer						Level 1	
COPD						Level 1	
Stroke						Level 1**	
Dementia						Level 1***	
Parkinson's						Level 1	
Multiple sclerosis						Level 2	
Tinnitus						Level 2	
Cochlear disorders						Level 3	
Dental procedures						Level 1	
Pain management						Level 1	
Psychiatric disorders							
Depression						Level 2	
Insomnia						Level 1	
Autism						Level 2****	
ADHD						Level 3	
Well-being							
Cognitive enhancement						Level 2	
Exercise						Level 1	
Pregnancy and birth						Level 1	
Stress reduction						Level 1	
Healthy ageing						Level 2	

*Based on the Oxford Centre for Evidence Based Medicine guidelines for treatment benefits.

**Level 1 evidence for improvements in gait function. Level 2 evidence for upper limb rehabilitation and cognition.

***Level 1 for reduction in depression. Level 2 for other outcomes.

****Level 2 evidence for improvements in social communication. Level 3 evidence for other language outcomes.

Level of evidence

Using the framework laid out by the Oxford Centre for Evidence-Based Medicine, we have evaluated the level of the evidence for an effect of the intervention in each field. The rating reflects the confidence that we can have in the results with Level 1 as the most solid evidence. The rating is determined by the type of studies available within each field:

Level 1 Systematic review of randomized trials

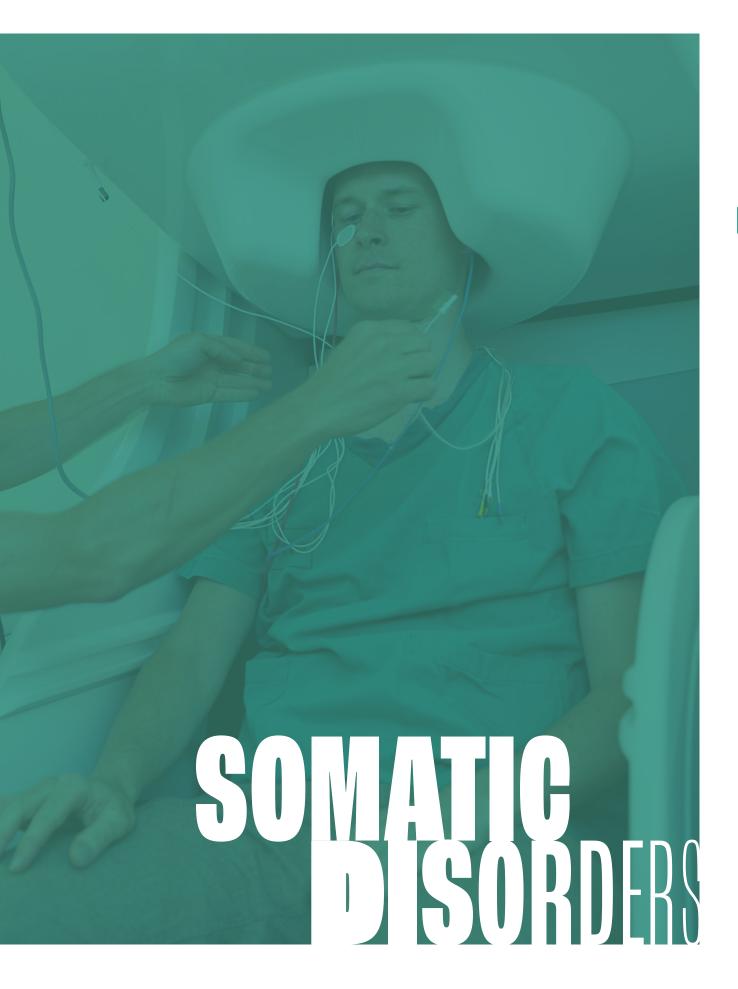
 $\ensuremath{\textbf{Level 2}}$ Randomized trial or observational study with dramatic effect

Level 3 Non-randomized controlled cohort/follow-up study

Based on "The Oxford 2011 Levels of Evidence" by the OCEBM Levels of Evidence Working Group, https://www.cebm.ox.ac.uk/resources

Table 1. Overview of health domains, intervention mechanisms and level of evidence.





MUSIC INTERVENTIONS IN HEALTH CARE · WHITE PAPER

Operations/invasive medical procedures

FACTS: Music interventions reduce anxiety, pain intensity, cortisol levels and sedative requirements before, during and after operations in many patients.

DESCRIPTION: When undergoing medical procedures people often experience increased anxiety and stress in anticipation of the potential painful procedures and recovery they are facing. Music interventions before, during and after invasive medical procedures has been widely studied, and there are numerous randomized controlled trials and several systematic reviews on this subject.

EVIDENCE: Music interventions are reported to reduce anxiety before (Bradt et al., 2013; Buffum et al., 2006; Cooke et al., 2005; Gillen et al., 2008; Hayes et al., 2003; Ikonomidou et al., 2004; Wang et al., 2002; Yung et al., 2003), during (Chang and Chen, 2005; Lembo et al., 1998; Lepage et al., 2001) and after operations (for a review see (Kühlmann et al., 2018)). A recent systematic review of 92 randomized controlled trials indicated that even though music interventions at all timepoints reduced anxiety, the effect may be largest when the music intervention is used before operation (Kühlmann et al., 2018). This review also reported that postoperative music interventions were more likely to reduce pain. Accordingly, music interventions are associated with a decrease in the analgesic and sedative requirements during and after invasive medical procedures (Ayoub et al., 2005; Cepeda et al., 2006; Ganidagli et al., 2005; Harikumar et al., 2006; Koch et al., 1998; Koelsch et al., 2011; Lepage et al., 2001; Rudin et al., 2007; Zhang et al., 2005).

When comparing music listening to anxiolytic drugs, two studies have found that patients undergoing painful operations showed a similar or larger decrease in preoperative anxiety with relaxing music compared to the standard treatment of oral or intravenous midazolam (*Bringman et al., 2009; Graff et al., 2019*). In line with the anxiety reducing effect, music interventions have also been shown to reduce cortisol levels before, during and after invasive medical procedures (Koelsch et al., 2011; Leardi et al., 2007; Miluk-Kolasa et al., 1994; Nilsson et al., 2005; Schneider et al., 2001; Uedo et al., 2004).

Music can be delivered to patients in different ways. One study found that patients undergoing coronary angiographic procedures experienced a positive effect of listening to specially designed music, and that listening to music through an audio pillow was preferred to loudspeakers, by both the patients and staff (Weeks and Nilsson, 2011). Other studies have used noise-cancelling headphones during medical procedures, but there is a risk that this may impair communication between patient and staff (Graff et al., 2019). Thus, it is important that the choice of audio equipment is suitable for the specific situation and hospital setting (Nilsson, 2008). Despite the promising results, research in this field is still limited by both methodological shortcomings increasing the risk of bias and large heterogeneity with regard to the nature of the operations and medical procedures studied. And it is important to notice that not all studies find a significant effect of music interventions for hospitalized patients (Nilsson, 2008). One reason for this may relate to differences regarding the choice of music. For example, one study found no anxiety reduction in a group of patients listening to researcher-chosen music before and during bronchoscopy (Jeppesen et al., 2016). In a follow-up study, the same research team compared the effect of three conditions: 1. researcher-selected music, 2. patients' choice among five playlists of different genres and 3. a no music control group (Jeppesen et al., 2019). All patients were undergoing bronchoscopy, and the results showed a significant reduction of anxiety in the patient-selected music group, but not in the researcher-selected group. This example highlights the importance of taking individual preferences into account. Still, meta-analyses show an effect of both researcher-chosen and participant-chosen music, even though the effect size tends to be higher when participants can choose among different playlists (Bradt et al., 2013; Kühlmann et al., 2018).

How do music interventions before, during and after operations work? The mechanisms underlying the positive effects of music before, during and after invasive medical procedures cover most of the mechanisms described in the introduction, namely auditory masking, positive emotions and reward mechanisms, distraction, familiarity and arousal regulation.

The mere presence of an alternative **auditory** stimulus to the existing noise on the medical ward might give a more relaxed atmosphere. When listening to music the patient can deliberately direct their attention towards the pleasant stimulus and might be less affected by sudden loud noises from the equipment or conversations among the personnel.

Cognitive distraction might also be of central importance to the pain relieving effects of music. Previous studies using pain stimulation in healthy individuals have found that other types of distraction, such as for instance mental arithmetic, are equally instrumental in reducing pain intensity compared to unfamiliar music (*Villarreal et al., 2012*). It does, however, seem that individualized/preferred music is more effective than experimenter-selected music in creating pain relief (*Mitchell and MacDonald, 2006*), and also more effective than other means of distraction (*Mitchell et al., 2006*). Accordingly, there is a correlation between music pleasantness ratings and reductions in pain intensity (*Roy et al., 2008*).

The role of pleasure highlights the importance of positive **emotions**. The engagement of the reward system might therefore be a central contributor to music's anxiety-relieving effects. Also, multiple functional imaging studies have

"Familiar music may be capable of creating a sense of familiarity even in completely unfamiliar settings such as in the case of hospitalizations" demonstrated an association between anxiety and enhanced amygdala activity (*Phan et al., 2002*). Thus, the modulatory effect of music on the amygdala and the overall **arousal** modulation by the music might be relevant for the anxiety-reducing effects. Accordingly, significant reductions in **cortisol** levels have been found after postoperative music listening (*Nilsson, 2009a*), suggesting reduction of stress and anxiety. Finally, music also provides beauty and aesthetic experiences (**Cognition**), which many, especially hospitalized patients may not have energy to pursue elsewhere. However, these aspects of music intervention have not been widely investigated.

In general, familiar music has the highest impact on emotional responses and activity in the reward system (Pereira et al., 2011a). Another central element is that familiar music may be capable of creating a sense of familiarity even in completely unfamiliar settings such as in the case of hospitalizations. Listening to familiar music might give a sense of control over an otherwise completely unpredictable environment. Nonetheless, the most common type of music interventions in studies of operations/invasive procedures is where the patient chose from a selection of music compilations offered by the researcher. Few studies have used individualized musical material, and it is unclear if the beneficial effect is larger if patients bring their own music (Kühlmann et al., 2018).

IN SUMMARY: Systematic reviews and meta-analyses provide Level 1 evidence for positive effects of music interventions on anxiety, pain and sedative requirements before, during and after invasive medical procedures, and no studies report adverse effects. This provides strong support for utilizing music during elective medical operations, particularly patient-preferred music. It should, however, be noted that the effect of music varies between studies, but the potential of music to reduce the need for sedatives and anxiolytics, even if only by a small amount, may still have major clinical implications.

5, 2 Cancer

FACTS: Music interventions have a positive impact on anxiety, mood, pain and fatigue in cancer patients. In addition, music may have beneficial effects on heart rate, respiratory rate and blood pressure.

DESCRIPTION: Cancer can affect most organ systems in the body, leading to a variety of cancer types with varying severity and prognoses for the patients. Nonetheless, most cancer diagnoses are associated with high levels of anxiety, rumination, and numerous painful procedures for the individual. Music interventions have been used to alleviate symptoms and treatment side-effects.

EVIDENCE: Anxiety and depressive symptoms are associated with having a life-threatening disease, such as cancer. It is estimated that 20-50%of cancer patients experience severe anxiety, and 50-75% have depressive symptoms. Music interventions provide significant anxiety reduction when applied during cancer operations, bone marrow biopsy, mastectomy and when the music is played directly before chemo- and radiation therapy (Bradt et al., 2016; Bro et al., 2018; Zhang et al., 2012). Furthermore, RCT studies have found that music interventions have positive effects on mood in cancer patients (Bro et al., 2018), and some studies also find an improvement in depressive symptoms, but the results are inconsistent across studies and thus should be interpreted with care (Bradt et al., 2016).

Besides the affective consequences of going through cancer treatment, cancer often causes severe pain, not only from the disease itself, but also from numerous injections, blood draws and invasive procedures. A systematic review found a large pain-reducing effect of music interventions in cancer patients (*Bradt et al., 2016*), and single studies also indicated that music may reduce the need for anesthetics and analgesics. Furthermore, studies have found that music may reduce fatigue in cancer patients and reduce heart rate, respiration rate and blood pressure (*Bradt et al.,* 2016). On average heart rate was reduced with three to four beats per minute, and respiration rates were reduced with an average of two breaths per minute.

The observed improvements in anxiety, mood, pain and fatigue are important as these are essential aspects of quality of life. The results are generally consistent across studies, yet, the quality of the existing studies is still limited, and more high-quality studies with larger sample sizes are needed.

How do music interventions in cancer treatment work? Like other operations and invasive procedures (see section 5.1 above), the mechanisms underlying the effect of music interventions in cancer patients are most likely positive emotions and reward mechanisms, arousal regulation and cognitive factors like distraction and associations with the music. A recent study evaluated the music ability of the included patients and found that this was not a determining factor for the effect (Bro et al., 2019). Still, it remains unclear if other aspects of music appreciation or sensitivity to music may play a role. The impact of music on physiological measures such as heart rate and respiration suggest an arousal-regulating effect of music in cancer patients, but though other fields of research have found that music promotes relaxation and reduces stress this has not been widely investigated in relation to cancer. Psychological stress seems to be linked to up-regulation of inflammatory processes that promote tumor growth, and potential use of music to reduce stress should aim for early interventions, but more research is needed to evaluate if such applications are valuable.

IN SUMMARY: Findings regarding the use of music interventions during cancer procedures overall seem to be consistent and well-replicated across studies. With a number of systematic reviews in this field, there is Level 1 evidence for beneficial effects of music on anxiety, mood and pain in cancer patients. Besides, the research

"Music interventions provide significant anxiety reduction when applied during cancer operations, bone marrow biopsy, mastectomy and when the music is played directly before chemo- and radiation therapy"

methods used seem appropriate for generalizing findings to everyday clinical implementations. The majority of these studies allow patients to select pre-recorded music before the medical procedure, and patients listen to the music in headphones during and after the procedure (see Table 1 and 2 in (Archie et al., 2013)). Meanwhile, most empirical studies only investigate the effect of music in restricted situations such as during operations or chemotherapy, but the effect of music interventions on a larger time scale remains to be investigated more fully. Findings from quality of life studies are not consistent, and methods vary considerably from study to study (including live music sessions, music therapy or passive listening). Besides the short-time administrations commonly used pre- or peri-operatively, no guidelines exist for the frequency, duration or type of music used in interventions aimed at cancer patients.

5.3

Chronic Obstructive Pulmonary Disease (COPD)

FACTS: Group singing can improve health and quality of life in adults with COPD

DESCRIPTION: COPD is a lung disease characterized by long-term breathing problems and poor airflow. The condition typically worsens over time and causes difficulties with everyday activities such as walking or getting dressed. Consequently, COPD is often associated with reduced quality of life, anxiety and social isolation. COPD is estimated to affect 174.5 million people worldwide, and it is considered the third leading cause of death worldwide (*Lozano et al., 2012*).

EVIDENCE: Studies have evaluated the effects of singing for adults with COPD and found positive effects of group singing on health-related quality of life, anxiety and depressive symptoms (*Lewis et al., 2016; Liu et al., 2019*). To address if the effects were specific to singing, a randomized controlled study compared weekly group singing to a weekly film club and found a positive effect on health status only in the singing group (*Lord et al., 2012*). In addition to improvements in breathing technique, participants in the singing group also reported benefits in terms of mood, enjoyment and social support (*Lord et al., 2010; Lord et al., 2012*).

Yet, a systematic Cochrane review points out that the quality of the existing studies is not optimal, and there is a need for larger studies to determine the effect of singing compared to stan-

"Singing involves training a sustained exhalation and breath control similar to respiratory approaches used to reduce breathlessness in people with COPD" dard rehabilitation (*McNamara et al.*, 2017). The largest study to date has recently been conducted by Mette Kaasgaard at Center for Music in the Brain in Denmark in collaboration with the Respiratory Research Unit, Region Zealand comparing the effect of weekly group singing training to standard physical rehabilitation. The study included 270 COPD patients and showed that singing training led to the same improvement as physiotherapy on a 6-minutes walking test (*Kaasgaard et al.*, 2021). Thus, these results support the use of singing training in COPD rehabilitation.

How do music interventions for patients with COPD work? Singing involves training a sustained exhalation and breath control similar to respiratory approaches used to reduce breathlessness in people with COPD (Gosselink, 2004). As such, singing training can affect your physical functions. When you learn to sing, you train the respiratory muscles, including diaphragmatic breathing, breath co-ordination and improved posture, and this may lead to improvement in respiratory outcomes and health-related quality of life (McNamara et al., 2017). Furthermore, emotional aspects are also important. Singing can enhance mood, distract attention, relieve stress and provide social cohesion, as reported by qualitative studies investigating the experiences of people with COPD involved in a group singing program (Lord et al., 2010; Skingley et al., 2014). Thus, group singing may also alleviate some of the psycho-social consequences of COPD which can be an additional factor of motivation for participation.

IN SUMMARY: Singing for lung health has received a growing interest the last years, and two systematic reviews provide Level 1 evidence suggesting a beneficial effect of singing training on health-related quality of life. One large RCT found that singing training was non-inferior to standard physiotherapy rehabilitation in improving physical capacity. Future studies should replicate this finding using large sample sizes and comparing the effect to standard rehabilitation.

5,4 Stroke

"A systematic review and meta-analysis of 38 studies involving 968 stroke patients found medium-to-large effects of rhythmic auditory cueing on gait velocity, stride length, cadence and postural stability"

FACTS: Rhythmic cueing is beneficial for gait rehabilitation and postural control in stroke patients, and music interventions also show a positive effect in the rehabilitation of upper limb function. Musical intonation therapy seems promising to facilitate speech recovery in patients after stroke, but the evidence base is still limited. Music listening might improve cognitive functions and prevent negative mood in stroke patients.

DESCRIPTION: Stroke causes severe damage to the brain regions that have been without oxygen supply during the blockage or hemorrhage of the blood vein. Stroke patients often lose control of the functions undertaken by the affected brain region and might be paretic (unable to walk or move certain parts of the body) if parts of the motor cortex are affected, or aphasic (unable to speak or understand speech) if parts of the auditory and frontal cortex are affected. Thus, rehabilitative interventions often focus on improving/regaining speech, cognitive abilities and motor control.

EVIDENCE: Rehabilitation with focus on improving gait in hemi-paretic patients has found that rhythmic cueing, i.e. by a metronome or by a rhythmically simple instrumental piece of music, shows positive effects on gait function (Wittwer et al., 2013). A systematic review and meta-analysis of 38 studies involving 968 stroke patients found medium-to-large effects of rhythmic auditory cueing on gait velocity, stride length, cadence and postural stability (Ghai and Ghai, 2019). The results of this review suggest a training dosage of 20-45 minutes' sessions for three to five times a week for optimal effect. Rhythmic cueing has also been shown to improve timing, velocity and acceleration of arm movements in stroke patients (Whitall et al., 2000). Similarly, other studies show beneficial effects on upper limb motor rehabilitation, and by integrating motor and multimodal stimulation music interventions show beneficial effects in rehabilitating

arm paresis after stroke in both sub-acute and chronic patients (*Grau-Sánchez et al., 2020*; *Sihvonen et al., 2017*). Here, one approach is music-supported therapy, in which fine and gross movements are trained through playing music instruments. In such active rehabilitation efforts auditory-motor coupling plays an important role, since patients practicing with muted instruments show smaller improvements than those receiving auditory feedback from the instrument (*Tong et al., 2015*).

Having had a stroke affecting one or more of the brain's language areas can result in aphasia, but even patients who are unable to speak a word can often sing the lyrics of songs. This has been known for more than 100 years and has led to the development of melodic intonation therapy as a useful intervention for aphasia (Schlaug et al., 2010). Melodic intonation therapy includes intensive training in singing of sentences, instead of speaking, while tapping the left hand (Norton et al., 2009). Studies show that intelligibility and naturalness of speech is improved after melodic intonation training in patients with aphasia (Johansson, 2011). Only small randomized studies have been conducted, and the results suggest a positive effect on language production in subacute stroke patients (Van der Meulen et al., 2014), but less clear effects for patients in the later stages post stroke (Van Der Meulen et al., 2016). Yet, these studies should be followed up by full-scale randomized controlled trials to clarify the effect and optimal timing of the intervention.

Besides, rhythmic cueing, music-supported therapy and melodic intonation therapy, music can also be used as an 'enriched environment' to improve recovery of patients more globally. One study found improved verbal memory, focused attention and less depression in patients with middle cerebral artery stroke after listening to their favorite music every day during two months compared to listening to audiobooks or not getting any intervention (*Särkämö et al., 2008*). The positive effects of daily music listening on cognitive rehabilitation were recently replicated by a similar trial (*Baylan et al., 2020*).

How do music interventions for stroke work?

The mechanism underlying improved performance by rhythmic cueing is probably a direct sensory-motor coupling, where **rhythmic** cues drive motor action directly possibly through neuronal entrainment, without much involvement of cognitive modulation or initiation. This is supported by the fact that rhythmic cues add stability in motor control immediately and does not require learning. Rhythmic cues may thereby increase symmetry of muscle activation and facilitate even timing of gait or arm movements. Such direct sensory-motor coupling most likely goes through brain stem neurons to **motor regions** in the brain.

Melodic intonation therapy facilitates **plastic brain** changes of the right arcuate fasciculus, a fiber bundle connecting language areas in the left hemisphere of the brain, so after melodic intonation therapy parts of language processing seem to be transferred from the left to the right hemisphere (*Zipse et al., 2012*). In addition, tapping with the left hand during melodic intonation therapy activates sensorimotor and premotor cortices on the right side that might prime articulation (*Johansson, 2011*). Neuroimaging studies of music-supported therapy have found increased activation and connectivity between auditory and motor regions of the brain, suggesting plastic brain changes related to improvements

"A neuroimaging study investigated the brain regions associated with long-term music memory and found that these regions, anterior cingulate gyrus and the ventral pre-supplementary motor area, were particularly well preserved in patients with Alzheimer's disease despite a general pattern of cortical degeneration" in motor function (*Ripollés et al., 2016*). Similarly, the improvements in cognition and mood after daily music listening were associated with increased grey matter volume in prefrontal and limbic regions of the brain, supporting the view that in addition to behavioral improvements, music listening can also facilitate neuroanatomical changes in stroke patients (*Särkämö et al., 2014a*).

Importantly, the facilitating effect of music on focused attention was more pronounced in patients with damage to the language-dominant hemisphere (*Särkämö et al., 2008*), suggesting that some types of patients gain more from music interventions than others.

IN SUMMARY: Music-based rehabilitation strategies for stroke patients have focused on motor control, speech and cognitive abilities. With regard to motor control, studies show consistent improvements of gait function in stroke patients after music interventions using the method of rhythmic cueing. Level 1 evidence documents the effect and suggests that the frequency and duration of the intervention influence the outcome. Studies addressing upper limb rehabilitation find beneficial effects of interventions such as music-supported therapy involving motor rehabilitation through playing music instruments. Audio-motor coupling through neuronal entrainment seems to be an essential mechanism, and neuroimaging studies show that neuroplasticity underlies the behavioral effects. With regard to speech rehabilitation in stroke, studies have focused on melodic intonation therapy that show promising results. There are, however, only few randomized controlled trials providing Level 2 evidence, and more research is needed to confirm the results. One of the main challenges in rehabilitative physiotherapy is to keep people motivated to do repetitive exercises for months and months, sometimes with minor results. Here music might be particularly useful because it enhances the pleasure and motivation for completing training and can have positive effects on mood too.

5,5 Dementia

FACTS: Music interventions may improve affective, social, cognitive and physiological symptoms in patients with dementia.

DESCRIPTION: Dementia typically affects elderly people, and the prevalence is found to double between 65 and 80 years. According to the WHO around 50 million people have dementia worldwide in 2019 with almost 10 million new cases every year. Dementia is marked by progressive memory impairments in combination with cognitive disturbances and is often accompanied by a range of affective reactions such as agitation, depression and/or aggressiveness. There is no cure for dementia, but the progression of the disorder can be slowed down by medication. The main challenge for health care professionals working with people with dementia is to promote quality of life and an active day-to-day life for the patients.

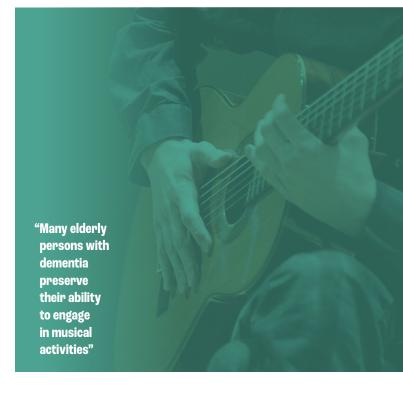
EVIDENCE: A review including both randomized and non-randomized trials found positive effects of music interventions on cognitive symptoms (attention, category fluency and autobiographical memory) and physiological symptoms (heart rate, breathing rate and blood pressure), with the patient's preferred music being the most effective (Vasionyte and Madison, 2013). A more recent systematic review included only RCT studies and found evidence for a reduction of depressive symptoms with music-based interventions, but no clear results for quality of life, cognition and behavioral problems (van der Steen et al., 2017). Yet, this review included a wide range of music and music therapy interventions. One small review including four RCT studies focused on individualized music listening interventions and found preliminary evidence of a beneficial effect on behavioral and psychological outcomes such as agitation, anxiety and depression (Gaviola et al., 2020). Yet, no meta-analysis was carried out as only few studies reported on each outcome.

Individual studies report additional positive effects. For example, one study found that listening to individualized/preferred music for 30 minutes a day, significantly reduced anxiety levels in a group of patients suffering from dementia (Sung et al., 2010), while two recent pilot studies indicate that music listening can improve sleep quality in adults with dementia (Jespersen et al., 2020; Weise et al., 2020). A randomized controlled trial included caregivers to enhance the use of singing or music listening in everyday care. Eighty-nine persons with dementia and their caregivers were randomized to singing, music listening or usual care with weekly singing or music listening coaching sessions for 10 weeks (Särkämö et al., 2014b). The results showed a beneficial effect of both singing and music listening on mood and cognitive function compared to the control group. Singing additionally promoted working memory and caregiver well-being, whereas music listening improved quality of life. Correspondingly, a qualitative study found that music enabled people with dementia to participate in activities that were stimulating and personally meaningful (Sixsmith and Gibson, 2007). They also found music to be a source of social contact and belonging, which gave people a sense of empowerment and control in everyday situations. Other qualitative studies have provided evidence that music contributes to positive self-esteem, enhances feelings of competence and independence, and lessens the experience of social isolation in older people in general (Creech et al., 2013; Hays and Minichiello, 2005). It is worth noticing that the benefits of music found in some of these studies do not seem to be specific to people with dementia, but can benefit elderly people all together.

How do music interventions for patients with dementia work? The mechanism underlying the effect of music interventions in dementia seems to be cognitive engagement such as eliciting memories and associations, as well as social and emotional functions of music (*Baird and Samson*, 2015; Särkämö, 2018). For example, a neuroimaging study investigated the brain regions associated with long-term music memory and found that these regions, anterior cingulate gyrus and the ventral pre-supplementary motor area, were particularly well preserved in patients with Alzheimer's disease despite a general pattern of cortical degeneration (Jacobsen et al., 2015). For implementing music interventions with dementia patients, it is worth considering that many elderly people might have hearing loss, and that reduced attentional control can make unwanted sounds more difficult to exclude. Therefore, it seems central that the person with dementia is in control of the music intervention. Also, the positive effects of music interventions on loneliness suggest that many people with dementia can benefit from group interventions. Listening to music together, or maybe even singing or playing instruments, might release oxytocin in the brain and promote feelings of social belonging in dementia patients. The positive effects of music interventions may not be entirely specific to music, since other pleasant activities may be equally valuable in improving function in persons with dementia (Baird and Samson, 2015).

IN SUMMARY: Though results are mixed, there seems to be a great potential for music interventions in patients with dementia (Narme et al., 2014). One systematic review provides Level 1 evidence for a reduction of depressive symptoms with music interventions, but for other outcomes, the results are more mixed. Randomized controlled trials and observational studies provide Level 2 evidence of a beneficial effect of music interventions on cognitive function, behavioral problems and physiological measures. Studies consistently find that preferred music is more effective than standardized music, and it seems particularly important to address individual preferences in music interventions for dementia (Vasionytė and Madison, 2013). One set of guidelines exists for using and evaluating the effect of music in patients with dementia (Gerdner and Schoenfelder, 2010). However, many studies on the effects of music intervention in dementia suffer from poor methodological quality (i.e. small sample sizes and failing to have proper

control groups or randomization). In addition, data from studies using music therapy (a therapeutic process) and non-therapy music interventions (e.g. music listening, choir singing) are often collapsed in meta-analyses making the findings hard to interpret. Yet, the existing studies suggest positive effects of both passive interventions involving music listening and active interventions involving music making. Many elderly persons with dementia preserve their ability to engage in musical activities (Baird and Samson, 2009), such as humming or tapping to a beat, even at late stages of the disorder, so even though they often suffer from illnesses other than dementia and have reduced dexterity in general, music might be readily accessible to most patients. Thus, more research is needed to investigate the effects of active music engagement, such as drumming, dancing and singing in people with dementia.



5.6

Parkinson's Disorder

FACTS: Music interventions improve motor function, cognitive and emotional symptoms in patients with Parkinson's disorder.

DESCRIPTION: Parkinson's disease is characterized by progressive cell death of dopaminergic neurons in the basal ganglia and is associated with severe motor dysfunction, cognitive decline and emotional flattening.

EVIDENCE: Music interventions for Parkinson's disease have primarily focused on enhancing motor function, and systematic reviews show a positive effect of rhythmic cueing on gait parameters such as gait velocity and stride length (*de Dreu et al., 2012; Ghai et al., 2018*). These positive effects on gait may also prevent falls (*Thaut et al., 2019*). Still, there are individual differences in the degree to which patients experience improvements with rhythmic cueing interventions. Studies suggest that these individual differences relate to the rhythmic skills of the patients so that patients who are better able to synchronize their movements to a beat benefit more from the intervention (*Bella et al., 2017; De Cock et al., 2018*).

Rhythmic auditory stimulation is used as a pacemaker during gait training, and the rhythmic cues can be provided with music or a metronome, but music has been found to have a superior effect compared to metronome cues (Wittwer et al., 2013). Training duration varies between 20 and 60 minutes per session with a frequency of 1 to 5 sessions per week. The total duration of the intervention periods is also different in different studies, and it remains unclear what dose, frequency and duration are needed for an optimal effect. Another interesting finding is generally improved motor function after listening to a preferred piece of music (Sacrey et al., 2011). Overall, focusing on the enjoyment of moving to music instead of the current mobility limitations of the patient seem to have a positive effect on the motivation to engage in rehabilitation exercises.

A number of studies have also looked at the effect of dancing on motor and cognitive function

in Parkinson's patients. The studies have focused on a variety of dance genres including tango, Irish set dancing and contact improvisation, and the results indicate positive effects of dance on gait, timed up and go test performance and global cognition as summarized by two systematic reviews (Kalyani et al., 2019; Shanahan et al., 2015). The quality of the evidence is limited by moderate risk of bias and relatively small sample sizes. Furthermore, there are still too few trials to determine the effect of specific types of dance intervention or the most beneficial music. A third type of music intervention includes singing to improve speech, functional communication and quality of life in people with Parkinson's disease. Parkinson's is often associated with speech changes and vocal fatigue, and singing might provide a useful intervention for alleviating these symptoms and in addition, communal singing can also provide meaningful social contact and thus train functional communication and increase quality of life. Few studies have been conducted in this field, but a review found beneficial effects of singing on speech in five of seven studies (Barnish et al., 2016). Yet, randomized controlled trials are needed to establish the effect.

How do music interventions for Parkinson's disorder work? External rhythmic cues seem to facilitate movement, potentially by engaging the brain mechanisms controlling timing, sequencing and coordination of movements such as the cerebellum and basal ganglia (Koshimori and Thaut, 2018; Schwartze et al., 2011)(Rochester et al., 2010). Even in Parkinson's disorder where degeneration of movement centers in the midbrain is widespread, the ability and urge to entrain with rhythms seem to be preserved (McIntosh et al., 1997). A part of the explanation could be that the external rhythmic cue compensates for the impairments in internal rhythm generation (Bella et al., 2017). Another mechanism may relate to the fact that emotional and pleasurable music can cause midbrain dopamine release, which might cause improvement in Parkinson's patients who

suffer from dopamine depletion in the midbrain (Sacrey et al., 2011).

IN SUMMARY: Overall, studies show a beneficial effect of music interventions using rhythmic cueing on gait parameters in Parkinson's patients. Systematic reviews of randomized controlled trials provide Level 1 evidence of this effect, but the optimal duration and frequency of the interventions remain unclear. Other studies have assessed the effects of dance interventions and Level 1 evidence suggests positive effects on walking and global cognition, even though the results are limited by methodological shortcomings and small sample sizes. Evidence on singing interventions for speech impairments is still limited, but non-randomized studies provide Level 3 evidence suggesting a positive effect. When considering music interventions for Parkinson's disease, it should however be acknowledged that the recognition of emotions in music may change in Parkinson's patients, especially in the more severe stages of the disease (Lima et al., 2013; van Tricht et al., 2010). Since the emotional impact of music seem to be what makes us enjoy listening to music, the pleasurable and motivating power of music might be reduced in some patients.

"Systematic reviews show a positive effect of rhythmic cueing on gait parameters such as gait velocity and stride length"

5, 7 Multiple Sclerosis

FACTS: Music interventions can improve motor functions in persons with multiple sclerosis, including walking parameters and hand dexterity.

DESCRIPTION: Multiple sclerosis is caused by degeneration of the myelin sheets covering the nerve cells in the brain and spinal cord. This damage can disrupt the signals of the nervous system and lead to different physical and mental symptoms, including fatigue, sensory disturbances, motor impairments and impaired cognitive functioning. The number of people affected varies around the world from less than 5 to more than 30 persons per 100,000 persons. Disease onset is often between the age of 20 and 40, making multiple sclerosis one of the most common neurological diseases in the young adult population.

EVIDENCE: Music has been used as intervention to improve both walking abilities and hand dexterity in persons with multiple sclerosis. An early pilot study suggested a positive effect of rhythmic auditory cueing on gait parameters in 10 patients with multiple sclerosis (Conklyn et al., 2010). Recently, two randomized controlled trials have demonstrated a positive effect of rhythmic-cued motor imagery on walking speed and distance using both music and metronome for rhythmic cueing (Seebacher et al., 2017, 2019). Both music-cued and metronome-cued motor imagery also improved fatigue and quality of life, but music-cued motor imagery was more effective (Seebacher et al., 2017). Sensory-motor synchronization was suggested as mechanism of action, and this is supported by a series of studies investigating gait synchronization to music and metronome (Moumdjian et al., 2019a; Moumdjian et al., 2019b; Moumdjian et al., 2019c). In one study, persons with multiple sclerosis were asked to synchronize their steps to the beat for 3 minutes of either preferred walking tempo or systematically increased tempi. The researchers found that participants could walk at a higher tempo with less fatigue with music (Moumdjian et al., 2019b). In another study, the

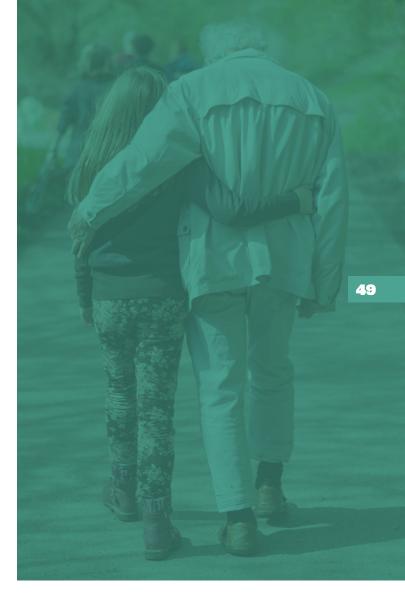
researchers found that intentional synchronization to the beat was more efficient than spontaneous synchronization in a 3 minute walking test (*Moumdjian et al., 2019c*). These results suggest that both motor imagery with music and intentionally coupling walking to music could be a promising walking training strategy for persons with multiple sclerosis.

In addition to research on walking parameters, one study has investigated the effect of playing keyboard with and without auditory feedback on hand rehabilitation in 19 persons hospitalized for multiple sclerosis rehabilitation (Gatti et al., 2015). Participants in this study were randomly assigned to playing finger movement sequences with and without sound for 30 minutes per day for 15 days. The results showed that the group playing keyboard with auditory feedback experienced significantly larger improvement in the functional use of their hand than the group with no auditory feedback (Gatti et al., 2015). Thus, playing keyboard seems to be a useful method for recovering hand dexterity in persons with multiple sclerosis.

How do music interventions for multiple

sclerosis work? Similar to the beneficial effect of rhythmic cueing on gait parameters in Parkinsons' patients, the improved walking abilities in persons with multiple sclerosis are linked to audio-motor coupling. Audio-motor coupling entails that the steps of the walker (motor system) and the beat of the music (auditory system) interact and become aligned in time. This synchronization process is called entrainment, and it engages alternative neural pathways (Moumdjian et al., 2019a; Thaut, 2015). These mechanisms seem to be preserved in multiple sclerosis and may thus counterbalance the disruption of nerve signals caused by de-myelination.

In addition, the **emotional** aspects of music have been highlighted. Moving to music is generally perceived as pleasurable (*Witek et al.,* 2014), and the richness of the music stimulus may increase motivation and thereby explain the



"The researchers found that participants could walk at a higher tempo with less fatigue with music"

superior effects of music compared to a metronome. Similarly, the keyboard playing task was perceived as more motivating by participants receiving auditory feedback than by those doing the finger movements with no sound (*Gatti et al.,* 2015). Music playing may also facilitate activity-dependent **neuroplasticity**, including changes in brain structure and function, as seen in healthy individuals receiving music training (*Sihvonen et al.,* 2017).

IN SUMMARY: Music-based interventions for multiple sclerosis is a relatively new and rapidly growing field, with a number of randomized controlled trials and experimental studies published. This Level 2 evidence suggests beneficial effects of music interventions for improving walking abilities and hand dexterity in persons with multiple sclerosis.

5,8 Subjective Tinnitus

FACTS: Several music interventions for tinnitus exist, such as hearing devices with built-in-music generators, portable devices with modified music spectrum, music making/singing and "notched" music. All interventions are supported by clinical studies, but only few are randomized controlled trials. Many different management strategies are used in clinical practice, but individuals have highly variable responses, and evidence for benefit in most cases has not yet been conclusively shown (*Hall et al., 2011*).

DESCRIPTION: Subjective tinnitus is known as a phantom sound. It involves the conscious perception of an auditory sensation such as noise or ringing sound in the absence of a corresponding external stimulus. Tinnitus can be constant or intermittent, and many patients experience more than one sound. It can be localized to one or both ears, or centrally within the head. Between 10% and 15% of the adult population suffer from tinnitus, and for some the condition can have a significant negative impact on the patients' emotional state and quality of life (Bhatt et al., 2016). The main risk factor is hearing loss, but this association is not straightforward as some people with troublesome tinnitus have normal hearing, and many people with hearing loss do not report tinnitus (Baguley et al., 2013). Decreased sound tolerance (hyperacusis) is a common accompanying symptom, and tinnitus is also associated with increased levels of anxiety, depression, stress, lack of concentration, and insomnia.

Although cochlear abnormalities and most commonly sensorineural hearing loss (SNHL) could be the initial source of tinnitus, the subsequent maladaptive neural reorganization of the auditory pathways and auditory cortex seems to contribute to the generation and maintenance of tinnitus (*Norena, 2011*). Tinnitus is also seen as a plasticity disorder in the sense that it is a result of the brain plastic adaptation to the decreased auditory input due to peripheral damage. This increased central auditory activity is believed to cause tinnitus perception (*Kaltenbach et al., 2005*). **EVIDENCE:** Since there is no cure available for tinnitus, most interventions aim at alleviating the tinnitus sound or accompanying symptoms, or in other words, mitigate the reactions to tinnitus. Sound stimulation or sound enrichment is often used in tinnitus therapies to help the patient habituate to the tinnitus sound. Other types of sound therapy focus more on the tinnitus suppression, with the sound individually tailored to the hearing loss and tinnitus characteristics to interrupt the maladaptive neuroplasticity driving the tinnitus sensation.

Use of the amplification is often recommended for tinnitus treatment, and several studies have shown how amplification in itself is effective in the treatment of tinnitus (Kochkin and Tyler, 2008; KochKin et al., 2011; Searchfield, 2005). Methods of sound stimulation for tinnitus treatment most commonly use a broadband noise as stimuli, but also other sounds such as music are used, and among a list of nine treatment methods tinnitus patients report that after hearing aid treatment, treatment with music is the treatment with the highest percent of efficacy (KochKin et al., 2011). Music compensated to an individual's hearing loss and with additional broadband mask in the frequency of the tinnitus has been used to reduce sensitivity to tinnitus. In this context, music is used to provide relaxation and distraction from the tinnitus and to induce positive emotions. Over time it was found to lead to reduction of tinnitus awareness and a induce a sense of control over the tinnitus (Davis et al., 2008). In another approach, hearing aids with a build-in fractal music generator has also been used for tinnitus treatment. Studies show significant reductions in tinnitus-related distress over six months when counseling is combined with the use of the hearing aids with fractal music (Johansen et al., 2014; Simonetti et al., 2018; Sweetow et al., 2015; Tyler et al., 2017). Finally, other researchers have focused on chronic tinnitus patients listening to self-chosen, enjoyable music, which was modified ("notched") to contain no energy in the frequency range surrounding the individual tinnitus

"Sound stimulation or sound enrichment is often used in tinnitus therapies to help the patient habituate to the tinnitus sound."

frequency. They found significant reductions in both tinnitus loudness and tinnitus-related auditory cortex-evoked activity in the group of patients who had listened to music (Okamoto et al., 2010). This study has been followed up by two randomized controlled trials. In one study participants with tinnitus were randomized to receive classical music that was either unaltered (control group) or spectrally modified based on individual tinnitus characteristics (intervention group). After 3, 6 and 12 months, participants in the intervention group reported lower levels of tinnitus distress compared to the control group (Li et al., 2016).

How do music interventions for tinnitus

work? In general, the tinnitus is perceived worse in quiet environments. The tinnitus can be masked by external sounds, but such a masking may be intolerably loud. Masking can give instant relief, but will not in itself give any longterm effect. A partial **auditory** masking reduces the contrast between the tinnitus sound and the background sound. The uncomfortable inner sound is replaced by a less disturbing external sound. The effect is that the perceived loudness of the tinnitus signal can be reduced, and finally this gives the patient a sense of being in control. Over time this can help the patient to habituate

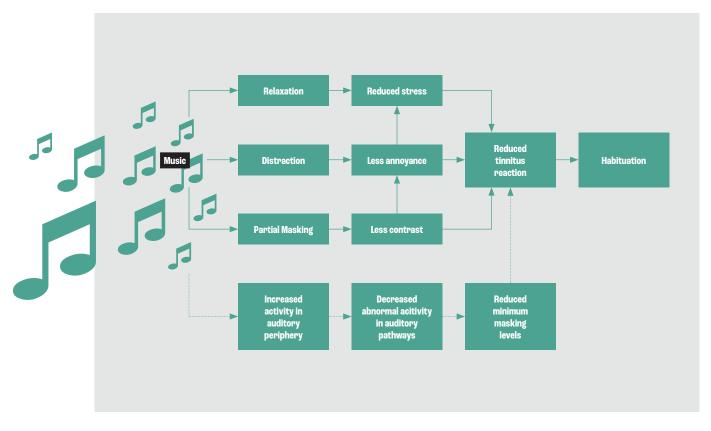


Figure 6: The effect of music on tinnitus reactions

Music may reduce tinnitus reactions both through relaxation, distraction and partial masking. The path with the dotted lines shows how sound stimulation, and thus music, can be used to compensate for the lack of peripheral auditory input and thereby potentially reduce the abnormal activity in the auditory pathways and tinnitus loudness (Kaltenbach et al., 2005).

to the tinnitus and thereby reduce the tinnitus reaction of the patient. Sound stimulation is also used to **distract** attention away from the tinnitus sound.

The main mechanism underlying the effect of 'notched' music on tinnitus is through neural plasticity. The neurons in the auditory cortex, which are not stimulated due to the notch, are presumably suppressed via lateral inhibitory inputs originating from surrounding neurons (Okamoto et al., 2010). This might contribute to the neurons being less easily activated over time and potentially also to a reversal of the maladaptive plasticity of the auditory cortex, such that the deprivation from auditory input in the frequency range of the tinnitus have change the neurons' connection strength and over-activity (Stein et al., 2015). In general, tinnitus interventions are more effective when applied early after tinnitus onset (Theodoroff et al., 2014), and this may also be important for the efficacy of music interventions (Pienkowski, 2019). The mechanisms of music when used as sound stimulation in a tinnitus treatment are shown in figure 6.

IN SUMMARY: Different music interventions for tinnitus have been studied, including music as masking, hearing aids with fractal music and "notched" music that may enhance neural plasticity in the affected auditory area. Studies suggest positive effects of these interventions, but few randomized controlled studies exist, limiting the quality of the evidence. Most studies provide Level 3 evidence, and two RCT studies provide level 2 evidence for a beneficial effect of "notched" music.

Cochlear Implants (CI)

FACTS: Music interventions with cochlear implant (CI) users aim to improve the encoding, perception or appraisal of music. Recent technological advancements attempt to overcome or bypass the device limitations when transmitting music, but the field is still under-researched. While there are clear significant positive clinical effects of music training, the degree of benefit is variable. There remains a need for high-quality randomized controlled trials to confirm the effectiveness of music as a rehabilitation tool for CI users.

DESCRIPTION: A CI is a surgically implanted device for children and adults with severe permanent hearing loss who do not receive adequate benefit from hearing aids. In 2016 there were more than 170,000 CI users in Europe including both adults and children (*De Raeve et al., 2020*). CIs work differently than hearing aids. Rather than turning sound up like a hearing aid, they bypass the natural transmission of sound and convert acoustic signals into electrical signals which are delivered directly to the auditory nerve. The CI is made of external and internal components, see Figure 7 for an illustration of a CI.

EVIDENCE: Music represents a substantial technical challenge for CIs as it is typically a highly complex acoustic signal containing multiple simultaneous harmonic and inharmonic sounds. CI users perceive some aspects of music better than others; they are often as good as their normal hearing counterparts in the perception of rhythm but are less accurate in the perception of pitch and timbre. CI users prefer solo instruments over ensemble or orchestra music and prefer simple and regularly structured music (e.g., pop or country) over complex musical arrangements (e.g., classical music) (Jiam et al., 2017; Nogueira et al., 2018; Riley et al., 2018). These findings are also reflected in studies using electroencephalography (EEG) to detect automatic brain responses to changes in musical features such as pitch, timbre, intensity and rhythm. Studies

"Cl users perceive some aspects of music better than others; they are often as good as their normal hearing counterparts in the perception of rhythm but are less accurate in the perception of pitch and timbre"

have reported intact neural abilities for music processing in both adult and adolescent CI-users (*Petersen et al., 2020; Petersen et al., 2015; Timm et al., 2014*), even though the neural responses were reduced in amplitude compared to normal hearing controls, particularly for pitch.

When it comes to improving music perception and appreciation in CI users, there are two primary approaches; refining the encoding of the signal that is delivered through the device and improving the listener's ability to decode the incoming signal using musical training. In the encoding approach, some techniques aim to enrich the information carried by the electric signal itself by enhancing the harmonic information and their temporal nuances. Other techniques aim to improve the quality of the encoding of the signal, specifically to reduce and control the electrical and neural spread of excitation to reduce channel interaction. The results of these studies are promising; however, while many studies reported better spectral resolution and improvements in speech perception, the benefits for individual listeners have been mixed. A review discussing the recent advancements of CI signal processing technology for music can be found in Nogueira et al (2018). Alternative approaches attempt to complement audition with other senses (e.g. vison and touch) and have demonstrated benefits of providing tactile information for improving speech perception in noise (Fletcher and Verschuur, 2021) and music (Fletcher, 2021).

Music training has been popular as an intervention with CI users both because of the sociocultural significance of music but also because music is thought to enhance processing at multiple levels of the central auditory system (e.g., Looi et al., 2012). Training with music has been shown to improve the ability of CI listeners to discriminate musical pitch, identify melodic contours, recognize and identify familiar melodies, identify the timbre of musical instruments, and improve overall music appreciation and enjoyment (Looi et al., 2012). For example, a behavioral 6 months' one-to-one musical ear training program on CI users found a pronounced improvement on music perception and high levels of joy from engaging in musical activities (Petersen et al., 2012). Compared with adults, children with CIs have shown the greatest benefits from music training, particularly singing and instrument playing (Gfeller, 2016). Several studies have shown that music training is not only effective for improving the perception of music but that learning often generalized to improvements in speech understanding abilities and quality of life (Ab Shukor et al., 2021; Torppa and Huotilainen, 2019). Still, the evidence in this field is limited due to the lack of sufficient control groups/tasks and insufficient numbers of test participants (McKay, 2021), and there remains a need for high-quality randomized controlled clinical trials to properly evaluate the effectiveness of music-based training approaches in CI users.

How do music interventions for CI users

work? The prime mechanism through which music might exert positive effects in CI users is through neural **plasticity**, particularly in basic auditory brain regions. Several overlapping brain regions subserve both music and language processing. Thus, by improving music perception the hope is that this will also benefit speech perception in CI users. Plastic changes are primarily promoted by active engagement with musical material (Petersen et al., 2009), whereas passive music listening might be perceived as aversive due to the impoverished sound transmission of the CI device. To improve the signal processing techniques of the CI device for complex stimuli such as music, machine learning may become essential in processes like optimization, automatization and performance prediction (Crowson et al., 2020).

IN SUMMARY: Conventional CI technology does not faithfully convey the detailed information necessary for complex auditory stimulus such as music to be perceived accurately. Encoding approaches are being developed to make mu-

sic more accessible. However, the perception of pitch, melody and timbre remains poor for most CI listeners. While there are clear positive clinical effects of music training, from perception to psychosocial benefits, the current research only provides Level 3 evidence, and there remains the need for high-quality randomized controlled trials to confirm the effectiveness of music as a rehabilitation tool for CI users.

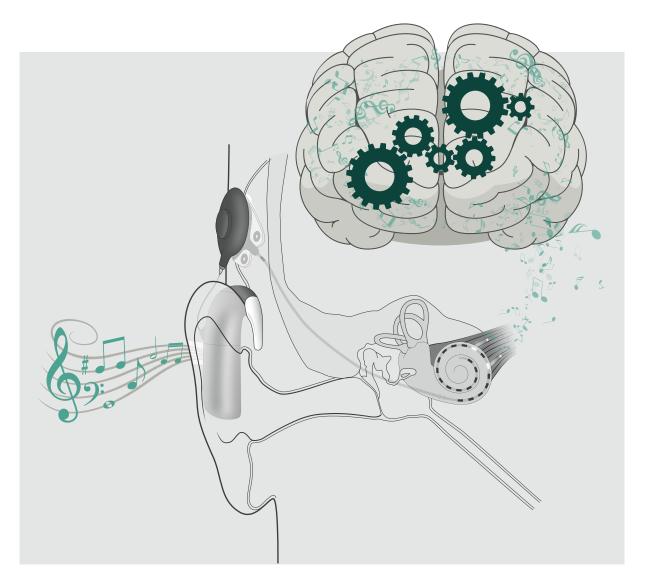


Figure 7: External and internal components of a cochlear implant

The external sound processer sits behind the user's ear. It contains a microphone and picks up sounds and converts them to digital signals. The signals are then transmitted across the skin using radio frequency signals to the internally implanted receiver stimulator. The implant converts these signals into electrical pulses which are sent to an electrode array that is surgically inserted into the cochlea. The electrode array has electrode contacts spaced along the length of the array to stimulate different regions of the cochlea that in turn stimulate groups of auditory neurons.

5.10

Dental procedures

FACTS: Music interventions can be beneficial for reducing anxiety in adults undergoing dental procedures. The evidence for an effect in children is inconclusive as studies show mixed results.

DESCRIPTION: Regular dental care is essential for well-being, as poor oral health is related to dental pain, disturbed sleep and may be a risk factor for other diseases. Yet, dental procedures induce anxiety in many people as they can be experienced as uncomfortable and potentially painful. Around 10-20% of the general adult population experience dental anxiety, and in children up to 40% are affected. Dental anxiety can complicate treatment and may lead to avoidance of dental visits, resulting in deterioration of dental and oral health.

EVIDENCE: Studies have found that music listening can be a beneficial intervention to reduce dental anxiety in adults. In one study, including 90 adults with dental anxiety, the authors reported a significant reduction of anxiety in the participants listening to music during the treatment of simple caries compared to the no-music control group (Lahmann et al., 2008). Another study found that listening to slow, soothing music for 10 minutes before attending standard dental hygiene treatment significantly reduced anxiety compared to a silence control group (Thoma et al., 2015). Similarly, anxiety reduction was found in anxious adults listening to music while waiting for dental surgery (tooth extraction) (Miyata et al., 2016). This study also showed reduced sympathetic activation as measured by heart rate variability in the music group compared to controls, suggesting an effect on the autonomous nervous system.

In general, systematic reviews find evidence in support of a beneficial effect of music interventions for reducing dental anxiety in adults (*Burghardt et al., 2018; Moola et al., 2011*); yet, the effect on children is less clear (*Ainscough et al., 2019*). Some studies find that music listening reduces anxiety in children undergoing dental procedures (*Jindal and Kaur, 2011; Marwah et al., 2005; Singh et al., 2014*), whereas others show no effect of the intervention (*Aitken et al., 2002; Gupta et al., 2017*). Interestingly, one study that found no effect of the music on anxiety reported that the children enjoyed the intervention with 90% of the children stating that they would like to listen to music at their next visit (*Aitken et al., 2002*). The effect of music interventions in children may vary depending on the type of procedure, the age of the child and the nature of the music intervention. Importantly, some of the studies in children include only 15 participants in each group, leading to low statistical power.

How do music interventions before and during dental procedures work? Anxiety has physiological and psychological components with the two aspects influencing each other. The physiological component involves increased arousal, and some studies have reported that music interventions reduced arousal as measured in heart rate and heart rate variability (Gupta and Ahmed, 2020; Miyata et al., 2016). In addition, music may alleviate dental anxiety by addressing cognitive aspects such as attention. Music may reduce anxiety by distracting the patient from thoughts and fears about the upcoming dental procedure. During the procedure, music may also provide distraction from sensory input such as tactile sensations or the sounds. Finally, the emotional impact of music may also be an important factor in how music interventions can alleviate anxiety before and during dental procedures.

IN SUMMARY: A number of studies have shown that music interventions can help reduce anxiety in adults before and during dental procedures. The results are summarized in systematic reviews providing Level 1 evidence for a beneficial effect in adults. The results regarding the effect in children are mixed, and more high quality studies are needed.

5.11

Pain management

FACTS: Music is a useful tool for managing pain, and listening to music can relieve both acute, post-operative and chronic pain.

DESCRIPTION: Pain is an unpleasant sensation and emotional experience linked to actual or potential tissue damage. Pain allows the body to react swiftly to damaging stimuli and thereby prevent further damage. Pain is a common human experience, and most often the pain subsides when the painful stimulus is removed and the body is healed, but in some cases, it may persist despite apparent healing of the body. In addition, pain can sometimes arise without any detectable cause. We experience pain when nociceptive nerve signals travel through the spinal cord to the brain for interpretation, and there are large individual differences in how we perceive pain. In many countries, pain is the most common reason for consulting a physician, and it is a symptom underlying many medical conditions. Pain can significantly reduce quality of life and impair general level of functioning, and thus, efficient management of both acute and chronic pain is essential.

EVIDENCE: Clinical studies have repeatedly shown that listening to music can reduce the sensation of pain. The analgesic effects of music have been subject to research since the 1960s, and it is one of the most studied topics in music and health research. Accordingly, systematic reviews including up to 87 randomized controlled trials report a consistent and significant effect of music for alleviating both acute (Cole and LoBiondo-Wood, 2014; Lee, 2016) and chronic pain (Garza-Villarreal et al., 2017; Lee, 2016). These studies include both experimental studies, evaluating the analgesic effects of music during acute experimentally induced pain, and clinical studies testing the impact of music on pain perception in patient populations. Clinical studies have shown that in addition to lower pain ratings after medical procedures, music listening also resulted in reduced use of analgesic drugs (Nilsson et al., 2003; Nilsson et

al., 2005). Thus, music may serve as a valuable adjuvant approach to pain management in hospital settings.

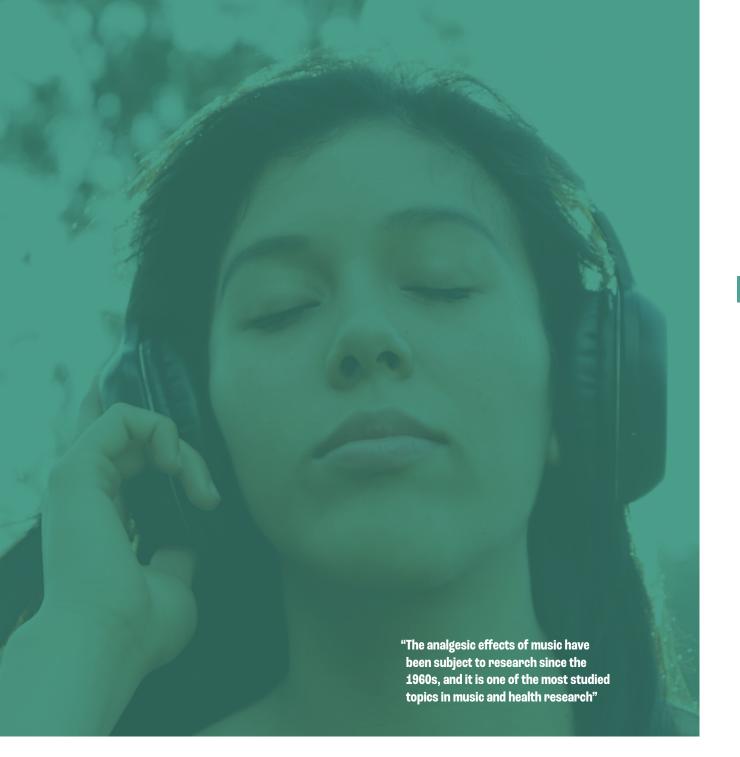
In addition to pain management in hospitals, studies have also found that music can be beneficial for persons with chronic pain conditions. One study found that listening to pleasant self-chosen music reduced pain in adults with fibromyalgia and increased functional mobility compared to a control group (*Garza-Villarreal et al.*, 2014). Similar results are reported in other studies with chronic pain patients (*Guetin et al.*, 2012; *Siedliecki and Good*, 2006).

The pain relieving effects of music are most well-documented in adults, but research suggests an equally beneficial effect in children (*Lee*, 2016). Furthermore, studies suggest that preferred or self-chosen music may be more efficient than researcher-chosen music even though a pain relieving effect is found in both groups (*Gar*za-Villarreal et al., 2017; Mitchell and MacDonald, 2006).

How do music interventions for pain work?

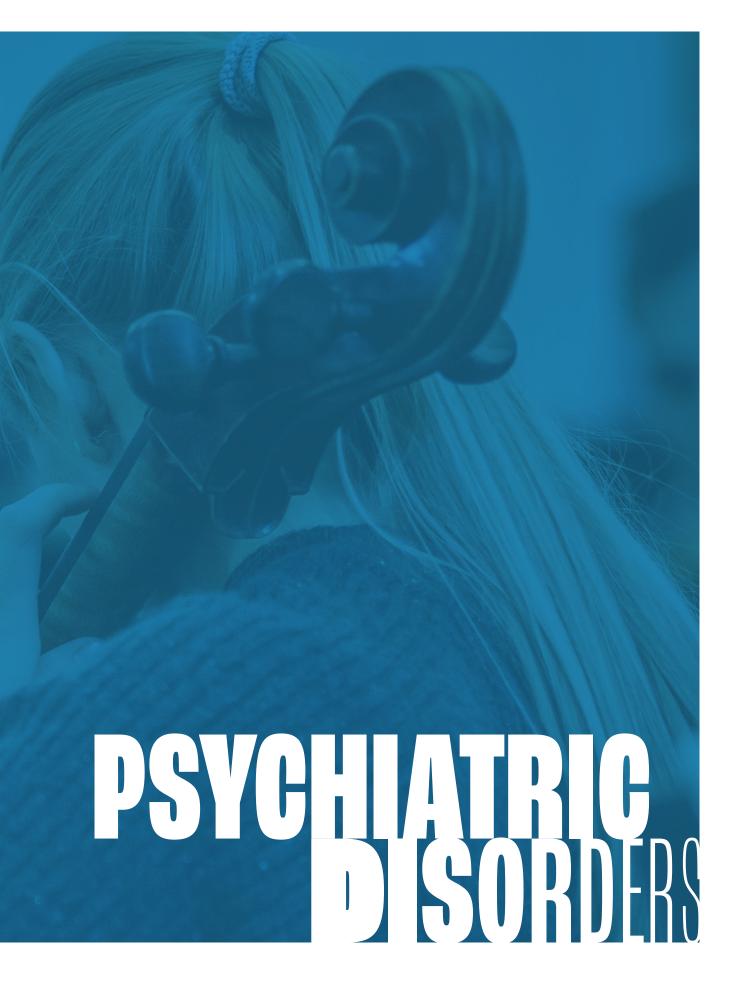
A number of different factors may underlie the analgesic effects of music. First, one of the most commonly discussed mechanisms underlying music-induced analgesia is distraction (Garza Villarreal et al., 2012). Music may reduce pain by attracting the attention of the listener and thereby providing distraction from the pain. In addition to these cognitive effects, music-induced emotions may be another key element. Music can affect our emotional state and elicit pleasurable responses (Salimpoor et al., 2013), and these emotional responses can modulate pain perception (Rhudy et al., 2008). Third, arousal regulation also seems to play a role in the analgesic effect of music. Pain is related to increased arousal, and since music can down-regulate arousal, it may thereby facilitate pain relief (Lunde et al., 2019).

A recent neuroimaging study found that music-induced analgesia in fibromyalgia patients was related to a shift in neural connectivity from pain-related areas to executive and cognitive control areas (*Pando-Naude et al., 2019*). These results



suggest a neural top-down regulation of the pain experience involving distraction, relaxation and positive emotions or a combination of these factors. The pain relieving effects of music have also been associated with release of dopamine in the brain or with the opioid system. However, a recent study found no evidence of the involvement of dopamine and endogenous opioids in a pharmacological manipulations study (*Lunde et al., 2022*). Instead, non-musical factors such as expectations and beliefs about pain may play an important role in how music can relieve pain (*Lunde et al., 2022; Lunde et al., 2019*). IN SUMMARY: The analgesic effect of music has been documented in numerous experimental and clinical studies. Systematic reviews provide Level 1 evidence showing that music is efficient for relieving both acute, post-operative and chronic pain, and the results indicate that music can serve as an adjuvant approach to pain management in hospital settings. Preferred and self-chosen music seems to be more efficient than researcher-chosen music, and both adults and children can benefit from the analgesic effects of music.





MUSIC INTERVENTIONS IN HEALTH CARE · WHITE PAPER

6 , ⊥ Depression

FACTS: Music interventions seem to lead to a reduction in depressive symptoms.

DESCRIPTION: Depression is a serious mental disorder affecting up to 20% of the population at some point in their life. Many people also experience depressive symptoms during challenging life periods without fulfilling the diagnostic criteria for depression. A key symptom of depression is *anhedonia*, the lack of interest and enjoyment in previously pleasurable activities. Besides, significantly lowered mood, energy and motivation are common in depression.

EVIDENCE: Investigating neural responses to pleasant music in people with depression, one study found increased activity in the brain's reward system (Osuch et al., 2009), suggesting that the ability to enjoy music and become emotionally affected by music is still intact in people with depression. Similarly, another study found that people with depression use music for emotion regulation in the same way as non-depressed individuals (Sakka and Juslin, 2018a), even though the level of depression may impact the emotional response (Sakka and Juslin, 2018b). In general, studies find significant reduction in depressive symptoms after music interventions (Chan et al., 2011; Leubner and Hinterberger, 2017) and particularly when patients listen to their own choice of music (Chan et al., 2011). There furthermore seems to be improvement over time, indicating a cumulative dose effect. The average time needed for significant reductions in depressive symptoms were 2-3 weeks (Chan et al., 2011). Yet, the positive effect seems to remain even after the music intervention is terminated. Studies vary significantly in how often the patients listen to music, but most studies have evaluated daily music listening practices. Studies evaluating the effect of music listening on depressive symptoms cover a wide range of populations from students (Gupta and Gupta, 2005; Harmat et al., 2008) to elderly persons with dementia (Guetin et al., 2009). Furthermore, a cohort study found that music listening during



"Music has been shown to modulate the activity of the subcallosal cingulate brain region, an area with decreased activity in patients with depression"

the third trimester of pregnancy was associated with reduced symptoms of postnatal depression in a group of 395 new mothers (*Fancourt and Perkins*, 2018), particularly among women with lower baseline levels of well-being.

The results on music for depression are promising, but it is worth noting that most studies have focused on changes in depressive symptoms in various populations, and few studies have focused on persons with a diagnosis of depression. Thus, the results do not suggest that music is an efficient treatment for major depression. Furthermore, it should be noted that study quality varies among studies, and more high quality randomized controlled trials are needed.

How do music interventions for depression work? The mechanism through which music influences people with depression is most likely the **emotional** impact of music. Music has been shown to modulate the activity of the subcallosal cingulate brain region (*Blood et al., 1999; Pereira et al.,* 2011b), an area with decreased activity in patients



with depression. Also, concentrations of the neurotransmitter serotonin, which is typically reduced in patients with depression, are found to be increased in humans exposed to euphonic music but decreased in humans exposed to cacophonic music (*Evers and Suhr, 2000*). This suggests that positive emotional music should be chosen for potential music interventions for depression. The effect of music seems to be accumulative over time, and durations of minimum 2-3 weeks should be recommended. Overall, there does not seem to be one style of music that is superior to other styles of music; instead most studies advocate using the music that the patients find enjoyable.

IN SUMMARY: Level 2 and 3 evidence suggest that music may be used to alleviate depressive symptoms in various populations, such as students, pregnant women and elderly persons with dementia. Music can constitute a pleasant stimuli that can directly affect brain activity, and more research is needed to evaluate both effects and mechanisms. Meanwhile it is also worth taking into account that the pharmacologic agents available for mood disturbances take weeks to months to take effect, so interventions that provide more immediate benefits may warrant further investigation.

6,2 Insomnia

FACTS: Music interventions have a well-documented effect on sleep quality in people suffering from sleep difficulties.

DESCRIPTION: Sleep problems are common in modern society with around 30% of the adult population experiencing insomnia symptoms such as difficulties initiating and/or maintaining sleep, early morning waking, or non-restorative sleep (*Ohayon*, 2002). While insomnia has a negative impact on daily functioning, medical treatments have numerous side-effects and should be avoided over longer time intervals (*Riemann et al.*, 2017).

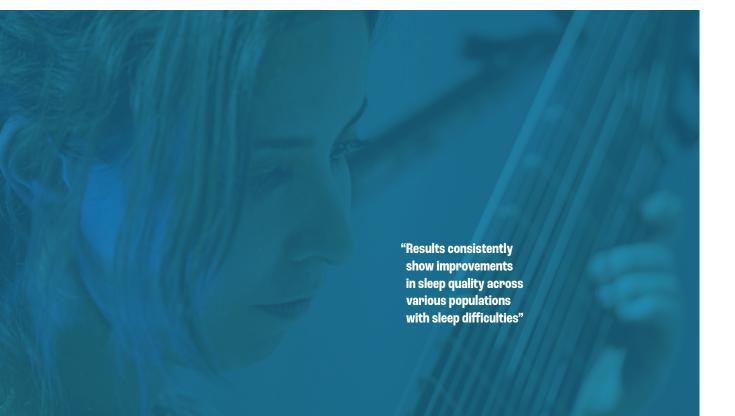
EVIDENCE: A number of studies have evaluated the effect of music on sleep problems, and the results consistently show improvements in sleep quality across various populations with sleep difficulties. Some studies have focused on the use of music for age-related sleep problems (Chen et al., 2021; Petrovsky et al., 2021; Wang et al., 2021), others have used music for pregnancy-related sleep problems (Liu et al., 2016; Shobeiri et al., 2016), or sleep problems related to mental health challenges such as depression and trauma (Deshmukh et al., 2009; Jespersen and Vuust, 2012). Another line of research has focused on the use of music to improve sleep quality in hospitals where sleep is essential for recovery, but often challenged by environmental noise. Under these conditions, music has proved a useful intervention for improving sleep (Hansen et al., 2018; Hu et al., 2015; Su et al., 2013).

Studies show that many people listen to music when they have difficulties sleeping (*Brown et al., 2017; Morin et al., 2006*), and music can be used as a self-help strategy to facilitate sleep. In other cases, it may be offered as an intervention at health care institutions such as hospitals or nursing homes. A meta-analysis summarized the findings of five studies (264 participants) including adults with poor sleep and found a clear improvement in sleep quality (*Jespersen et al., 2015*). Yet, only one study included objective measures of sleep. This study showed that participants listening to soothing music four nights at bedtime showed shortened stage 2 sleep and prolonged REM sleep as measured with polysomnography in a sleep lab (*Chang et al., 2012*). However, the results on objective sleep measures are mixed. A recent RCT study found no changes in objective sleep measures in adults with insomnia disorder listening to bedtime music for three weeks even though participants in the music group experienced sleep improvement as reported in questionnaires (*Jespersen et al., 2019*). The relationship between subjective and objective sleep measures is not simple, and larger studies may be needed to see changes in objective sleep measures.

How do music interventions for insomnia

work? A number of mechanisms have been proposed to underlie the effect of music on sleep. The effect of music on **arousal** is one important factor, and musical parameters such as slow tempo, stable dynamics and a simple structure are important for promoting arousal reduction that can lead to sleep improvement (*Bernardi et al., 2009; Bernardi et al., 2006; Trehub and Trainor, 1998).* Another important factor is the **emotional** impact of music. Sleep problems are often associated with difficult emotional states, and music may facilitate sleep by improving emotional well-being. In addition, **cognitive** factors can also play a role in how music can improve insomnia, for instance listening to music might distract attention away from rumination and involuntary thought that often 'pop up' at bedtime. Finally, music can also be used to mask or cover a disturbing sound environment as mentioned in the studies on the use of music for sleep improvement in hospital environments (*Dickson and Schubert, 2019*). This mechanism may also be relevant for people with sleep problems related to traffic noise.

IN SUMMARY: There is substantial evidence supporting a beneficial effect of music as sleep aid. A number of systematic reviews provide Level 1 evidence showing that listening to music at bedtime can improve sleep quality. However, there is limited knowledge on the impact of music on objective measures of sleep reflecting, for example, the amount of sleep spent in the different sleep phases.



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6.3

Autism Spectrum Disorder (ASD)

FACTS: Neuroimaging studies show intact processing of musical emotions in autism, and some individuals with ASD may even be particularly musically gifted. Music may be a fruitful intervention for teaching emotion recognition and social communication.

DESCRIPTION: Autism Spectrum Disorder (from here on referred to as autism or ASD) is a neurodevelopmental disorder affecting about 1% of the population. Autism is characterized by impairments in communication, social and emotional interaction, in combination with stereotyped and repetitive behaviors and interests. Early language development is often significantly delayed in children with autism, and language abnormalities, such as atypical intonation, volume or rhythm patterns or idiosyncratic use of words typically, remain throughout life. It is estimated that about 25% of individuals diagnosed with ASD remain non-verbal throughout life. A central concern of many parents to children with ASD is the lack of emotional communication and reciprocity. Furthermore, people with autism often have issues with coordination and regulation of movement and sensory information.

EVIDENCE: While many studies have reported abnormal processing of language in people with ASD, promising results exist in the field of music perception. Recent research shows that people with autism enjoy listening to music, become emotionally affected by music, and often are musically talented. Behavioral studies have shown that people with ASD process musical contour and intervals just as well as a healthy control group (Heaton, 2005), and that they in general have superior pitch processing (Bonnel et al., 2003; Heaton, 2003; Heaton et al., 2008b) and memory (Heaton, 2003; Stanutz et al., 2012). In addition, behavioral studies have shown that children and adults with ASD correctly identify a wide range of emotions in music just as well as control participants (Allen et al., 2009; Caria et al., 2011; Gebauer, 2013; Heaton et al., 2008a; Heaton et al., 1999; Quintin et al., 2011). A qualitative

study by Allen & Heaton (2009) found that adults with ASD listened to music as often as people without ASD, and when asked why they listened to music, they reported being emotionally affected by the music and feeling a sense of belonging to a particular musical culture. Moreover, it is shown that physiological responses and brain processing of music are intact in people with ASD (Allen et al., 2013; Caria et al., 2011; Gebauer, 2013). Building on the musical interest and abilities in children with ASD, an intensive music intervention strategy labelled auditory-motor mapping training has been shown successful in teaching language to completely non-verbal children with ASD (Wan and Schlaug, 2010). Furthermore, a study demonstrated improved social communication in children with ASD after a music intervention (Sharda et al., 2018). In this study, 51 children with ASD were randomized to a music intervention, involving an improvisational approach with songs and rhythm, or to a non-musical intervention. After the 8-12 weeks' intervention period, scores of social communication were higher in the music group compared to controls, and interestingly, resting-state functional brain connectivity involving auditory, subcortical and frontal regions was also increased in the music group compared to controls (Sharda et al., 2018).

How do music interventions for ASD work? Music interventions for people with ASD work by creating emotions that do not depend on being together with other people or the ability to describe emotions using language. Music listening may thus be a rewarding stimulus that activates the dopaminergic system (Quintin, 2019) as well as limbic and paralimbic structures in the brain. The release of oxytocin during music listening might also be fundamental for creating the sense of belonging, which this group of people often have difficulties experiencing elsewhere. The auditory-motor mapping training utilizes auditory motor integration, and many of the same mechanisms as described in relation to melodic intonation therapy in stroke rehabilitation.

Music engagement may enhance sensorimotor integration and facilitate modulation of neural networks involved in atypical sensory processing (Sharda et al., 2018).

IN SUMMARY: Neuroimaging studies show typical activation of neural networks related to reward and emotion with music, and several studies suggest that music might be a particularly fruitful intervention type in the population. Evidence concerning the effect of music interventions in children and adults with ASD are sparse. Yet, pioneer studies provide Level 2 and 3 evidence for a beneficial effect of music interventions for improving language abilities in non-verbal children with ASD and for improving social communication.

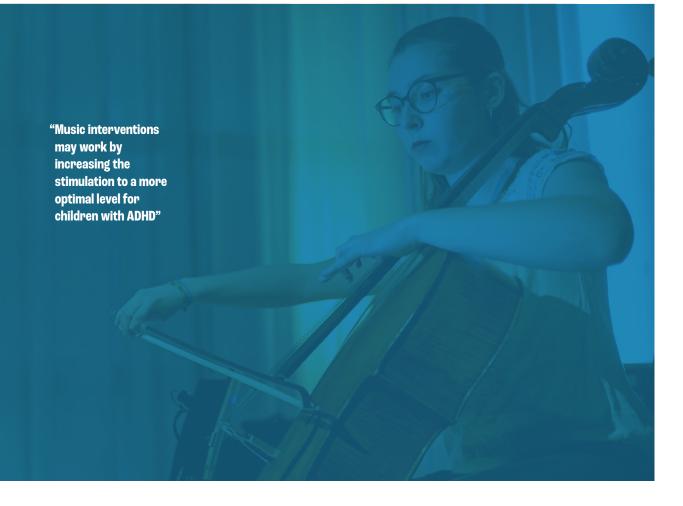
"Behavioral studies have shown that children and adults with ASD correctly identify a wide range of emotions in music just as well as control participants" **FACTS:** Background music may increase attentional performance in children with ADHD. However, the effects are small and randomized controlled studies are needed to establish higher level evidence.

DESCRIPTION: ADHD is an abbreviation for Attention Deficit Hyperactivity Disorder. It is one of the most common neurodevelopmental disorders in children, and it is most often diagnosed in childhood, but may last into adulthood. Children with ADHD have trouble paying attention, and they may be overly active and impulsive. These difficulties can challenge many aspects of the child's life, including school performance.

EVIDENCE: Research into music interventions for ADHD has mainly focused on whether background music can help school children sustain their attention during academic tasks. One early study compared arithmetic performance of children with ADHD and healthy control children under three conditions: high stimulation (self-chosen music), low stimulation (speech) and no stimulation (silence). The performance of the control group was not affected by the conditions, but the children with ADHD performed better during the music condition (a self-chosen radio station playing rock or rap music), particularly when the music condition was presented first (Abikoff et al., 1996). Another study used a similar design and found substantial individual differences in the response to music. Some children with ADHD benefitted from the background music and others performed worse compared to silence (Pelham et al., 2011). The results in this field are promising, but it is important to keep in mind that the size of effects are small to moderate, and high quality studies are still lacking (Maloy and Peterson, 2014).

Another line of research shows that shortterm orchestral music training can increase inhibitory control and reduce hyperactivity in healthy children (*Fasano et al., 2019*). These results could be relevant for children with ADHD, and





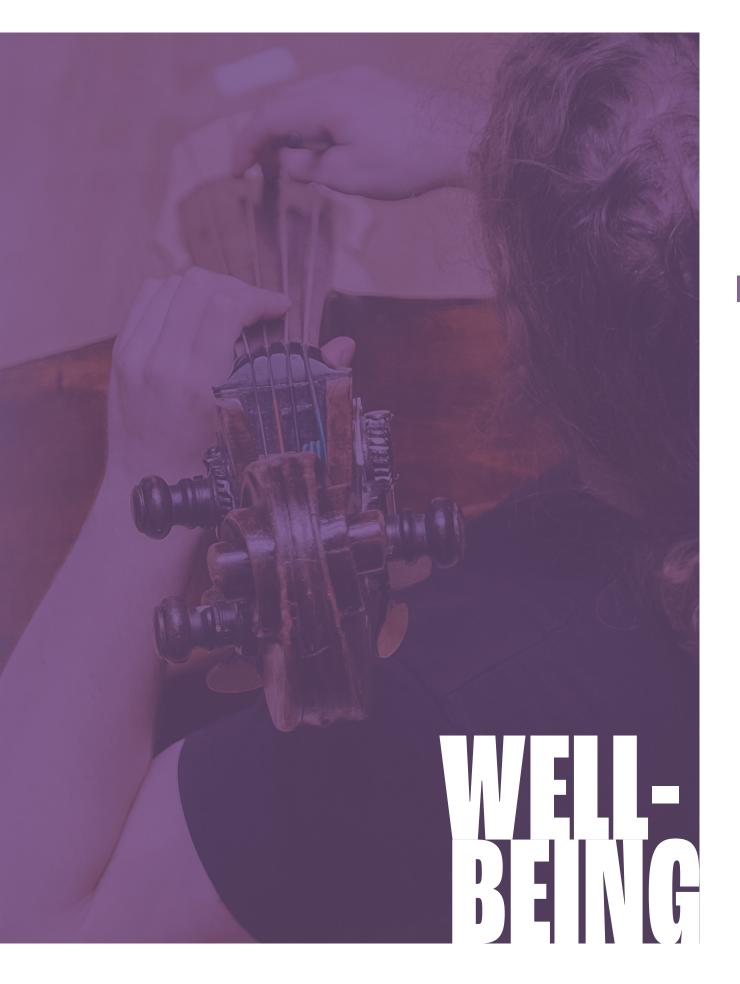
future studies will investigate if the findings can be expanded to this group of children.

How do music interventions for ADHD work?

Children with ADHD often have difficulties with attention and hyperactivity in situations with low levels of stimulation. Music interventions may work by increasing the stimulation to a more optimal level for children with ADHD (*Maloy and Peterson, 2014*). This way of regulating **arousal** can lead to improved attention and thus, improve behavior and school performance. In addition, the neurotransmitter **dopamine** which often co-occurs with adrenalin and has been suggested as a key element in ADHD may play a role in the effect of music interventions for this population. The pleasurable effect of music is generally believed to be mediated partly by dopamine release in the striatum (*Salimpoor et al., 2011*).

IN SUMMARY: Studies suggest a small to medium effect of background music on attentional skills in children with ADHD during school tasks. This Level 3 evidence should be improved by implementing randomized controlled trials. Furthermore, orchestral music training can improve inhibitory control and reduce hyperactivity in children with normal development. This may also be a promising intervention for children with ADHD.





Cognitive enhancement

FACTS: Evidence suggests a temporary effect of music listening on spatio-temporal reasoning mediated by mood and arousal.

DESCRIPTION: The positive transfer effect of music to cognitive performance has been much debated since the finding of 'the Mozart effect' in 1993 (*Rauscher et al., 1993*). In addition, researchers have tried to disentangle to which degree the benefits of musical training generalize to cognitive functions unrelated to music. The putative use of music as a cognitive enhancer would have an impact both on rehabilitative and academic use.

"Brain plasticity associated with musical expertise is seen in various brain areas, including those involved in general cognitive functions"



EVIDENCE: In the original study on the Mozart effect, the researchers found that participants who listened to Mozart's sonata for two pianos (K. 448) for 10 minutes, performed better on a spatial reasoning task. Yet, the effect only lasted for about 10-15 minutes (Rauscher et al., 1993). This line of research has, nonetheless, received quite extensive critique. One study showed that Schubert and a narrated story was equally effective for enhancing spatio-temporal reasoning as listening to Mozart (Nantais and Schellenberg, 1999). Similarly, pop music may be more effectful in e.g. young adolescents than K448 (Schellenberg and Hallam, 2006). Furthermore, the finding of the Mozart effect suffered from methodological issues and failed attempts to replicate the Mozart effect question the generalizability of the findings (for a review of this literature see (Schellenberg, 2012)).

Looking at musicians, many studies find improved cognitive abilities (i.e. IQ, working memory/attention, speech-in-noise perception) (Hansen et al., 2012; Khalil et al., 2013; Kraus et al., 2012; Schellenberg, 2011), but whether this is the product of extensive musical training or innate abilities that drive people towards playing music is not clear. One line of research has focused on language and phonemic awareness and found that music training may improve linguistic skills (Benz et al., 2016). In a longitudinal study, 8-year-old children were assigned to either music or painting classes for 2 years, and the results showed improved speech segmentation skills only in the music group (Francois et al., 2013). Other studies have focused on executive functions, attention and memory (see Benz et al. 2016 for a review). In a longitudinal study, 147 primary school children were randomized to music, visual arts or no arts. The results showed improved scores on inhibition, planning and verbal IQ in the music condition compared to the two control groups suggesting a transfer effect of long-term music training on executive and verbal functions in children (Jaschke et al., 2018). These findings may underlie the association between music participation and academic achievement (Guhn et al., 2019; Jaschke et al., 2018).

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How do music interventions work? 'The Mozart effect' has subsequently been described as a function of the positive emotional arousal induced by listening to e.g. Mozart, or to any other liked music for that matter (Jenkins, 2001; Thompson et al., 2001). Another suggestion is that, since the brain regions activated by music (particularly prefrontal, temporal, and precuneus regions) also are central for spatial reasoning, music might facilitate engagement of these regions during spatial reasoning tasks (Jenkins, 2001). Similarly, learning to play an instrument facilitates both structural and functional changes in the brain (Jäncke, 2009). Brain plasticity associated with musical expertise is seen in various brain areas, including those involved in general cognitive functions (James et al., 2014), and may thus be a key mechanism in the effect of music training on cognitive function.

IN SUMMARY: Evidence suggests that listening to music that is enjoyable may temporarily improve performance in tests of spatial-temporal abilities in healthy subjects. Furthermore, there is a positive association between music training and general cognitive functions such as language skills, working memory and executive functions. The causal relationship is not yet clear, but emerging evidence from a few randomized longitudinal studies with an active control group provides Level 2 evidence for a beneficial effect of music training on general cognitive skills.

Physical exercise

FACTS: Studies of music interventions during physical exercise have investigated psychological, physiological and ergogenic effects, and studies support a beneficial effect on performance and affective responses, as well as reduced exertion and improvement in oxygen consumption.

DESCRIPTION: The health benefits of physical exercise across the lifespan are receiving increasing attention these years. Many people use music as an aid to keep up motivation during exercise and to keep improving their strength and condition. For elite athletes competition is high and even minor adaptations that can lead to improved performance are pursued. Thus, music might be a valuable motivational and ergogenic aid for both elite and recreational athletes.

EVIDENCE: Studies find that music interventions can lead to a range of benefits that include enhanced positive affect, lower perceived exertion, greater energy efficiency and faster time trial performances (Karageorghis and Priest, 2012a). Listening to music synchronized with the speed of running seems to have a range of positive results, such as less exhaustion (approximately 19% longer endurance), improved mood and motivation, lower oxygen consumption (1.80±0.22 L.min-1), and thus better running economy (Bacon et al., 2012; Terry et al., 2012). In swimming, asynchronous music during a high-intensity training is shown to increase motivation and performance (but only by 2 %, (Karageorghis et al., 2013) but see (Szczepan and Kulmatycki, 2012)). Moreover, listening to self-selected music was found to increase performance and mood during explosive exercise such as bench press and jump squat (Biagini et al., 2012). Listening to high-tempo music during warm-up was found to have a positive effect on peak speed and mean speed during a 30 s. anaerobic high-intensity cycling test (Chtourou et al., 2012; Jarraya et al., 2012). An extensive review summarizing the results from 139 studies, including 3,599 participants, evaluated the effect of music in exercise and sports (Terry et al., 2020). Through meta-anal"Level 1 evidence suggests beneficial effects of music in exercise and sports on affective valence, performance, exertion and oxygen consumption"

ysis they found beneficial effects of music on affective valence (i.e. emotional state during training), physical performance, reduced exertion and oxygen consumption. The largest effect was on affective valence with a moderate effect size, and thus music can be an important factor for increasing enjoyment and motivation and thereby promote regular training and optimize health benefits (Terry et al., 2020). The effect on physical performance was small, but very consistent, and it was moderated by tempo, indicating that fast music yielded a stronger performance effect than music with a slow-moderate tempo (< 120bpm). Small effects were also seen on perceived exertion and oxygen consumption, but there was no significant effect of music on heart rate during exercise or sports (Terry et al., 2020).

How do music interventions work? The most likely mechanisms underlying the effect of music listening on physical exercise is through rhythm and tempo. Rhythm and tempo regulate arousal and thus have a direct impact on physiological responses. Overall, it seems that the tempo of music affects the tempo of activities being performed while listening to the music (Kämpfe et al., 2011). Correspondingly, it has been hypothesized that listening to music with a synchronous rhythm to the movements being performed can enhance performance, while asynchronous music might impair performance (Karageorghis and Priest, 2012a, b). However, this assumption was not confirmed in a large meta-analysis (Terry et al., 2020). In this review, synchronous vs. asynchronous use of music had no impact on performance. Still, studies on synchronous use of music in sports and exercise are scarce, and the hypothesis warrants further research. The cognitive distraction provided by the music also seems to be important for improved performance and reduced exertion (Terry et al., 2020; Terry et al., 2012). However, when doing high-intensity anaerobic exercise all attention should be devoted to the exercise, and music might be irrelevant to performance or even impair performance.

In addition to rhythm/tempo and distraction, the emotional impact of music also seems to be central for the increased motivation associated with listening to music during physical exercise (Terry et al., 2020). In terms of selecting music, most studies use self-selected music. Yet, one study compared self-selected with experimenter-selected music and found that self-selected music increased mood and motivation more in participants compared to experimenter-selected music, but that both types of music were equally effective in increasing performance (Terry et al., 2012). However, music preference as indicated by self-selected vs researcher selected had no impact on any of the outcomes in an extensive meta-analysis (Terry et al., 2020). Interestingly, it seems that men often perceive music interventions during exercise more positive than women, but that it is women who benefit the most from listening to music during physical exercise (Karageorghis et al., 2010). Finally, there might be special strength in using a musical piece, which is associated with a particular experience or emotion (like hearing the national anthem before an international game).

IN SUMMARY: Level 1 evidence suggests beneficial effects of music in exercise and sports on affective valence, performance, exertion and oxygen consumption. Music can improve emotional states during physical activity and improve physical performance. However, the effect sizes for performance, exertion and oxygen consumption are small. Music have been used for a range of different exercise modes (cycling, running, swimming etc.), it has been used before, during and after exercise intervals, and with varying effects and in both elite and recreational athletes. This magnitude of music applications across studies point towards the numerous ways in which music can be used to improve performance or motivation during physical exercise.

7.8

Pregnancy and birth

FACTS: A number of studies find that music can relieve anxiety and improve sleep during pregnancy. Music is also beneficial for relieving anxiety and pain during labor.

DESCRIPTION: Pregnancy includes a series of changes in the life of the expectant woman. Many pregnant women experience an increase in worries and anxieties related to health and the change of life situation, and 7-13% develop postnatal depression symptoms (*Parsons et al., 2012*). Maternal well-being and fetal health is related so strategies for improving well-being and mental health during pregnancy are important for both mother and child. Furthermore, the pain of giving birth can be intense, and many women seek methods to reduce the intensity of labor and improve their experience of giving birth.

EVIDENCE: Music listening can be a beneficial strategy for relieving anxiety during pregnancy. A recent RCT study including 409 women found that listening to slow soothing music regularly during the third trimester reduced anxiety in the pregnant women (Garcia-Gonzalez et al., 2018). These results are supported by a systematic review from 2017. Here, the authors also found evidence that music interventions may reduce anxiety in pregnancy, even though the included studies were of low to moderate quality (van Willenswaard et al., 2017). Another beneficial effect of music during pregnancy is the potential alleviation of pregnancy-related insomnia (Liu et al., 2016; Shobeiri et al., 2016). Around 50-60% of all pregnant women suffer from insomnia, and here music can provide a safe and viable intervention.

"A systematic review including 14 studies with a total of 1310 participants found that music listening during the delivery process reduced anxiety scores and physiological measures such as heart rate and blood pressure" Well-being during pregnancy is also related to the process of delivery, and a number of studies have examined the effect of music on anxiety and pain during labor. A systematic review including 14 studies with a total of 1310 participants found that music listening during the delivery process reduced anxiety scores and physiological measures such as heart rate and blood pressure (*Lin et al., 2019*). Similar results have been reported for women undergoing caesarean section (*Hepp et al., 2018*). In addition, studies have also demonstrated that music listening during delivery can reduce the perception of pain, provide psychological support and facilitate the progression of labor (*McCaffreg et al., 2020; Smith et al., 2018*).

How do music interventions work? The beneficial effects of music during pregnancy and birth can be related to a number of factors. The main mechanism is the arousal-reducing effects of music, which is reflected in both psychological and physiological measures. Music can facilitate relaxation and may thereby relieve anxiety and pain. Furthermore, the pleasure of listening to music can induce positive **emotions**, by engaging reward networks in the brain. This process may counteract anxiety and improve general well-being. Finally, there can also be a **cognitive** factor, because listening to music can distract us from worries and fears by diverting our attention. This shift in attention to the music as a pleasant stimuli is also important for the pain-relieving effects of music (Lunde et al., 2019; see also section 5.11).

IN SUMMARY: With a number of good systematic reviews in this field, there is Level 1 evidence to suggest that regular music listening during the third trimester can improve anxiety in pregnant women. Similarly, music listening during delivery can reduce anxiety and improve physiological measures compared to controls with no music. Studies also indicate that music can relieve pain during delivery and reduce anxiety in women undergoing caesarean section. Yet, more high-quality studies are needed to evaluate the latter effects.

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Stress reduction

FACTS: Listening to relaxing music decreases stress and anxiety and reduces cortisol levels, heart rate and blood pressure in people of all ages.

DESCRIPTION: Modern lifestyle has led to increasing levels of stress in the population. As such, the biological stress response is adaptive in the short-term perspective, since it ensures survival by preparing the body for fight or flight, while prioritizing resources. Yet, prolonged periods of stress have detrimental consequences for physical and psychological well-being. Long-term stress responses lead to chronic activation of the HPA axis including high release of cortisol, which becomes neurotoxic, so it destroys brain cells and promotes inflammatory processes. Thus, lifestyle choices that can reduce stress are much in demand, and music might be a good candidate.

EVIDENCE: Listening to 'relaxing music' has been shown to reduce stress and anxiety in healthy subjects (*Dileo and Bradt, 2007; Knight and Rickard, 2001; Pelletier, 2004*). A recent review and meta-analysis summarizing 104 experimental and clinical RCT studies found that music can reduce both physiological measures of stress (heart rate, blood pressure and stress-related hormones) and psychological measures of stress (de Witte et al., 2019).

Studies have shown that relaxing music can decrease cortisol levels in healthy participants (Fukui and Yamashita, 2003; Khalfa et al., 2003; McKinney et al., 1997), suggesting that music has a direct impact on the HPA axis and physiological responses to stress. Music listening is also found to lower heart rate and systolic blood pressure in healthy individuals (Knight and Rickard, 2001), and both in young (Labbé et al., 2007) and elderly people. In addition, research indicates that music can reduce stress in two ways. Firstly, listening to researcher-chosen relaxation music during a stressful task can attenuate the response to a stressor (Khalfa et al., 2003), and secondly, music listening can lead to a faster recovery from the stress response (Thoma et al., 2013). Many of these studies have been conducted in experimental settings, but a study of music listening in daily life also documents that music listening can reduce both subjective stress levels and cortisol concentrations (*Linnemann et al.*, 2015). The stress-reducing effect was largest when participants listened to music in order to relax or when they listened to music together with other people (*Linnemann et al.*, 2016).

The choice of music seems to be important for creating stress reduction. One study compared relaxing classical music with techno music and found that techno heighted activation of the sympathetic nervous system and the release of cortisol (*Gerra et al., 1998; Hébert et al., 2005*). For similar results comparing heavy metal, classical and self-chosen music see (*Labbé et al., 2007*). These studies suggest that the reduction of cortisol depends on musical features, in particular a slow tempo. Likewise, slow musical tempo is found to lead to a decrease in heart rate and blood pressure, while faster music increases heart rate and blood pressure (*Bernardi et al., 2009*).

Another study compared preferred sedative and stimulating music to non-preferred sedative and stimulating music and found a stress-reducing effect of both preferred sedative and stimulating music (*Jiang et al., 2013*). For the non-preferred music only, the music characterized as sedative had a stress-reducing effect. Other studies support that music preference plays an important role for stress reduction, but find that familiarity is less crucial (*Jiang et al., 2016; Tan et al., 2012*).

In a recent review, the way the music was selected (researcher-chosen or participant-chosen) did not seem to influence the stress reduction effect (*de Witte et al., 2019*). Yet, different studies have used varying definitions of what is considered researcher-chosen or participant-chosen. For example, studies where participants are given a choice among a pre-defined set of music playlists have been characterized both as researcher-chosen and participant-chosen.

How do music interventions for stress reduction work? The mechanism through which mu-

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sic has an effect on stress reduction is primarily through its **arousal** regulating effect. The rhythmicity and tempo of music is known to modulate brain stem activity (*Griffiths et al., 2001*). Since the brain stem is critically involved in regulating heart rate, pulse, blood pressure, temperature, skin conduction and muscle tension, it seems that the rhythmic components of music are of particular importance for its effect in stress reduction (*Chanda and Levitin, 2013*). Besides, music might also contribute to lowering of stress by inducing positive **emotions**.

IN SUMMARY: Level 1 evidence shows that music can have a positive effect on reducing stress and anxiety, modulating heart rate, blood pressure and respiration, and on reducing cortisol levels in people of all ages. Though most people who regularly listen to music probably know these effects, this exciting potential of music in stress management is not widely used in a systematic way.

"Music can reduce both physiological measures of stress (heart rate, blood pressure and stressrelated hormones) and psychological measures of stress"

Healthy ageing

FACTS: Music interventions seem promising for improving well-being, motor and cognitive functioning in older adults.

DESCRIPTION: Keeping the brain active is a central goal during a healthy aging process. But when the body starts to decline this might not be straightforward. Thus, activities that bring enjoyment and engage the brain are promising tools for promoting positive aging.

EVIDENCE: Aging can be associated with physical and mental decline, affecting, among other things, mobility, sleep quality, hearing and communication. Indeed, music applications may be beneficial for reducing most of these declines. Studies investigating music interventions for improved gait (and reduced risk of falls) have found positive effects in older adults (Maclean et al., 2013; Trombetti et al., 2011). In addition, studies found that music improves sleep quality in older adults (Lai and Good, 2005; Shum et al., 2014). With regard to mental decline, correlational and longitudinal studies suggest that musical training provide a neuroprotective effect (Criscuolo et al., 2019; Roman-Caballero et al., 2018). This is seen in studies where experienced older musicians perform better than older non-musicians in tasks related to working memory, verbal fluency, episodic memory, cognitive control, spatial judgements and processing speed (Roman-Caballero et al., 2018; Sutcliffe et al., 2020). It has been suggested that music training as a complex cognitively demanding activity may enhance cognitive reserves and thereby protect from age-related cognitive decline. Yet, the causal relationship is not clear from these correlational studies (see section 7.1).

Another line of studies has evaluated the effect of music interventions for enhancing general cognitive abilities. For example, older adults aged 60 to 85 without previous musical experience exhibited improved processing speed and memory after just three months of weekly 30-minute piano lessons and three hours a week of practice, whereas the control group showed no changes in these abilities (Bugos et al., 2007) (for a review see Sutcliffe et al. 2020). These studies are encouraging. Yet, since the control group received no intervention it is unclear if the effect may be related to the extra attention and engagement of the music group. Thus, randomized controlled trials with active control groups are needed to establish the effect of music per se.

One of the symptoms of age on the auditory system is impoverished speech-in-noise perception. This is experienced as very frustrating and tiring, since extra attention is required to follow conversations whenever background noise is present (which it almost always is). Older musicians (45-65) do, however, show superior speech-in-noise perception and auditory working memory compared to older non-musicians (Parbery-Clark et al., 2011). Music training leads to better processing of speech in the auditory brainstem and cortex and to better understanding of speech in noise. Correspondingly, older musicians do not have the same brainstem timing delays in their speech-evoked responses that older non-musicians do (Parbery-Clark et al., 2012). Overall, this suggests that music training may be important for preventing such problems and might also prove to be an effective rehabilitation strategy for improving speech-in-noise perception in older adults (for reviews see (Alain et al., 2013) and (Kraus and Anderson, 2013)).

A fundamental aspect of well-being is being socially connected with other people. Yet, some older individuals might not have the physical strength or mental capacity to do this, which often results in isolation and depression. However, music processing and memory seem to be preserved in old age (*Halpern and Bartlett, 2002*), and music activities may be an important resource to enhance social engagement and combat loneliness among the elderly. For example, a study of 390 community-dwelling adults above the age of 60 showed that those randomized to a community choir for 6 months experienced significant reduction in loneliness and increased interest in life compared to the waitlist control group (*Johnson et al., 2020*). How do music interventions work? Music, in particular active music making, seems to be a valuable way of keeping the brain active in old age (Särkämö, 2018). As demonstrated in Figure 3, music activates regions all across the brain, which are also associated with motor abilities, language processing, cognitive abilities and many other relevant functions. The mechanisms by which music improves speech-in-noise perception seem to be through neural plasticity of the auditory system, in particular early auditory regions in the brain stem. The improvement of gait is most likely supported by mechanisms identical to those described in relation to Parkinson's and stroke (see section 5.3 and 5.5), particularly rhythm and motor-related entrainment mechanisms. Similarly, the mechanisms underlying improvements in sleep quality are the same as described in the insomnia section (see section 6.2). Finally, the positive effects on well-being and social cohesion may be related to the emotional qualities of music and the release of oxytocin, which is considered fundamental for the companionship and positive feelings related to music interaction.

IN SUMMARY: Music interventions can, like any other mental or motor activities, contribute to healthy aging in a number of areas such as motor stability, sleep, cognition, speech perception and social engagement. Musicianship seems to lessen age-related cognitive decline, and Level 2 evidence suggests that music interventions may serve to maintain cognitive functions and enhance well-being also in non-musicians. Additionally, filtering speech from background noise seems to be a potential fruitful target for music interventions in healthy elderly individuals.





EVIDENCE SUMMARY and VES for ONS in **H**

SUMMARY

Evidence, challenges and perspectives for music interventions in health care

Biomedical and psychological evidence has emerged, demonstrating the beneficial effects of music in a variety of somatic and psychiatric disorders and for improving general well-being in healthy individuals. In this updated Whitepaper, we have reviewed the mechanisms through which music may exert these effects. We have described music's influence on auditory, motor, arousal, emotional and cognitive brain systems and linked these mechanisms on the beneficial effects of music intervention for a range of somatic and psychiatric disorders and for improving well-being in healthy individuals.

The perspectives for music as an effective supplementary tool in health care are promising, and the research has increased substantially in both quality and quantity within the last years. In this updated white paper, we used the guidelines from the Oxford Centre for Evidence-Based Medicine to evaluate the quality of the evidence within each field. This enables comparison with other fields and gives an impression of how confident we can be in the results. Level 1 is the highest level of evidence, and it requires the existence of systematic reviews of randomized controlled trials. In this white paper, we found Level 1 evidence for the effect of music on anxiety in operations and cancer treatment, COPD rehabilitation, gait rehabilitation in stroke and Parkinson's patients, depressive symptoms in dementia, dental procedures, pain management, insomnia, exercise and stress reduction. Level 2 evidence indicates the existence of randomized controlled trials or observational studies with a dramatic effect. Here, we found Level 2 evidence for the effect of music on cognitive and upper limb rehabilitation in stroke patients, gait rehabilitation of multiple sclerosis, tinnitus, depressive symptoms, social communication in autism, cognitive enhancement and healthy aging. In these fields solid evidence has emerged for a beneficial effect of music; yet, more randomized trials are needed to facilitate systematic reviews and ensure that the findings are robust across

trials. Level 3 evidence reflects the existence of non-randomized controlled studies, and in this white paper, we found Level 3 evidence in the fields of cochlear implant rehabilitation, ADHD and language training in autism. These fields all show promising results and provide interesting fields for future research and development of novel intervention methods. Music interventions have also been tested in other fields not included in this white paper. For example, interesting research has been done related to cerebral palsy rehabilitation (*Marrades-Caballero et al., 2018*) and epilepsy (*Bodner et al., 2012*).

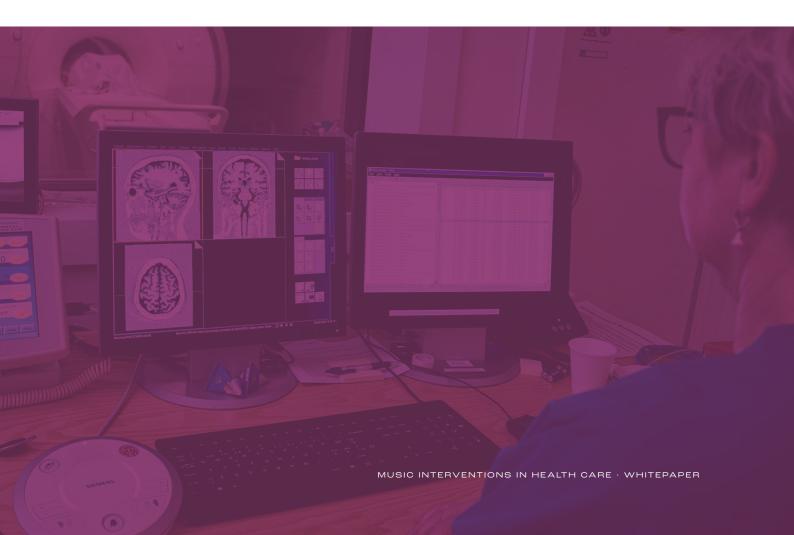
Despite the impressive progress in this field, a number of challenges persist. Important limitations in many of the scientific studies in this

> "The research has increased substantially in both quality and quantity within the last years"



field are lack of proper active control groups, differences in the methodological approaches across studies and limited sample sizes. This is further complicated by the probable variability in musical taste, experience and training between participants, and cultural differences in both musical material and practice.

When using music as an intervention, a number of things must be considered. To ensure high-standard treatments it is imperative that music interventions 1) are evidence-based, 2) offer the technology to adjust interventions according to specific requirements of medical procedures and to the individual preferences of the patient, and finally, 3) are easy to use for health care personnel and patients alike. Certainly, music cannot replace good medical treatment, but it can supplement it and lead to a more individualized and effective treatment of patients. Even moderate effects gained by music interventions might have great clinical importance. Music interventions are low cost, easy to apply, can be tailored to individual preferences, are enjoyable and have no side effects. Therefore, the potential that lies in music interventions should be pursued to ensure optimal health benefits from implementing music in novel settings, such as the health care system.



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