MUSIC INTERVENTIONS IN HEALTH CARE

WHITE PAPER

BY LINE GEBAUER AND PETER VUUST

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ABOUT THE PUBLICATION

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PREFACE

This publication is the result of an innovation project entitled "Music Interventions in Health Care". The project is financed by the Danish Sound Innovation Network through a grant from the Danish Agency for Science, Technology and Innovation. The project has been completed in 2013 and was managed by Aarhus University and project manager Peter Vuust. The following project participants have provided in-kind contributions: Widex, SoundFocus and DKsystems.

ABSTRACT

Chances are that you have listened to music for several hours during the past week. A recent Danish survey found that 76 % of adults between 12 and 70 years listened to music for more than one hour daily (Engagement, 2010). Indeed, music is consistently rated to be among the top ten pleasures that people value the most in life (Rentfrow and Gosling, 2003), but music can do more than just lift your spirit. Throughout the past decade, solid biomedical and psychological evidence is beginning to emerge, demonstrating the beneficial effects of music for a variety of somatic and psychiatric disorders, and for improving general well-being in healthy individuals. In this 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. 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.

CONT

ENTS

INTRODUCTION

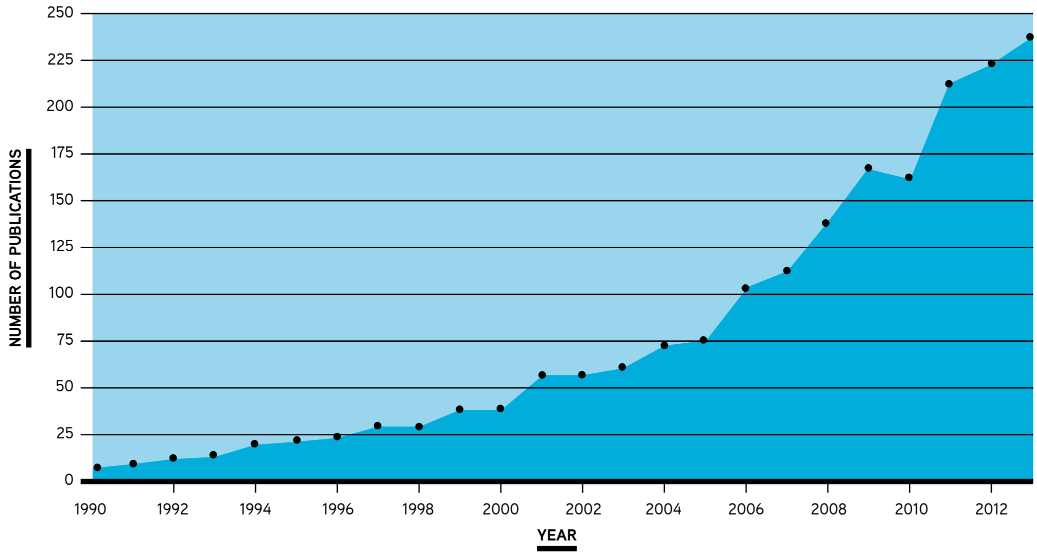
1

1.
INTRODUCTION

The assumption that the environment is an essential part in recovery from disease has recently gained increased attention among healthcare 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. Music interventions in particular have received extensive scientific interest. When doing a literature search for scientific publications[1] which include the word "music intervention", only 10 papers were published during 1990, 40 papers in 2000, and a total of 235 scientific papers in 2013 (Figure 1). Indeed, a meta-analysis from 2012 found that, compared with other environmental adjustments, music was the most widely studied and most effective intervention in hospital settings (Drahota et al., 2012). Thus, interest in integrating music into healthcare settings is blooming.

FIG. 1: SCIENTIFIC PUBLICATIONS ON "MUSIC INTERVENTION" FOR EACH OF THE YEARS 1990-2013

Publication statistics extracted from the scientific database Scopus.com from the years 1990-2013. A total of 1,939 publication were identified. Scopus-data were extracted on January 6, 2014.



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 1,939[1] 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. The majority of studies included focus on passive music listening to a recorded musical piece, 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 healthcare 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 for different somatic and psychiatric disorders and for 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 healthcare. ■

[1] *Output on the search term "music intervention" in the online scientific database Scopus.com on January 6, 2014.*

THE BUILDING BLOCKS OF MUSIC

2

2.
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 traced back about 50,000 years (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; McDermott and Hauser, 2005; Patel, 2010).

2.1
HOW MUSIC WORKS

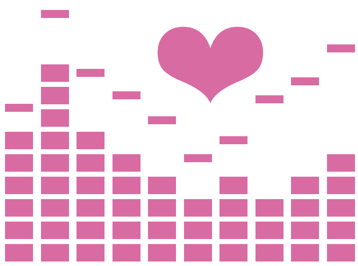
Essentially, what makes music 'music', and not just a string of random sounds, is the structure. Just like language relies on grammatical rules for acquiring meaning, music relies on specific structures or syntax (Patel, 2003). Some structural elements seem to be universally present across different cultures and musical traditions (Drake and Bertrand, 2001), whereas others are created by the conventions of a specific genre or culture (Cross, 2003; Vuust et al., 2012). The songwriter, Harlan Howard famously described country music as "three chords and the truth", and at least illustratively speaking that pretty much goes for all music. Even though this is obviously 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 the statistical regularities of musical structure and brain responses is the tonal system of musical harmony, where EEG (electroencephalography) and MEG (magneto-encephalography) measurements, such as the early right anterior negativity (often referred to as ERAN) and the mismatch negativity (MMN), are reliable markers for processing 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 in the immediate musical context (Gebauer et al., 2012). Just through listening to music, we implicitly learn the statistical probabilities between the 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 (Gebauer et al., 2012; Vuust et al., 2009). 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

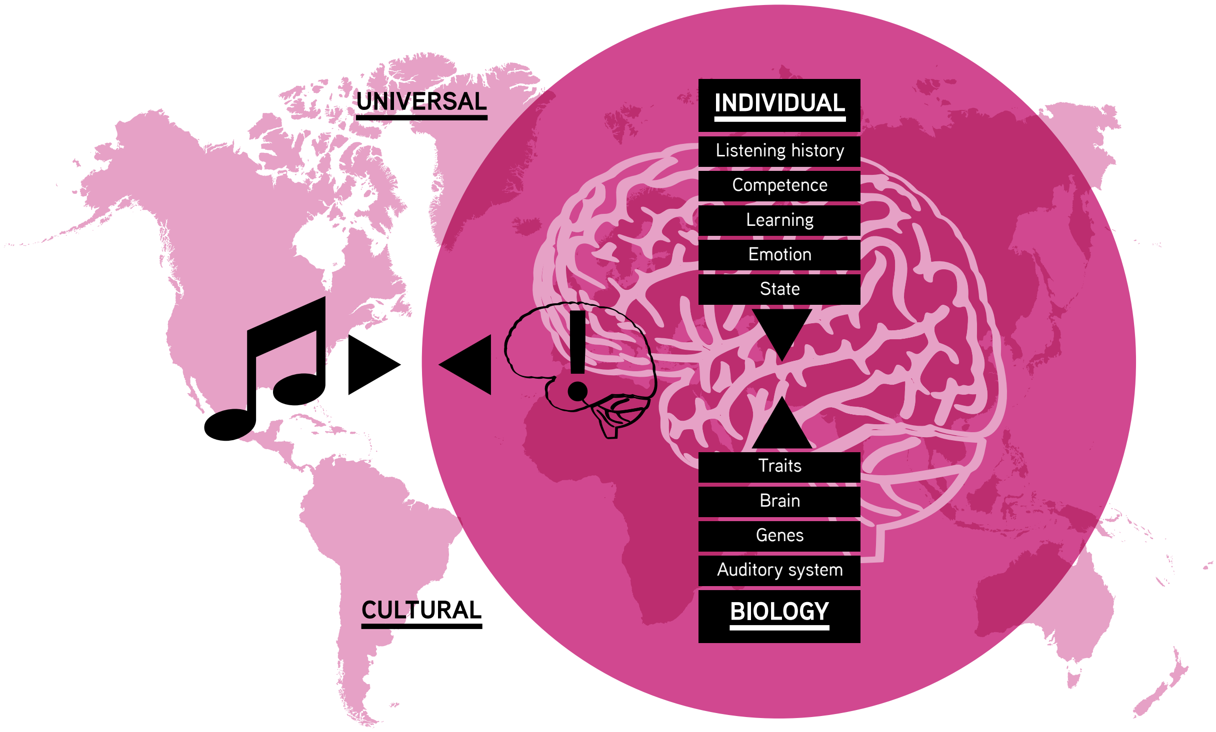
When asked why they listen to music, people consistently answer that it is because it creates emotions and pleasure. Music emotions are sometimes described in terms of valence and arousal. Arousal describes whether a person is relaxed (low arousal), or alert and energized (high arousal). Arousal covers 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, for instance the sensation of swing or groove. 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.



How music is capable of creating such strong emotions and pleasure is not, however, 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. These reflexes 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 response to dissonant or loud/ unpredictable music. (2) **Evaluative conditioning** is when a piece of music becomes associated with an emotion solely because the music and emotion have repeatedly occurred together in time. So for instance kids might really like the tune from the Friday-evening cartoon because that tune has become associated with having candy. (3) **Emotional contagion** 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 are likely to be perceived as sad if they are low-pitched, slow and have a low sound level. (4) Some music might arouse **visual images** which create 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 met. (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 spend substantial amounts of their time listening 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 the universal, cultural or individual aspect of music. This is central for designing effective products and for modifying existing music products to new markets.

FIG. 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 musical rules. Thus, when evaluating the effect of music applications 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.



2.3
UNIVERSAL ASPECTS OF MUSIC

There exist numerous universals in both the way music is used and in the structure of music (Brown and Jordania, 2013). 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. Mothers sing lullabies for their newborns, and music-making is very often one of the earliest activities that infants engage in (Trehub, 2003).

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, 2011). Across cultures the same musical modulations are used to intensify the emotional expressions. For instance it has 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 makes us more alert and energetic, while, music with a slow tempo, low pitch and low intensity will make us calm down. 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. This is identical across people and it is independent of cultural background or individual history. Interestingly the use of music therapeutically also seems to be extremely common both across cultures and back in time (Brown & Jordania, 2011).

2.4
CULTURAL ASPECTS OF MUSIC

When listening to music from tribes in Africa which have had very little contact with Western music, after just a few seconds it becomes apparent that, despite the musical universals described above, large cultural differences exist in musical styles, 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).

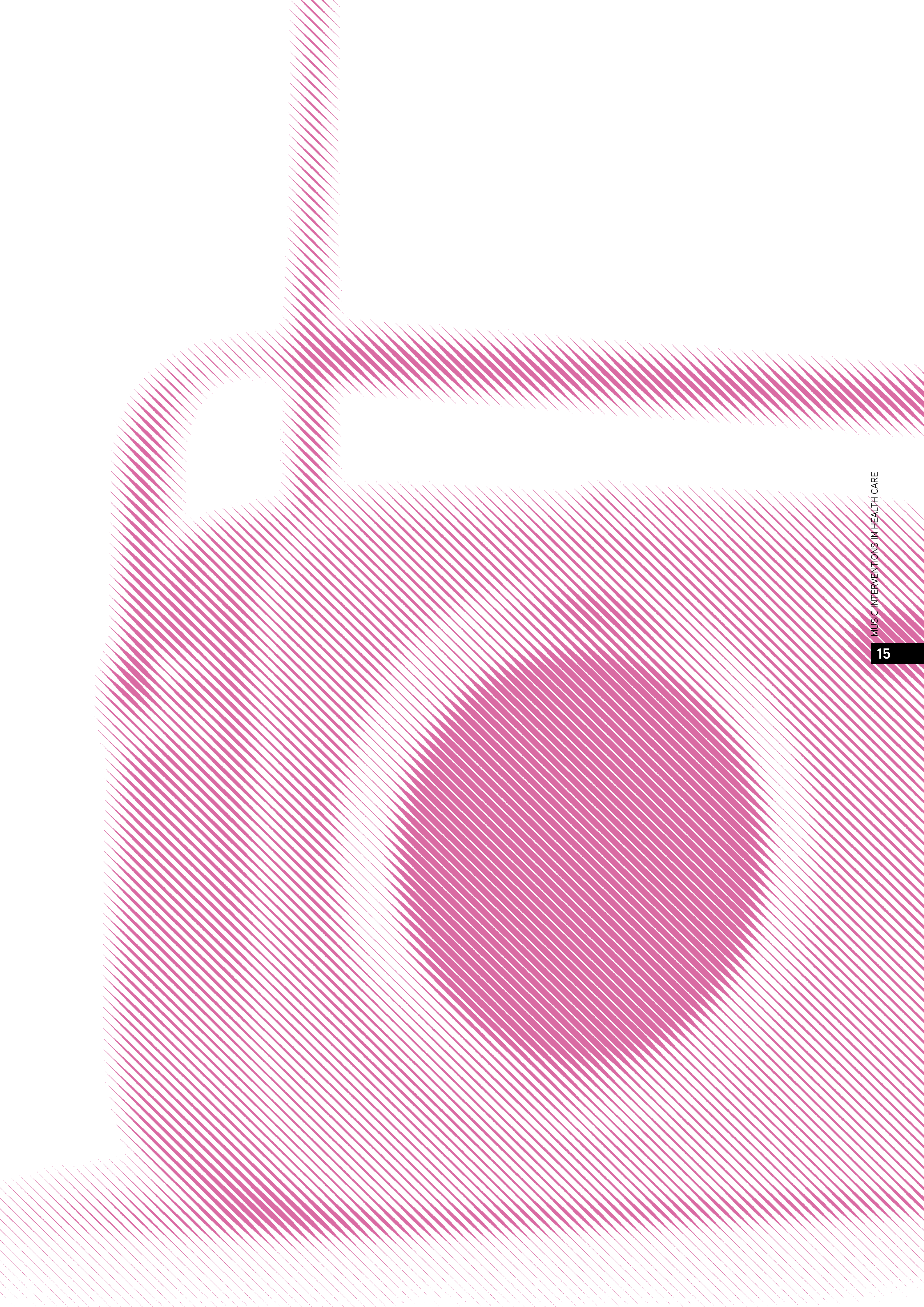
The musical culture that we grow up in, and is affected by throughout life, has a large effect on the way we perceive music, and on our musical taste. Our musical expectations are highly dependent on the statistical regularities we have learned through all the music that we have listened to on the radio, sung in school, danced to with our first true love, or played in the garage. 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 with which they are not familiar.

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 heard by rebellious and 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 they 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 throughout life. However, there is 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 genre (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 a tremendous impact on how 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., 2011b). 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 we 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. ■



3

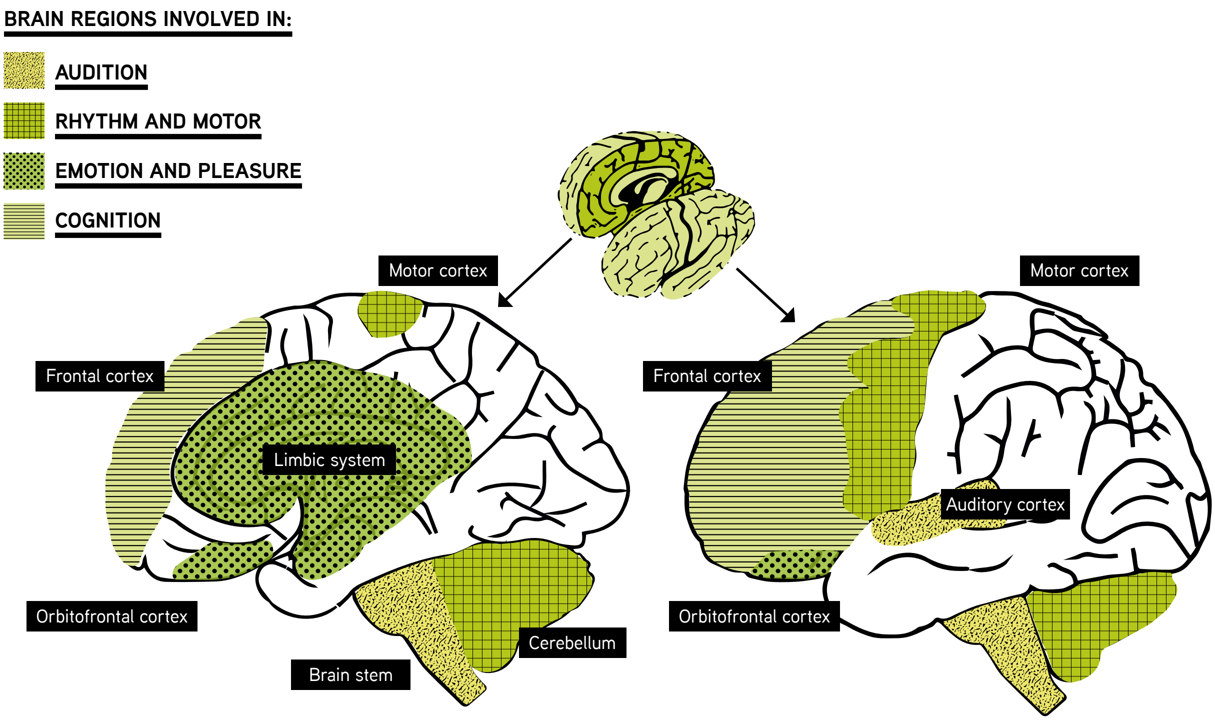
3.
MUSIC IN THE BRAIN

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 of music-making on neural plasticity over both the short and long terms (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 finally cognition.

FIG. 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.



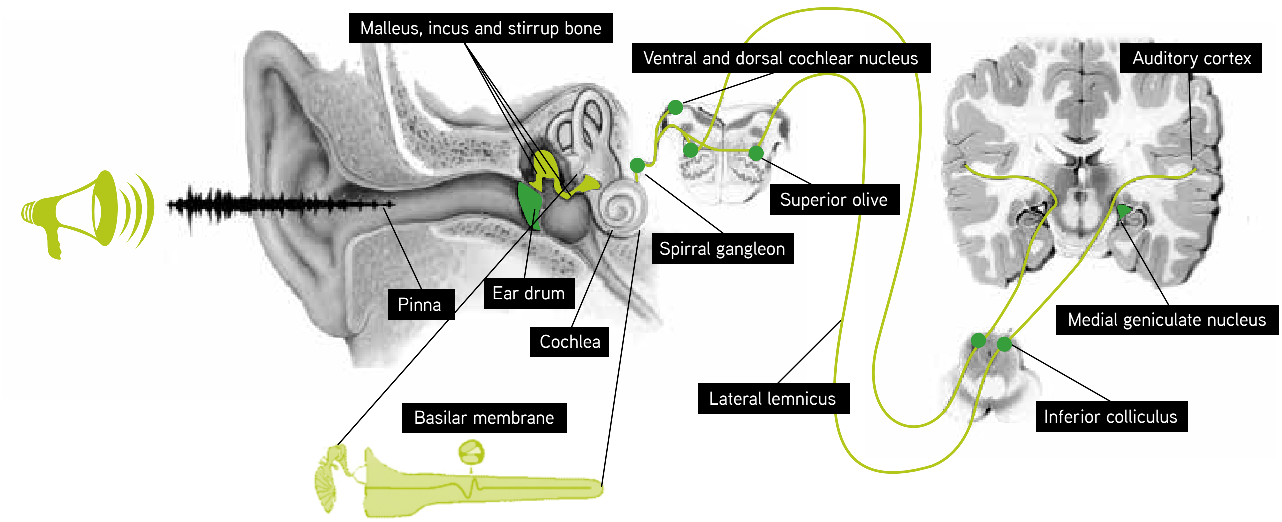
It should, however, be emphasized that though the brain can be divided into auditory, rhythm/motor, emotion and cognition regions for illustrative purposes, such clear borders do not exist in the real, living, human brain. The brain is a complex dynamical system, consisting of around 85,000,000,000 neurons. Each neuron has up to 10,000 synaptic connections with other neurons, resulting in a total of around 60 trillion connections that pass information around in the brain. The assumption that specific information remains in a restricted area of the brain is not true. Music, and all aspects of music, is processed across the entire brain. What is true, however, is that the described brain regions have a higher specialization for specific information. Not surprisingly, the auditory cortex 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.

3.1 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 travel through the ear canal and reach 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 create 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 signals from the inner hair cells are transmitted via the auditory nerve to auditory parts of the **brain stem**, to relay structures in the midbrain, and to primary and secondary **auditory cortices** in the temporal lobe (Figures 3 and 4). The brain stem processes low-level elements of the music, such as localization of the sound in the surroundings, on the basis of which ear 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 is typically 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 and this can be utilized in patients suffering from tinnitus or people with cochlear implants.

FIG. 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.



3.2

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 dancing. 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).

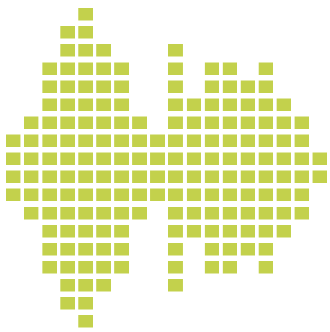
The rhythmic structure of music is primarily processed in the brain stem, cerebellum and motor regions. Besides being one of the early regions in the auditory pathways, the brain stem is essential in processing rhythm and involved in regulating physiological responses such as heart rate, pulse, blood pressure, temperature, skin conduction and muscle tension. 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.

All parts of the body are represented on the **motor cortex** in the so-called homunculus or 'little man' (Figure 5). 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 are activated, even when people are lying fixed 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 the cerebellum is also important for keeping rhythm (Parsons, 2001; Penhune et al., 1998).

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. As such, music which reduces arousal can be experienced as relaxing and may reduce negative emotions such as anxiety, while music which increases arousal can be experienced as energizing and may create strong positive emotions. Music that increases arousal will also facilitate motor activity and create an urge to move, which for most people is experienced as very pleasurable (Witek et al., 2011).

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**, as well as the brain's reward system (Koelsch, 2010). These structures include the amygdala, hippocampus and parahippocampal gyrus, ventral striatum and nucleus accumbens, insula and orbitofrontal cortex. These brain structures also respond when observing emotional expressions from faces, visual scenes, or voices (Adolphs, 2001). In particular the **amygdala**, an almond-shaped nucleus in the limbic system, is central to emotion processing. The amygdala was originally believed to be only involved in fear processing (Davis, 1992), but more recent investigations have shown that the amygdala is equally important in processing positive emotions and rewards (Baxter and Murray, 2002). Yet for music, the amygdala seems to be more specialized for scary, sad or fearful music. A study of a woman with a damaged amygdala, but otherwise unimpaired music perception, showed that she was worse at recognizing scary and sad music (Gosselin et al., 2007). Similarly, studies of healthy individuals who listen to sad or unpleasant music show activation of the amygdala (Koelsch et al., 2006; Mitterschiffthaler et al., 2007). The **hippocampus** and **parahippocampal gyrus** are closely 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.



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 is primarily located in the limbic system and consists of the **ventral tegmental area, nucleus accumbens** and **orbitofrontal cortex** (Berridge and Kringelbach, 2008). In addition to the 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 are evaluated (Gebauer et al., 2012; Salimpoor et al., 2013).

3.4
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 of distraction by directing attention towards the music.

3.5
BRAIN PLASTICITY

All activities we engage in affect the way our brain is wired, and the evidence for musical activity as an inducer of neural changes in the brain has been mounting significantly during the past decade. 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 gray 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 perfect pitch, the ability to name a tone without the aid of reference tones, are equipped with relatively more gray matter in the Planum Temporale, an auditory area on the dorsal temporal lobe of the left hemisphere, than musicians or non-musicians without perfect pitch. By comparing the cortices of twenty professional musicians with the cortices of twenty amateur pianists and forty non-musicians, the researchers also found enlargement of the cortex in pre-motor, motor, and sensori-motor cortices (areas probably 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 the motor cortex of string players has 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). The corpus callosum, the main fiber connection between the two hemispheres, is also enlarged in musicians compared to non-musicians, indicating enhanced coordination between the two hemispheres (Schlaug et al., 1995). In other words, practicing music stimulates and preserves areas essential to music and language. So even though the issue of how to interpret the thickness of the cortex is currently under debate, it appears that daily music practice leads to structural changes in areas of the brain related to motor and auditory activity, and probably also certain areas essential to language.

3.6
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 listening to music. One of the neurotransmitters that has 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 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).

Dopamine interacts with other neurotransmitters in the brain - of special interest here is oxytocin and the opioid system. In particular, 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). 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) leads 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). On the one hand, opioids might be central for the peace and relaxation we can experience from certain music, but on the other hand, opioids also seem to be responsible for the strong emotions or pleasure we experience from listening to music. 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, as well as the analgetic effect of music.

Finally, music affects the **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. The effect of music on the HPA axis is closely linked to the general effect on arousal, and contributes to both the relaxing and energizing properties of music. Music has also been shown to modify heart rate, respiration rate, perspiration, and other autonomic systems (Loomba et al., 2012), which has importance for the potential use of music in the healthcare system. ■

HOW CAN MUSIC BE USED IN HEALTH CARE?

4

4.
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 (heart beat, 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/watching a performance), 2) whether it is a live performance or a recorded piece, 3) whether the music is self-chosen or chosen by healthcare professionals, music therapists, or others. In the studies reviewed below, we have primarily focused on passive listening to 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, as well as general well-being, there are an excessive amount of studies available. It is thus a considerable challenge to summarize them 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. ■

Connection between specific disorders/well-being challenges and the effects of music intervention based on auditory, cognitive, rhythm/motor, arousal or emotional mechanisms.

QUALITY OF EVIDENCE

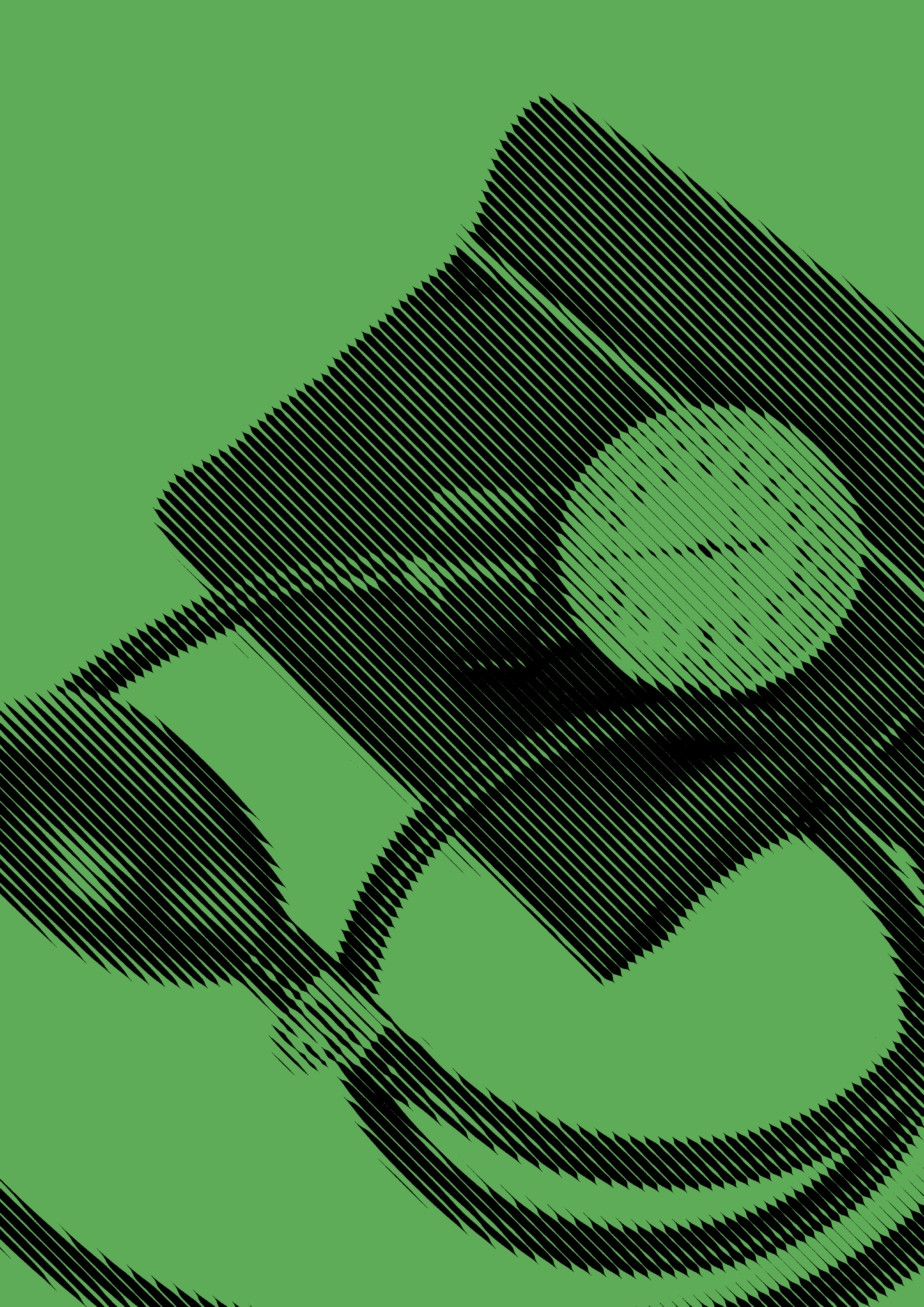
GOOD *evidence indicates the inclusion of Random Controlled Trials (RCT) and well conducted meta analyses.*
SOME *evidence indicates some agreement across studies, but more studies and better study design is needed to clarify the effect of music interventions.*
PROMISING *indicates promising application but evidence is sparse/inconsistent, and more research is needed.*

INTERVENTION MECHANISM

	Audition	Cognition	Rhythm/Motor	Arousal	Emotion	Level of evidence
SOMATIC DISORDERS						
Operations	■	■		■	■	Good
Cancer	■	■		■	■	Good
Stroke*			■		■	Some
Dementia		■			■	Some
Parkinson's			■		■	Good
Tinnitus	■	■			■	Some
Cochlear disorders	■				■	Promising
PSYCHIATRIC DISORDERS						
Depression					■	Some
Insomnia		■		■		Good
Autism	■		■		■	Promising
WELL-BEING						
Cognitive enhancement		■		■		Promising
Exercise			■	■	■	Some
Stress reduction				■	■	Some
Healthy ageing			■		■	Promising

**Rhythmic cueing for rehabilitation in stroke patients qualifies for some evidence, whereas melodic intonation therapy only qualifies for promising evidence.*

5



5.1
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 elective medical procedures, people often experience increased anxiety and stress in anticipation of the potential painful procedures and recovery they are facing. The effect of music interventions before, during and after invasive medical procedures is probably the most widely studied use of music intervention, with a number of randomized controlled trials and Cochrane reviews.

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 (Cepeda et al., 2006)). For instance, one study found that patients undergoing painful operations showed a larger decrease in preoperative anxiety with relaxing music than 0.05–0.1mg/kg of midazolam (Bringman et al., 2009). In extension to 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 interventions are also associated with reduced individual pain intensity ratings (Jafari et al., 2012; Ozer et al., 2013). 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). Similar results have been found in children undergoing operations (Nilsson et al., 2009). One study found that patients undergoing coronary procedures experienced a positive effect of listening to a specially designed piece of music, and that listening to music through an audio pillow was preferred to loudspeakers, by both the patients and staff (Weeks and Nilsson, 2011). While these findings are very promising, it should nevertheless be noted that another review reports that only half of the reviewed studies found a positive effect of music interventions on individual levels of anxiety and pain, while the other half of the studies reported no difference between the music intervention group and a control group (Nilsson, 2008).

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 described mechanisms; 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. By having 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 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 pleasantness ratings and reductions in pain intensity (Roy et al., 2008).

An additional impact of music on reducing pain during operations (including cancer procedures) is the release of endogenous **opioids** in the midbrain, which work as the body's own painkillers. Besides the analgesic effects of opioids, they are also tightly interconnected with the dopaminergic reward system, which creates pleasure and 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 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.

In general, familiar music also has the highest impact on emotional responses and activity in the reward system (Pereira et al., 2011a), and might therefore result in more endogenous opioids being released. 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. For improved pain reduction, individualized musical material should be offered. Another central element is that music is capable of creating a sense of familiarity, even in completely unfamiliar settings such as in the case of hospitalizations. Then listening to familiar music might give a sense of control over an otherwise completely unpredictable environment. 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 SUMMARY The majority of studies report 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 individualized/preferred music. It should, however, be noted that the effect of music varies greatly between studies, but the potential of music to reduce the need for analgesics and/or 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 acute pain, anxiety and mood in cancer patients.

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.

EVIDENCE Anxiety and depressive symptoms are associated with having a life-threatening disease, such as cancer. It has been 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 chemotherapy and radiation therapy (Bradt et al., 2011; Zhang et al., 2012). Furthermore, RCT studies have found that music interventions have positive effects on mood in cancer patients (this is however not seen as a reduction of depressive symptoms), and there is evidence suggesting improved quality of life from music interventions in palliative cancer patients (Archie et al., 2013; Zhang et al., 2012).

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. Music has been found to reduce heart rate and respiratory rates during cancer procedures; it has a statistically significant analgesic effect (Zhang et al., 2012), and it reduces analgesic requirements during painful procedures and up to 24-h post-operatively, also in cancer patients (Archie et al., 2013).

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, distraction, familiarity, and arousal regulation. Indeed, psychological stress seems to be linked to up-regulation of inflammatory processes that promote tumor growth, 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. Potential use of music to reduce stress should aim for early interventions, and more research is needed to evaluate whether 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. Besides, the research 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 timescale 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
STROKE

FACTS Rhythmic cueing has a moderate effect on motor control during gait and arm-reaching stroke patients. Musical intonation therapy is widely used to facilitate speech recovery in patients after a stroke, but randomized controlled trials are lacking. Listening to music 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 auditory and frontal cortex are affected. Thus, rehabilitative interventions often focus on improving/regaining speech, cognitive abilities and motor control.

EVIDENCE Gait is an intrinsically rhythmic movement, and rehabilitation with focus on improving gait in hemi-paretic patients has found that rhythmic cueing, i.e. by a metronome in a simple instrumental piece of music, shows positive effects (Wittwer et al., 2013). Studies report pronounced effects of rhythmic cueing on stride symmetry, gait velocity, weight bearing on the paretic leg, knee angle control, as well as mediolateral and vertical displacement of center of mass resulting in a smoother forward trajectory of movement (Thaut et al., 2001). Besides, gait recovery, rhythmic cueing has also been shown to improve timing, velocity and acceleration of arm movements in stroke patients (Whitall et al., 2000). Long-term rehabilitative interventions using rhythmic cueing have been shown to have superior effects to conventional physiotherapy (Thaut et al., 2001).

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 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). Yet, no randomized controlled trials of certified Cochrane reviews exist on the topic (van der Meulen et al., 2012), so more research is needed to clarify the effect of melodic intonation therapy more precisely.

Besides, rhythmic cueing and melodic intonation therapy, music can also been used as '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 over two months compared to listening to audio books or not getting any intervention (Särkämö et al., 2008).

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, without the involvement of cognitive modulation or initiation. This is supported by the fact that rhythmic cues add stability in motor control immediately, and do not require learning. Rhythmic cues may thereby increase the symmetry of muscle activation and even facilitate 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 the sensorimotor and premotor cortices on the right side that might prime articulation (Johansson, 2011).

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 other.

IN SUMMARY There are relatively consistent findings of improved gait in stroke patients after music interventions using the method of rhythmic cueing, while more conflicting findings exist with regard to arm movements (Richards et al., 2008). The study that was unable to replicate the findings of positive effects of rhythmic cueing on arm movements used a slightly modified training program, thus the method and duration of the training might be essential for positive outcomes. The results and neurological findings in support of melodic intonation therapy are promising, although there are only few well-controlled studies, and no randomized controlled trials have been conducted. Traditional melodic intonation interventions require a therapist, but new technologies might be valuable for supporting melodic intervention training without a therapist, thereby making costs lower and the number of training hours higher. 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 has positive effects on mood too. Meanwhile, it should be emphasized that there are only few studies investigating the effect of music interventions on cognition and mood, so no firm conclusions about the effectiveness can be drawn from this.

5.4
DEMENTIA

FACTS There is some evidence that music interventions improve affective, social, cognitive and physiological symptoms in patients with dementia. Yet, findings are not consistent across studies and very different methodologies make it difficult to draw any firm conclusions on the effectiveness of music interventions in dementia.

DESCRIPTION Dementia typically affects elderly people, and the prevalence is found to double between 65 and 80 years. It is estimated that dementia affects about 24 million people worldwide (Narme et al., 2014), and as the general population is increasingly living longer, the number of people diagnosed with dementia is growing rapidly. 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 healthcare professionals working with people with dementia is to promote quality of life and an active day-to-day life for the patients.

EVIDENCE Studies have 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 (Vasionytė and Madison, 2013). One study also 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), and evidence-based guidelines have been proposed for this type of music intervention in dementia (Gerdner and Schoenfelder, 2010). 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). A very recent RCT study compared music intervention with a non-musical intervention, here cooking, and found that both music and cooking had positive effects on patients' emotional state and a reduction in behavioral symptoms such as agitation/aggression, hallucinations, delusions, disinhibition and sleep abnormalities (Narme et al., 2014). Thus it seems that the positive effects are not as such specific to music, but that several activities might be equally valuable in improving function in demented patients. However, music is probably one of the most cost-effective and easy-to-use interventions, compared with e.g. cooking interventions. Finally, 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 in general.

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. The arousal-regulating effect of music has an impact on heart rate, breathing and blood pressure in demented patients, similar to that observed in healthy individuals. 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 vital 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.

IN SUMMARY Though results are mixed, there seems to be a great potential for music interventions in patients with dementia (Narme et al., 2014). Studies consistently find that individualized/preferred music is more effective than experimenter-selected (Vasionytė and Madison, 2013), and 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. failing to have proper active control groups). For critique see Vink, Bruinsma, & Scholten (2011), and data from studies using music therapy (active playing) and music intervention (passive listening) as they have a tendency of collapsing in meta-analyses making the findings less reliable. Meanwhile, many elderly people 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. Therefore, 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.

5.5
PARKINSON'S DISEASE

FACTS Music interventions improve motor function, speech production and emotional symptoms in patients with Parkinson's disease.
DESCRIPTION Parkinson's disease is caused 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-based movement therapy is found to improve gait, in particular walking velocity (de Dreu et al., 2012), and some evidence suggests that music interventions can improve motor control for speech in patients with Parkinson's disease (Thaut et al., 2001). Rhythmic auditory stimulation is used as a pacemaker during gait training, and consists of pre-recorded metronome-pulse patterns embedded into the on/off beat structure of rhythmically accentuated instrumental music. One study found rhythmic auditory stimulation to be significantly more effective than self-paced training on improving gait velocity, stride length and cadence in Parkinson's patients (Thaut et al., 1996).

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 seems to have a positive effect on the motivation to engage in rehabilitation exercises.

HOW DO MUSIC INTERVENTIONS FOR PARKINSON'S DISORDER WORK? External **rhythmic** cues seem to facilitate **movement**, perhaps by engaging the brain mechanisms controlling timing, sequencing and coordination of movements (Rochester et al., 2010). Even in Parkinson's disease, 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). One viable explanation for the finding of improved motor function after listening to favorite music is the finding that **emotional** and pleasurable music can cause midbrain dopamine release, which might cause great improvement in Parkinson's patients who suffer from dopamine depletion in the midbrain (Sacrey et al., 2011).

IN SUMMARY Overall, there seems to be a positive effect of music-based movement therapy on gait velocity in Parkinson's patients. However, there are many different approaches to using music interventions during gait training, and the distinctions between these and differences in effectiveness are not clear. For instance, music-based movement therapy and auditory rhythmic cueing are not identical protocols, but seem to have highly similar effects. More studies including more participants and identical methodologies are needed. Some studies have integrated music-based movement therapy into partnered dancing, but this was found to be less effective than gait-related training. The potential of increasing midbrain dopamine release in Parkinson's patients by listening to music or playing music has not been widely investigated. When considering such possibilities, it should however be acknowledged that Parkinson's patients in the more severe stages of the disease are impaired in recognizing emotions in music (van Tricht et al., 2010), and since the emotional impact of music seems to be what makes us enjoy listening to music, the pleasurable and motivating power of music might be reduced in these patients.

5.6
SUBJECTIVE TINNITUS

FACTS Several music interventions for tinnitus exist, such as desensitization, hearing devices with built-in music generators and 'notched' music. All interventions are supported by independent studies, but no randomized controlled trials exist to support conclusions about the effectiveness of music interventions on tinnitus perception.

DESCRIPTION Subjective Tinnitus is a common symptom of hearing disorders. It is a condition where a noise or a ringing sound is constantly heard without the presence of an actual sound. There are numerous causes of tinnitus, but for most cases a sensorineural hearing loss (SNHL) followed by a maladaptive neural reorganization of the auditory pathways and auditory cortex seems to contribute to the generation and maintenance of tinnitus. However, not all people with SNHL report tinnitus.

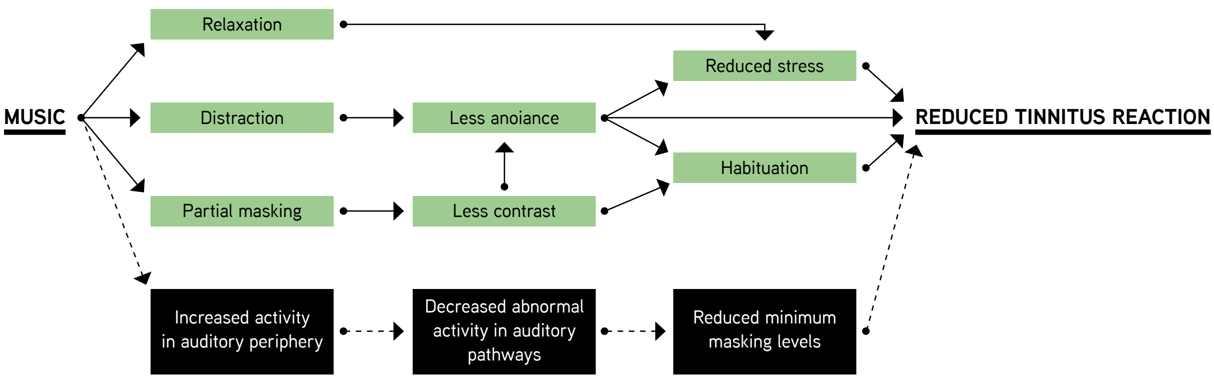
Tinnitus is a plasticity disorder in the sense that it is believed to be the result of the brain's plastic adaptation to decreased auditory input due to peripheral damage (Møller, 2011). The result is increased central auditory activity which is believed to cause tinnitus perception (Kaltenbach et al., 2005).

The sound heard differs from person to person. This can be ringing, buzzing, cricket-like sounds and others. Other disorders related to tinnitus are: hyperacusis, insomnia, anxiety, depression, stress and lack of concentration. Most people with tinnitus are not bothered about it, but some 20-40% has negative reactions to the condition. Tinnitus reactions and stress are often correlated (Hébert and Lupien, 2007). As no cure for tinnitus is known, most interventions aim to help the individual to better adapt to the tinnitus or, so to speak, mitigate the reactions of the tinnitus sufferer. Habituation and desensitizing are in other words the goal of the intervention or treatment. Sound stimulation or sound enrichment is often used in tinnitus therapies to help the patient habituate to the tinnitus sound.

EVIDENCE Music has been used as a systematic desensitizer for tinnitus. In this context music is used to provide relaxation and distraction from the tinnitus, and to induce positive emotions. Over time this is found to lead to reductions in awareness of the tinnitus and a sense of control over the tinnitus (Davis, 2006). Hearing aids with a build-in fractal music generator have also been used for tinnitus treatment. After six months of use, a significant tinnitus-reduction was measured on the Tinnitus Handicap Inventory questionnaire (Sweetow and Sabes, 2010). Use of hearing aid amplification is often a good tinnitus treatment. 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). Most commonly a broadband noise is used as stimulus, but also other sounds such as music can be used. One study had chronic tinnitus patients listen to self-chosen, enjoyable music, which was modified ("notched") to contain no energy in the frequency range surrounding the individual tinnitus frequency. The study 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). Among treatment methods tinnitus patients report that, after hearing aid treatment, treatment with music has the highest efficacy (KochKin et al., 2011).

FIG. 5: THE BENEFICIAL EFFECT OF MUSIC ON TINNITUS REACTIONS

Music can make people relax and relaxation can reduce stress. Furthermore music can distract the tinnitus patient in such a way that the attention can be drawn away from the tinnitus sound to the music. This can lead to less annoyance and again reduce stress and tinnitus reaction. Music listening may also induce partial masking of the tinnitus sound resulting in less contrast between tinnitus and other sounds. Over time this may help the patient to habituate to the tinnitus. The path with dotted lines show how sound stimulation and thus music can be used to compensate for the lack of peripheral auditory input and thereby maybe reduce the abnormal activity in the auditory pathways and tinnitus loudness (Kaltenbach et al., 2005).



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 masking may be intolerably loud. Masking can give instant relief, but will not in itself give any long-term effect. A partial **auditory** masking reduces the contrast between the tinnitus sound and the background sound. Sound stimulation is also used to distract attention away from the tinnitus 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 ultimately this gives the patient a sense of being in control. Over time this can help the patient to habituate to the tinnitus and thereby reduce the tinnitus reaction of the patient.

The main mechanism between 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 changes the neurons' connection strength and over-activity.

5.7
COCHLEAR IMPLANTS (CI)

FACTS There is no strong evidence of positive effects of music intervention on general auditory processing or language in patients with cochlear implants, but consistent findings of improved music perception, and joy of musical activities suggest large possibilities for music interventions in this novel field.

DESCRIPTION Cochlear implantation (CI) is a surgical treatment that effectively helps deaf people regain hearing abilities. At present there are over 150,000 CI-users worldwide (Petersen et al., 2009). The CI operates by an external signal processor, which breaks up sound into different frequencies, converts these into electrical signals and transmits them to an internal receiver through a radio-frequency link. The receiver passes the stimuli on to an implanted electrode array, which stimulates the remaining auditory nerve fibers in the cochlea. Hereby, the auditory nerve is activated, allowing sound signals to reach the brain's auditory system. Hence, the average CI-user recognizes above 80% of sentences and about 55% of monosyllabic words in quiet listening conditions after 12 months of practice with a unilateral CI.

EVIDENCE One study found that out of twenty-nine participants, 38% did not enjoy listening to music after the implantation and 86% reported that they spent less time listening to music after the implantation than before (Leal et al., 2003). Not surprisingly, surveys have shown that a majority of adult CI recipients' self-reported levels of music listening and enjoyment were significantly lower after having the cochlear implantation than before the hearing loss (Gfeller et al., 2000). On average, implant users seem to perceive rhythm as well as normal hearing controls, but recognition of melodies and timbre perception is poor (McDermott, 2004). However, CI-implantation has been found to result in better music perception in the form of improved pitch, rhythm and timbre discrimination compared to before the implantation (Leal et al., 2003). Since music is generally found to be an important source of joy and social belonging in most people's life, producers are continuously trying to improve the impoverished music transmission of the electrical cochlear implant. Indeed, a recent behavioral six-month one-to-one musical ear-training program on CI-users found a pronounced improvement in music perception and high levels of joy from engaging in musical activities (Petersen et al., 2012). A brain-imaging study from the same research group also demonstrated brain plasticity in auditory and language areas of the brain after CI-implantation (Petersen et al., 2013). Since, in many cases, music has been an essential part of these patients' cultural and social life prior to deafness, CI-candidates' hope of retrieving music enjoyment is an important incentive for choosing this treatment.

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 the 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, whereas passive music listening might be perceived as aversive due to the impoverished sound transmission of the CI device. Finally, it might be a goal in itself to regain some of the joy of listening to music from before the hearing loss. This might be done by improving CI devices or by intensive musical training (Petersen et al., 2009).

IN SUMMARY The study of auditory abilities, and in particular musical interventions to improve auditory abilities in CI users is a new field and very little research exists. However, the studies that have been conducted point to potential benefits for improving music perception and joy in musical activities. ■

PSYCHIATRIC DISORDERS

6

6.1
DEPRESSION

FACTS Music intervention seems 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. A key symptom of depression is anhedonia; the lack of interest and enjoyment in previously pleasurable activities. Besides significantly lowered mood, sleep and eating disturbances 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). This suggests that the ability to enjoy music and become emotionally affected by music are still intact in people with depression. In general, studies find significant reductions in depressive symptoms after listening to the patients' own choice of music (Chan et al., 2011). There also seem to be improvements over time, indicating a cumulative dose effect. The average time needed for significant reductions in depressive symptoms was 2-3 weeks (Chan et al., 2011). 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 there does not seem to be differences in the effect on depressive symptoms between daily and weekly music listening practices.

Another key symptom of depression is insomnia or hyper-somnia, and several studies suggest that music can have a positive effect on these conditions too (see section 6.2 on insomnia).

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 are 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 are 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. A set of best practice guidelines for using music interventions for depression has been developed (Institute, 2011).

IN SUMMARY Limited evidence exists on the effect of music interventions on people with depression. There are, however, promising findings, indicating that this should be investigated further. 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 subjective and objective measures of sleep quality in people suffering from insomnia.

DESCRIPTION Sleep disorders are common in modern society and insomnia symptoms are estimated to affect up to 40% of the adult population (Morin et al., 2011). Insomnia is defined as difficulty in initiating and/or maintaining sleep, early morning waking, or non-restorative sleep (Chang et al., 2012b). While insomnia has a severe negative impact on daily functioning, medical treatments have numerous side-effects and should be avoided over longer time intervals.

EVIDENCE Music interventions are widely used to promote sleep in insomnia patients. Both subjective and objective data show significant improvement of sleep quality through systematic music listening at bedtime (Chang et al., 2012b; De Niet et al., 2009; Harmat et al., 2008; Lai and Good, 2005). A recent meta-analysis of ten reviews of music-assisted relaxation found medium effects on improved sleep quality in insomniac patients (Gerrit, 2013). One study developed 'brain music' by recording the electrical activity of the brain of insomnia patients during different sleep phases and then converting this into music. Participants listened to the music based on their own brain waves before going to sleep, and 80% experienced positive effects both on subjective sleep evaluation and on neurophysiological and neuropsychological measurements (Levin, 1998). However, the efficacy of 'brain music' has not been tested in other studies.

HOW DO MUSIC INTERVENTIONS FOR INSOMNIA WORK? There is a limited understanding of the musical parameters underlying the effect of music on sleep, but a slow tempo and the impact on arousal regulation has been suggested to be of importance for reducing **arousal**. The timing of the intervention at bedtime and the use of soothing music for 45 min have been used to facilitate relaxation while attempting to sleep (Chang et al., 2012a). There might also be **cognitive** factors responsible for the impact of music interventions on sleep, for instance listening to music might distract attention away from rumination and involuntary thoughts that often 'pop up' at bedtime.

6.3
AUTISM SPECTRUM DISORDER

FACTS Music may be a fruitful intervention for teaching emotion recognition in autism, but studies are few. Novel music-based protocols are developing for improving language in non-verbal individuals with autism.

DESCRIPTION Autism spectrum disorder (from here on referred to as autism and 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 remains throughout life. It has been estimated that about 25% of individuals diagnosed with ASD remain non-verbal throughout life. A central concern of many parents of 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). Likewise, 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, has been 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 labeled auditory-motor mapping training has been show to be successful in teaching language to completely non-verbal children with ASD (Wan and Schlaug, 2010).

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. The release of oxytocin while listening to music 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.

IN SUMMARY Evidence concerning the effect of music interventions in children and adults with ASD are sparse. However, several studies suggest that music might be a particularly fruitful intervention type in the population. Overall there seems to be a good effect of music intervention for improving language abilities in non-verbal children with ASD. ■

WELL-BEING

7

7. 1
COGNITIVE ENHANCEMENT

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

DESCRIPTION The positive impact of music on cognitive performance has been much debated since the finding of 'the Mozart effect' in 1993 (Rauscher et al., 1993). The potential use of music as a cognitive enhancer would have a great impact, both in rehabilitative and academic use.

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 as effective for enhancing spatio-temporal reasoning as listening to Mozart (Nantais and Schellenberg, 1999); for similar results see (Rideout et al., 1998; Schellenberg and Hallam, 2005). 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. Meanwhile, findings of improved verbal IQ and executive function as a result of short-term music training exist

(Moreno et al., 2011). Likewise, a study from the same group that originally published 'the Mozart effect', found that children who were given music lessons in playing keyboard (Mozart and Beethoven) for 6 months performed 30% better on a spatial-temporal reasoning task than children of the same age but without musical training (Rauscher et al., 1997; Rauscher and Zupan, 2000).

HOW DO MUSIC INTERVENTIONS WORK? 'The Mozart effect' has subsequently been described as a function of the positive **emotional arousal** induced by listening to Mozart, or to any other music with similar musical characteristics for that matter (Jenkins, 2001; Thompson et al., 2001). However, a rat study from 1998 sought to test this hypothesis by having separate groups of rats listen to Mozart, minimalist music (Phillip Glass), white noise, or silence from before birth (in utero) and for 60 days after birth. Surprisingly, this study found that the rats that had listened to Mozart performed a maze task (requiring spatio-temporal navigation) significantly faster than the remaining groups (Rauscher et al., 1998). Thus, this study suggests that the positive effect on spatial reasoning of listening to Mozart is not caused by emotional arousal, since rats do not show any signs of emotional appreciation of music (neither Mozart nor any other genres). Another suggestion is that, since the brain regions activated by music (particularly prefrontal, temporal, and precuneus regions) are also crucial for spatial reasoning, music might facilitate engagement of these regions during spatial reasoning tasks (Jenkins, 2001).

IN SUMMARY Evidence suggests that listening to music that is enjoyable may improve performance in tests of spatial-temporal abilities in healthy subjects. This might be due to the effect of music on emotional arousal, or to the engagement of similar brain networks in music perception and spatio-temporal reasoning. However, the duration of improvements on spatio-temporal abilities is widely debated.

7.2
PHYSICAL EXERCISE

FACTS Studies of music interventions during physical exercise have investigated psychological, physiological and ergogenic effects, but results are not consistent and vary across exercise disciplines.

DESCRIPTION The health benefits of physical exercise across the lifespan are receiving increasing attention. 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 Some studies find that music interventions lead to a range of benefits that include enhanced positive effect, 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 high-intensity training has been 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 sec. anaerobic high-intensity cycling test (Chtourou et al., 2012; Jarraya et al., 2012). Meanwhile, other studies find no effect on music during anaerobic exercise (Atan, 2013). This might be because this type of exercise is so demanding that the distracting effect of music counteracts the focus needed to perform optimally, while listening to music before and after high-intensity performance might still have a positive effect. In addition to this, no effect has been found from listening to self-selected music during a 5-min (Bigliassi et al., 2012) or 10-km cycling competition (Hagen et al., 2013). Finally, one study demonstrated, that listening to music or rhythms after intensive exercise might shorten the time needed to recover (Eliakim et al., 2013).

HOW DO MUSIC INTERVENTIONS WORK? The most likely mechanisms underlying the putative 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, listening to music with a synchronous rhythm to the movements being performed seems to enhance performance, while asynchronous music might impair performance (Karageorghis and Priest, 2012a, b). The **cognitive** distraction provided by the music also seems to be important for improved performance and longer endurance (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 important for the increased motivation associated with listening to music during physical exercise (Karageorghis and Morton, 2006). In terms of selecting music, most studies use self-selected music. However, 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). Interestingly, it seems that men often perceive music interventions during exercise more positively 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 The reported findings on the effect of music interventions during physical exercise are not consistent across studies, and no meta-analyses exist. Music has 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 points towards the numerous ways in which music can be used to improve performance or motivation during physical exercise. Yet, due to the heterogeneity across studies and the low generalizability across exercise disciplines, or from elite to recreational athletes, no firm conclusions can be drawn from the existing literature. Overall, there seems to be some evidence for the effectiveness of music during running and swimming, but these applications need to be investigated further before conclusive arguments can be made.

7.3
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. Of particular concern are work-related stress reactions, where people may be experiencing severe physiological symptoms of stress before appropriate treatment is initiated. 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 wellbeing. 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). Furthermore, several studies have found that experimenter-selected relaxing music decreases 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. Listening to music has also been 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. Musical genre seems to be important for creating stress reduction. One study compared relaxing classical music with techno music, and found that techno heightened 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)). Thus, it seems that the reduction of cortisol depends on musical features such as slow tempo, low pitch, and no lyrics. Indeed, a study investigating the effect of rhythmic characteristics found that non-rhythmic music ('meditative' music) showed a significantly larger reduction in cortisol levels, than music with a regular or irregular rhythm (Möckel et al., 1994). 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).

HOW DO MUSIC INTERVENTIONS WORK? The mechanism through which music 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 their effect on stress reduction (Chanda and Levitin, 2013). Furthermore, music might also contribute to lowering of stress by inducing positive **emotions**.

IN SUMMARY There is good evidence to suggest, that music has 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.

7.4
HEALTHY AGING

FACTS Music interventions seem promising for improving well-being, motor and cognitive functioning in older adults. Though, very limited research exists on this topic.

DESCRIPTION Keeping the brain active is a central goal during a healthy aging process. However, 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). One study found that music improves sleep quality in older adults (Lai and Good, 2005). With regard to mental decline, one study found that having actively played music (or sung) was a strong predictor of intact cognitive abilities in old age (Hanna-Pladdy and MacKay, 2011). Moreover, 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).

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), 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 than 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 studies from music therapy suggest that music can facilitate friendship by providing people with opportunities to interact and share their life experiences with others (Hays et al., 2002).

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. As demonstrated in Figure 3, music activates regions across all 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 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, described with regard to friendship and well-being, seem to be created through music listening. In particular, the **emotional** qualities of music and the release of oxytocin might be fundamental for the companionship and positive feelings that we experience from listening to music together.

IN SUMMARY Filtering speech from background noise in particular seems to be a potential fruitful target for music interventions in healthy elderly individuals. Also music listening seems to be a valuable way of providing experiences to people who because of progressive age might no longer be able to pursue social and/or aesthetic activities on their own. Contrary to solving cross-words or reading the newspaper, music does not demand intellectual engagement or intact vision to be enjoyable. Thus, for older people experiencing cognitive decline, listening to music is still a viable option. Thus, there seems to be important areas of interventions where music could be important for improving positive aging, but more research is needed across all applications. ■

SUMMARY

8

8. SUMMARY: EVIDENCE, CHALLENGES AND PERSPECTIVES FOR MUSIC INTERVENTIONS IN HEALTHCARE

Lately, 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 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 to 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 healthcare are promising. Well-documented effects of music interventions are found on reducing pain and anxiety in operations and cancer. Music interventions are also found to ameliorate most symptoms for Parkinson's patients, and improve sleep quality in insomnia. For stroke rehabilitation, dementia, subjective tinnitus, depression, exercise and stress reduction, there are many promising new findings and emerging methods, but larger studies and meta-analyses are still needed. For the use of music in cochlear implantees, autism, and for cognitive enhancement and aging, evidence is still relatively scarce, but these areas nonetheless provide interesting fields for future research and development of novel intervention methods. Fields,

which are not included in this white paper, but also show great promise, are the use of music interventions during dental procedures (Aitken et al., 2002; Standley, 1986) and during child birth (Kushnir et al., 2012; Li and Dong, 2012).

The framework for understanding the brain processing of music presented in this white paper also hints at several novel areas for which music intervention could be effective. For instance, the development of a refined understanding of the neurochemistry of the brain and how music can affect a number of neurotransmitters and hormones related to reward, motor and attention systems in the brain, may hint at possible implementations of music treatments for patient groups such as attention deficit hyperactivity disorder (ADHD), schizophrenia, Tourette's syndrome, and auditory processing disorder.

However, a number of challenges and key factors to the success of the research and the putative applications exist. Important limitations in most of the scientific studies in this field are lack of proper active control groups, differences in the methodological approaches across studies and limited sample sizes, making strong conclusions and meta-analyses difficult. 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.

There are also a number of other things to consider with regard to using music as an intervention. 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) that music interventions and associated technology are easy to use for healthcare personnel and patients alike. Certainly, music cannot replace good medical treatment, but it can supplement it and lead to 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 potentials that lie in music interventions should be pursued, and new technologies need to be developed based on scientific evidence to identify appropriate applications of music, and to ensure optimal health benefits from implementing music in novel settings, such as the healthcare system. ■

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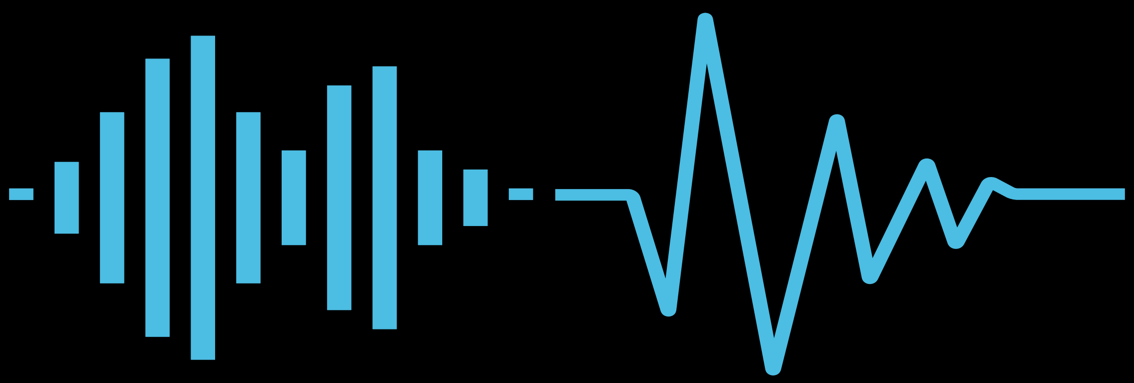

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