Full-Length Article

Medicine's Melodies: *Music, Health and Well-Being*

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Abstract
Most of what we hear about the connection between music and health is largely anecdotal. The past decade has seen a renewed interest in the connections from researchers conducting rigorous experimental studies. In this broad overview, I will review the current state of knowledge, touching on music therapy for both physical and psychological health, music for the management of pain, and musical interventions for dementia patients.

Keywords: ***music, medicine, health, well-being, therapy***

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Prelude

Beliefs about music's power to heal the mind, body and spirit date back to the Upper Paleolithic era, around 20,000 years ago, when ancient shamans used drumming in the hopes of curing a wide range of maladies, from mental disorders to wounds and illnesses [1]. Music was also used as therapy in Old Testament times [2] and Classical Greece [3]. During the 11th Century B.C.E., near the end of his life, King Saul suffered from periodic depressions and agitation. On such occasions he would summon David, reputed to be among the greatest musicians in the kingdom:

> "David would take the lyre and play it; Saul would find relief and feel better, and the evil spirit would leave him." [4]

In modern times, music therapy was reintroduced during World War II to treat wounded veterans [3]. Some of the beneficial effects across all these periods may have accrued by putting patients into a trance state [5], or by accessing the subconscious, thereby "opening the healing mechanism for the patient"[6]. Science has only recently confirmed what shamans and other faith healers knew: that listening to music facilitates entry into the brain's default mode network (DMN) [7], a path to the subconscious [8].

From Saul to Science

Across much of the last 40 years, most of what we knew about the use of music for medical interventions, both psychological and physical, came from anecdotes, speculation, and case studies rather than controlled experiments. Many practitioners lacked formal certifications in music therapy, and many had no training in medicine, scientific experimentation, psychotherapy or nursing. This is not to say that music interventions were not therapeutic, but there was little consistency or standardization as to how such therapies were delivered. Many approaches and doctrine lacked scientific evidence. Three important developments changed this in recent years.

First, the American Music Therapy Association became more well-known, and in 2008, they formally adopted the phrase "evidence-based" in their defining statement:

> "Music Therapy is the clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program" [9].

In the news media, there were approximately 4 articles mentioning evidence-based uses of music from 1998-2008, but between 2009 – 2019 there were 185, with nearly all mentioning the AMTA.

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Daniel J. Levitin, E-mail: dlevitin@minerva.kgi.edu| COI statement: The author received support for the research and writing of this article from the Kim & Glen Campbell Foundation. The author reports that he has previously received financial support from Fender Musical Instruments Corporation, Apple Corporation, and Sonos.

Second, researchers began to apply more rigorous methods and controls. Of 4718 articles indexed by PubMed on music therapy in the decade 2008 – 2018, one-third (1509) used a control group [10], an increase from only one-tenth in the previous decade [11]. Two developments were key: the invention of neuroimaging technologies allowing us to see the brain in action in real time, and personal computers with digital editing and playback software. This allowed researchers to parametrically vary stimuli with great precision, and to play them back the same way every time, even after multiple duplications of a file — something that was never possible in the age when stimuli were prepared by editing tape, and magnetic recording tape and vinyl records were used for stimulus presentation.

Third, dedicated University courses of study for music therapy have been established, with some of the more prominent programs being at The Frost School of Music (University of Miami), Western Michigan State University, Berklee College of Music, Arizona State, University of Georgia, and Colorado State in the U.S., and in Europe/U.K, Nordoff-Robbins, University of Augsberg, the University of South Wales, Anglia Ruskin University, University of Vienna, and Bergen University. The expansion of board certifications and licensure — and awareness of them — helped to bring more rigor to training and treatment plans.

Together, these developments have created an exciting climate of innovation alongside renewed interest and rigor in the scientific basis for music therapies and interventions. A wide range of journals now publish empirical articles relevant to these topics bringing them to the attention of a widening circle of researchers. In addition to specialized journals such as *The Journal of Music Therapy, Music and Medicine,* and *Music Therapy Perspectives,* the work of our colleagues is found in *Brain, Human Brain Mapping, Music Perception, Trends in Cognitive Science,* as well as *Nature, PNAS,* and *Science* among others.

All of this was buoyed by increased public and news media interest in music and the brain, as evidenced by popular books dedicated to the topic, beginning with the 1997 publication of journalist Robert Jourdain's book *Music, The Brain, and Ecstasy* [12] up through this year's publication of *Why You Like It* by Nolan Gasser [13], musicologist and chief architect of Pandora. In addition, the well publicized use of music therapy to aid in the recovery of shooting victim Congresswoman Gabby Giffords may also have a played a role in the public's curiosity about, and acceptance of music therapy as a serious medical option.

The neuroanatomy of music (a brief overview)

Music activates nearly every region of the brain that has so far been mapped [14].

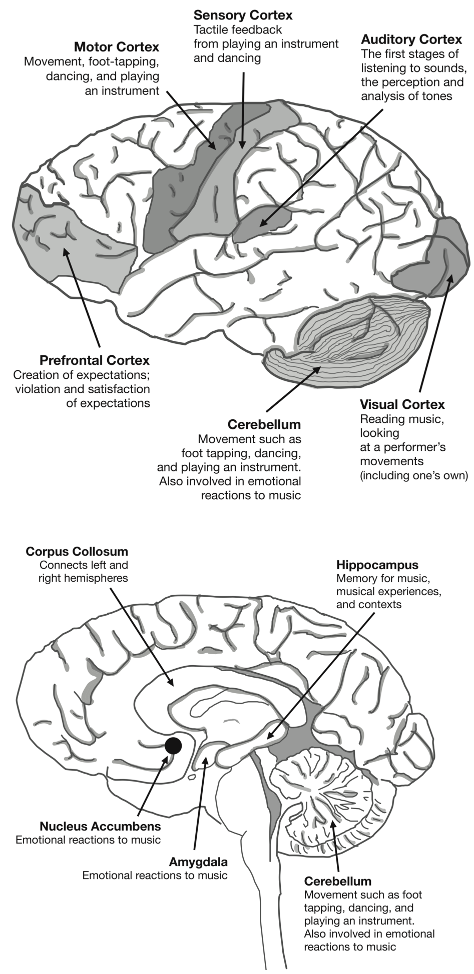

Figure 1. *Music activates a wide range of brain regions. Based on [15] and updated with new information.*

Sound waves in the air cause the tympanic membrane to vibrate, and as the resulting waves pass through the cochlea, frequency-selective neurons send signals upstream to the brain stem, inferior and superior colliculi, and primary auditory cortex (A1) [16–18]. From A1, the signal is sent to special-purpose processing circuits operating quasi-independently, and in parallel, to extract pitch, duration, loudness, timbre, and spatial location. The individual extracted pitches are strung together as sequences that yield perceptions of contour, melody, tonality (e.g. major/minor)[19] and harmony; the durational information is sequenced to yield tempo, rhythm, accelerando and ritardando [20]. The loudness information yields the dynamics that are so important in musical expressivity, including crescendo and decrescendo [21]. Although these different parameters are processed independently, it all comes together so quickly (on the order of tens of milliseconds) that we end up with the phenomenological impression of a holistic musical piece. The nature of these binding processes is an area of active investigation [22]. Evidence for the separability of musical parameter processing comes from case studies of people with congenital or acquired amusias [23, 24] as well as neuroimaging experiments [25].

Listening to music activates:

- motor cortex when we tap our feet, snap our fingers, and dance [26];
- pre-motor cortex and motor cortex even when listeners remain perfectly still, indicating that the cortical motor response is automatic and involuntary [26–28];
- sensory cortex as we obtain sensory feedback from our motor movements, plus vibratory stimulation of skin and through bone conduction [29–30], and, as above, even while remaining perfectly still [31];
- visual cortex as we watch musicians perform [32];
- pre-frontal cortical regions track music as it unfolds over time, generating expectations, and comparing those predictions with what actually occurs [33-37];
- emotional reactions to music tie together circuits in the cerebellum, frontal cortices, and the well-known "pleasure network" of the brain incorporating the nucleus accumbens, ventral tegmental area and amygdala [38];
- memory circuits in the hippocampus [39] as we try to index stored musical memories — patterns — that are similar to what we are hearing;
- autobiographical associations in memory [40-42]. For familiar music, this might be the last time we heard the song, who we were with, particular emotions it has evoked in us in the past, and other songs we know by the same artist. For unfamiliar music it will invoke sonic patters that the current piece may have in common with pieces we've heard before.

Why might music have therapeutic properties?

The ability of music to activate such a wide network of brain regions places it in a privileged position to effect physiological changes in the brain. When used as part of an evidence-based therapeutic program, it has been found to be effective in a wide range of health applications, from pain management, stress relief [43,44], mood induction, relief from anxiety, and cognitive difficulties often associated with Alzheimer's Disease, dementia, and cognitive impairment.

According to the model of Hillecke and colleagues [45], music therapy works through modulation of five factors: attention, emotion, cognition, behavior, and communication. To Hillecke's list, one might add social engagement, memory, and motor systems.

Stefan Koelsch has articulated 7 ways in which music may modulate emotional states, and thus lead to therapeutic outcomes, what he calls "the 7 Cs":

> "Humans have a need to engage in social activities; emotional effects of such engagement include fun, joy and happiness, whereas exclusion from this engagement represents an emotional stressor and has deleterious effects on health. Making music is an activity that involves several social functions:
>
> (1) when we make music, we make *contact* with other individuals (preventing social isolation);
> (2) music automatically engages *social cognition;*
> (3) it engages *co-pathy* … interindividual emotional states become more homogeneous (e.g. reducing anger… depression or anxiety… thus promoting interindividual understanding and decreasing conflicts);
> (4) *communication*…
> (5) *coordination* of movements (requiring the capability to synchronize movements to an external beat);
> (6) performing music also requires *cooperation* (involving a shared goal and increasing interindividual trust); and
> (7) as an effect, music leads to increased *social cohesion* of a group.
>
> Music seems to be capable of engaging all of the "Seven Cs" at the same time, which is presumably part of the emotional power of music" [46].

From a cognitive perspective, music's ability to trigger so many beneficial effects may derive from the same reason it is one of the last things to go in cases of severe memory impairment: its multidimensionality. Music is made up of both simultaneous pitches (chords) and sequential pitches (melody); durations which translate into tempo, rhythm, syncopation, "swing" and "groove"; tonal complexes (timbre); loudness (dynamics); and if the music has lyrics, semantics. It is a highly structured medium. There is a grammar for pitch, rhythmic and loudness sequences, and they cannot be combined in just any random order [47,48], leading to a complex interdependency in the way they become encoded in memory. And with lyrics, the mutually reinforcing cues of rhythm, accent structure and rhyme scheme provide additional structure and constraints. The components of music are so highly structured and intertwined that much of a musical representation could become damaged, and the music would still be recognized, and in many cases, perceptual completion processes would restore the missing components based in Helmholtz's principle of unconscious inference [49].

Embodied Cognition

Many musicians continue to thrive well into their late 80's and 90's — Pablo Casals, Artur Rubinstein, Arturo Toscanini, for example — and an emerging theory about why this is so is known as "embodied cognition." Our brains were built for exploring the environment. The enormous complexity of the human brain is primarily there to organize and support movement and action. When we cease to move, to explore our environment, when we no longer use our brains to organize physical action, they slow down, atrophy, and become disorganized [50]. Is an act of literal movement, and metaphorical navigation, as we explore and find our way around tonal and rhythmic space. A key to this is the recognition that playing a musical instrument always requires movement of some kind — there can be no sound without physical movement: plucking, bowing, breathing, fingering, pressing or banging. (And singing requires the movement of the vocal folds, jaw, tongue and lips). All of these activities require precise, fine muscle movements, coordinated with millisecond accuracy. Exploring our musical environment exercises those same areas of the brain that are activated when we explore our physical environment. Playing a musical instrument requires more training than becoming a neurosurgeon.

A systematic meta-analysis showed that for adults with mild cognitive impairment (MCI), exercise had a significant beneficial effect on memory [108]. Adults with MCI have a considerably increased risk of progressing to dementia, and the risk is increased by atrophy of the hippocampus [108]. Physical activity may be just as effective as pharmaceutical agents in improving and maintaining memory, as well as global cognition, and delaying the onset of dementia as well as other neurological diseases such as Alzheimer's and Parkinson's. And playing a musical instrument and singing may be just as effective, if not more, than the types of coarse movements required for exercise. Perhaps, as Cicero suggested, it is this kind of interaction that "supports the spirits, and keeps the mind in vigor".

The embodied cognition view further states that our cognitive and perceptual abilities are not a static endowment but rather emerge from fruitful and active exchanges with the environment. As children, we gain a sense of agency and control over the environment through our interactions with it. We can lose that sense of agency and control if we reduce our interactions with the environment, which can lead to a loss of motivation and confidence in our ability to interact, setting off a downward spiral. This is particularly a problem for older adults who are already experiencing three kinds of bodily changes that may spur them to interact with the environment less. First is loss of dexterity, which comes from a general slowing down of nerve transmission speed, loss of nerve conductance, and eye-hand coordination. Second is a loss of motivation, which may be born of isolation and feelings of loneliness. Third is a loss of joy and pleasure at doing things for oneself, partly owing to reductions in the production and uptake of dopamine, the brain's reward chemical signaling channels.

Taken together, these can lead people to curtail activities unnecessarily, that is, not for health or safety reasons. Abandoning a particular activity, such as playing a musical instrument or slicing vegetables, leads us to perceive ourselves as "someone who doesn't perform these kinds of actions anymore," and a self-image as a partial non-agent in the world. This can be one of the worst things about aging. There is currently no work (that I'm aware of) studying the intersection between embodied cognition and music making, but it may prove highly beneficial to do so.

Emotional Modulation

Many people intuitively use music to modulate their moods throughout the day, selecting certain kinds of music to help them wake up in the morning or calm them before sleep, to help with an exercise workout, comfort them after an unpleasant interpersonal encounter, or set a mood for a party [51].

Music elicits a wide range of emotions, including joy, exhilaration, calm, fright, sadness, and awe [52-54]. The most robust and well-established finding is that music can induce feelings of intense pleasure [14], euphoria [55], and trance states [56]. The neurochemistry of these feelings has been attributed to music's ability to modulate levels of dopamine, endorphins, and opioids in the limbic system [38, 57-61]. Pleasurable music can moderate dopamine, serotonin, and opioid levels; soothing music can moderate prolactin [62-64]. Techno music (which is known to induce trance states) was found to increase plasma cortisol, ACTH, prolactin, growth hormone and norepinephrine levels [65, 66]. A meditative piece of music (by Ravi Shankar) significantly reduced plasma levels of cortisol and norepinephrine [67].

An interesting, and perhaps counterintuitive finding is that people vary greatly in their judgments of what particular musical selections and musical features induce specific emotions. In one study, 200,000 people rated 20,000 different songs along 200 dimensions [68, 69]. The same songs often appeared in different categories. For example, *Back in Black* by the heavy metal band AC/DC was rated as "exhilarating" by some participants and "soothing" by others. On further investigation, the participants who found it soothing were habitual listeners of Swedish Speed Metal (a heavy metal subgenre) and so, by comparison, AC/DC was relatively calm.

Moreover, a given piece of music can evoke different emotional responses throughout one's life, even throughout the day; there are times when we don't even want to hear our favorite piece of music. This underscores the importance of musical interventions being performed in close consultation with the patient, rather than using "experimenter-selected" music as hundreds of studies and interventions continue to do.

Health, Immunity, and Pain

Several studies have investigated the effects of music on salivary immunoglobulin A (s-IgA), a principal immunoglobulin secreted externally in body fluids, including saliva and mucus of the bronchial, genitourinary and digestive tracts [70, 71]. Salivary IgA is a first line of defense against bacterial and viral infections and a reliable marker of the functional status of the entire mucosal immune system.

Following music therapy, immunoglobulin A (IgA) levels have been shown to rise [72], as well as melatonin [73]. Increased melatonin production in turn leads to increased cytokines and the production of t-cells. Epinephrine and norepinephrine increase following music therapy, increasing arousal and attention. Mood changes are also well established.

Patients who listened to joyful music showed significant increases in arterial dilation [74], to a level obtained with aerobic activity or statin therapy. Among Alzheimer's Disease (AD), Mild Cognitive Impairment (MCI) and dementia patients, music has been found to be effective at treating disruptive behavior, anxiety, and depression, and is linked to improvements in Quality of Life and cognitive function [75].

Listening to music prior to surgery was found to be as effective as diazepam in reducing pre-operative stress and anxiety [76, 77]. Music reduces pain [78, 79]. Participant-selected pleasurable music differentially activated a network of pain-related brain regions, including dorsolateral prefrontal cortex, periaqueductal gray matter, rostral ventromedial medulla, and dorsal gray matter of the spinal cord [80]. An emerging body of thought on the nature of pain proposes that rather than a "pain matrix" in the brain, there is a "saliency matrix [81]." This theory emerges from the common observation that similar sensory stimulation can evoke wildly different mental experiences. The identical pressure on the underside of your foot is interpreted differently depending on whether you just stepped on a rock, or you're in a spa receiving a foot massage, indicating that the experience of pain is a cognitive construction, owing to interpretation and context. Pleasant music accompanying pain may serve to re-contextualize the experience, just as music of differing emotional valences can profoundly affect our experience of a visually ambiguous movie scene [82-85].

Special Problems of Aging

Musical memory is relatively spared in patients with AD and dementia, sometimes extraordinarily so [86-88]. Memory is especially preserved for long-ago learned songs, as opposed to newly encountered ones, and this finding is consistent with the overall profile of AD and dementia-related memory impairment, that episodic and recent memory is affected more profoundly than semantic and long-held memory.

An emerging body of literature indicates that music can play a powerful role in treatment for patients with dementia, late stage Alzheimer's Disease (AD), and other brain disorders associated with aging. Even though memory deficits are a hallmark of dementia, and in particular AD, a number of studies have found that *musical* memory can be preserved, even in the face of profound amnesia for other aspects of a person's life [89]. Some, like musician Glen Campbell, can continue to perform music at a world class level [90]. And it's not just memories for old, well-known music that are intact — people with dementia can even learn new songs [91]. Music also reactivates autobiographical memories in patients, which can provide comfort, alleviate depression, anxiety and agitation [92].

The neurological basis for this is just being uncovered. When AD patients listen to music they chose, activation increases in motor areas of the cortex, along with widespread activation throughout the brain, linking together the cortex and the cerebellum. This may account for the sense of "being alive" again, and for improved mood, memory, sense of self, and reconnecting with personal emotions. Musical memory remains intact even in the face of massive lesions to canonical memory areas such as right medial temporal lobe, the left temporal lobe and parts of left frontal and insular cortex, with similar findings in patients with bilateral temporal lobe damage [93].

Methodological Issues in Music Research

For centuries music therapy remained undefined. The phrase was used loosely to describe pretty much anything people wanted it to be. In the past ten years, there has been a growing recognition that progress in the field of music as medicine depends on careful scientific observation and controlled experiments.

A century of experimentation on music and health, broadly defined, tended to use music selected by the experimenter as conveying, in the experimenter's own judgment, certain emotional qualities. The trade-off here is between controlling acoustic properties of the music versus the emotional or valence responses to that music. In conducting studies that inform music therapy do we want to ensure that every participant in the study receives the identical acoustic signal, regardless of whether or not they like the music or what emotion they associate with it (or even if it is familiar)? Or, if we're studying an actual live, thinking person's reactions to music, would we rather control for how much an individual likes the music, their emotional response, and whether or not they've heard it before? Much experimentation was conducted with music composed by the experimenter, not by trained composers, in what strikes me as a misguided effort to control the stimulus.

Andrea Halpern was perhaps the first cognitive psychologist in modern times to employ real-world, well-known songs in rigorous experiments [94], and the field has seen an increasing trend towards doing so since then [95].

Some guidelines for future research methodology in experiments of music therapy interventions include (but are not limited to):

(1) *Control for familiarity*. Ask listeners how familiar they are with a given piece of music, by using Likert scales. It's also possible to verify familiarity by playing short excerpts of the music, a la Krumhansl [96] and Schellenberg [97, 98].
(2) *Control for pleasantness.* Ask listeners how pleasant or enjoyable they find a piece of music.
(3) *Control for emotional quality*. Ask listeners, through free-response or forced-choice, to indicate what emotion they associate with the piece [99-101].

Comparing one musical stimulus to another, or to a non-musical stimulus, can help to elucidate a number of questions of utmost interest to music therapists. Is music special? Might I get the same effect from, say, an audiobook, guided meditation, or podcast? By equating familiarity, pleasantness, and emotional quality, we can home in on answers to these questions. When contrasting two or more pieces of music, or a piece of music with another stimulus (e.g. speech), we accomplish an ecologically valid, real-world control by equating the music and its control stimulus across all of these dimensions. It doesn't matter if the acoustical profile of the stimuli are the same — what matters is how the listener perceives them.

Future directions

One promising area that remains underexplored is the use of music in group settings. Although music therapy is primarily administered in a one-on-one basis between therapist and patient, an emerging body of evidence suggests that group music listening may confer additional benefits. Group music listening and group music making have been likened to physical grooming among primates, as it supports social bonding [109, 110]. For music listening in particular, the great advantage over speech is that large numbers of individuals can participate together, at the same time. In music, this creates a choir; in speech it creates cacophony.

When people listen to or sing music in groups increased levels of serum oxytocin are observed, a social saliency hormone associated with feelings of bonding and trust [102,103]. Music fosters a sense of community; a sense of connection to others; and provides a shared experience.

Several communities are experimenting with intergenerational choirs that bring together children, adolescents, and older adults with dementia. One studied changing attitudes of younger people toward older adults through the use of collaborative singing [104]. Students, starting with the first rehearsal, were "buddied up" with a person with dementia and that person's family members, and they sat next to each other during most rehearsals. At the beginning of each rehearsal, time was given (15 – 20 minutes) for socialization, a chance for the buddies to talk with each other. All choir members are treated as equals and called by their first names, regardless of the age difference. Songs were selected that had more repetition, fewer rhythmic or tempo changes, and included songs well-known by all including *Stand By Me* and *Over The Rainbow.*

Before the choir began, 65% of the words that young people used to spontaneously describe older adults were negative, such as *sadness, sick, helpless,* and *deterioration.* After three months in the choir, 75% of the words that young people used were positive, such as *unity, love* and *caring.* One student said, "Months ago I was afraid of not knowing what to say or what to do [around a person with dementia]. But the issue was with me, not with the folks with memory loss…Spending time with my new friends with Alzheimer's helped me to see that we are not hopeless when we start forgetting; we are hopeless when we give up and decide not to live." One individual with AD said "When I spend time with the students, I feel energized and accepted. It is fun being around young people."

Group singing constitutes a real-life activity in a setting that is organic and natural, rather than clinical. But it is not for everyone — older adults with mobility problems, or other issues that may make group singing stressful, may benefit from group music listening. This may be one of the most promising avenues for future research. Listening to music causes synchronization of brain activity, when people listen to the same piece of music [105]. No one has yet done the study, but based on the literature, a reasonable hypothesis is that such group listening to music may foster intra-group cohesion, increases in mood and feelings of well-being, and increases in oxytocin, serotonin, dopamine and endogenous opioids. As Pink Floyd sang in 1967, "Music seems to help the pain… to cultivate the brain,"[106] a sentiment echoed thirty-five years later by German artist Sarah Connor: "People have always been singing to wipe away tears, to ease all the pain. Music has always been healing."[107]

Finally, there are indications that one of the most promising areas for studying music, especially among older populations, is to adopt the embodied cognition approach to explore whether playing musical instruments and singing can delay the onset of cognition impairment, enhance quality of life, and possibly increase lifespan.

Conclusions

For decades, music therapists have combined art and science to develop therapeutic relationships and systematically deliver musical interventions that promote recovery, resilience, and enhanced quality of life. More recently, music therapy researchers have begun to generate evidence for the efficacy and effectiveness of these interventions, while cognitive psychologists and neuroscientists continue conducting rigorous scientific experiments to better understand the underlying mechanisms, and the effects of listening to and creating music on the brain. Future goals are to use what we are learning about the relationship between music and the brain to better understand how and why music therapy interventions work, to enhance their efficacy and generalizability, and to educate medical professionals about their benefits.

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Biographical Statements

Dr. Daniel J. Levitin is a cognitive neuroscientist specializing in studies of music, using a variety of converging approaches, such as neuroimaging, psychophysics, behavioral experiments, pharmacological interventions, genetics, and studies of patient populations. He is also a remusician who has performed with Rosanne Cash, David Byrne, Bobby McFerrin, and Victor Wooten among others. Levitin is Founding Dean of Arts & Humanities at the Minerva Schools at Keck Graduate Institute in San Francisco, and James McGill Professor Emeritus at McGill University in Montreal.