The Yale Medical Orchestra displayed exceptional talent and inspiration as it performed a timeless composition to celebrate Yale School of Medicine’s bicentennial anniversary during a December 2010 concert. Under the leadership of musical directors Robert Smith and Adrian Slywotzky, the richly emotional meditations of Mendelssohn, Dvorak, Schubert, and Yale’s own Thomas C. Duffy filled the minds and hearts of an audience as diverse as the orchestra. I intend to retrace the steps of that melodic journey in this essay, fully aware of the limits imposed on me to recreate the aural art form through the medium of text. While these symbols can be pale representations of the beauty and complexity of the music, I hope they will be the building blocks for the emotional experience of the audience. I describe the works’ inception and their salient musical features and then review what we know about the effects of melody, meter, and timbre on our brains. My intentions are to provide evidence to encourage the further use of music as a tool in medical practice, provide interest in the works explored by the Yale orchestra, support the orchestra itself, and investigate a personal passion.

“The sound of your voice are the keys to innumerable worlds.”
— The Hathors

The Yale Medical Orchestra, in association with the Program for Humanities in Medicine, displayed exceptional talent and inspiration as it performed a timeless composition to celebrate Yale School of Medicine’s bicentennial anniversary during a December 2010 concert. From the bustling excitement as the orchestra took the stage to the singular musical thought that spread through the room as they led us on our journey to the roar of applause echoing in majestic Harkness Auditorium, the night was a wholly encompassing expression of the power of music.

PERCEPTION OF HARMONY

The first work from this performance that I will examine is Schubert’s 8th Symphony. At age 25, Franz Schubert’s approach to his 8th Symphony was ambivalent at best. He wrote it for no iden-
tifiable reason or person and left it incomplete and in possession of his friend Anselm Huttenbrenner, who did not release the work until 37 years after the composer’s death [1]. The conductor Johann von Herbeck first brought the work to the orchestra in 1865, and it is commonly referred to as Schubert’s Unfinished Symphony. A nearly complete scherzo in three-quarter time complements the first two similarly metered movements, but a fourth movement to end in the home key of B minor is not thought to exist. It opens slowly in strings with a melody overlain by oboes and clarinet that climbs to a thrilling peak as the composition unfolds. A transition is made in only four measures, bringing the piece to a G major key with celli echoed in violins. A powerful closing features a strongly emphasized chord called a sforzando. The second movement begins with basses, horns, and violins playing in counterpoint to a resounding theme established by clarinets and oboes, alternating and elaborating in rich detail. Interwoven beautifully by the Yale Symphony Orchestra, it was a dynamic musical experience for the audience.

Despite Schubert’s lackluster enthusiasm, how does his composition remain orchestral poetry, able to be received and understood by our minds more than a century later? Indeed, at its most elemental level, how do vibrations of strings transfer frequency to air particles that alter neural activity in our brains, creating the rich tapestry of the Unfinished Symphony?

Allow us to begin within the human auditory cortex, which composes approximately 8 percent of the total cortical surface area and is located at the juncture of the Sylvian fissure and adjacent Heschl’s gyrus [2]. It is constructed of more than a dozen auditory cortical fields organized by frequency that receive projections from the medial geniculate body of the thalamus [3]. Each field is organized tonotopically at its core with surrounding belt and parabelt regions thought to further assess frequency-specific noises for features such as rhythm and timbre [4]. fMRI data suggests that other acoustic features such as location and quality also are interpreted in discrete regions similarly to the commonly known “what” and “where” pathways of the primary visual cortex [5-7]. Neuroimaging of healthy human subjects shows that anterior parabelt regions differentially activate in response to vocalization [8] and may play a role linking auditory stimuli with memory.

Evidence also demonstrates that the auditory system has evolved in dozens of species to support harmonic perception. A variety of studies show preference to harmonic pitches (frequencies that fall into stepwise, integer multiples of the fundamental, or base frequency of the key) in a range of species from fish, rats, and monkeys to humans [9]. Recognition of deviant and missing frequencies in harmonic tones also is preserved. In babies, disfavorable attention is given to inharmonic tones, and adults need not even be attending to discordant sound in order to show “object relative negativity” in evoked potential recordings [10]. A 1 to 2 percent mistuning of frequencies is sufficient to make these sounds inharmonic, perceived as separate tones. Electrophysiological data of multiunit activity shows oscillations (beats) corresponding to frequency differences in dissonant cords, but not in harmonic chords (octaves and perfect fifths). As a whole, these phenomena are theorized to arise from a “harmonic sieve” of the auditory system that preferentially recognizes features of a quantized set of frequencies. Lesional studies of bilateral Heschl’s gyri in macaque monkeys demonstrate impairment in harmonic recognition and a two-fold increase in detectable frequency differences in these monkeys vs. controls [11]. In humans, patients with right Heschl’s gyrus lesions can detect frequency differences only at intervals three times the size as those of controls, demonstrating a deficiency in pitch ordering and fine discrimination [12]. Population-wide coding of cat auditory nerve also has demonstrated temporal patterns of neural firing that resemble sound stimuli waveform, providing further evidence for how sound and music can be coded by and dissected into specific features in the primary auditory cortex [13].
MUSIC AND EMOTION

Before we continue our exploration, we must make a stop at the Hebrides archipelago, off the west coast of Scotland, to investigate our next masterpiece. In 1830, Felix Mendelssohn was inspired to visit the Hebrides shortly after his 20th birthday with his friend Karl Klingemann [14]. Accounts of a wild, desolate coast where “nothing is heard but the howling of the wind and roaring of the waves” drew him there. Ironically, on the boat, Mendelssohn became overpowered by the motion of the sea, and we must rely on Klingemann’s words for an account: “We were put out in boats and lifted by the hissing sea up the pillar stumps to the famous Fingal’s Cave. A greener roar of waves never rushed into a stranger cavern — its many pillars making it look like the inside of an immense organ, black and resounding, absolutely without purpose, and quite alone, the wide grey sea within and without” [15]. This vision inspired Mendelssohn to send a letter almost immediately after his trip to his sister in which the first measures of the dark and majestic score Fingal’s Cave were transcribed.

The work is unique in its classification as a concert overture as it does not precede a larger work, but yet remains as a standalone piece that sets a mood and paints a picture for the audience. It has two main themes: an introduction of a thinly veiled progression of fifths played by violas, cellos, and bassoons and a lyrical theme that captures the emotion and stunning beauty of the cave. Mendelssohn’s mastery allowed for the encapsulation of his emotional experience on the Hebrides in a poignant composition felt by audiences for hundreds of years after its conception. Professor Todd described the work in his book Mendelssohn: The Hebrides and Other Overtures by stating that “image became sound. [W]e can perhaps attribute this remarkable masterpiece to an ultimately unfathomable process of synaesthetic transformation” [14].

Such emotion transcribed to melody compels us to contemplate the consequences of music on our minds and our experience of the world. Evidence shows that music can affect three hallmarks of human cognition: theory of mind, recursion, and abstract representation [16]. Although it was hypothesized early that musical ability resided in the right hemisphere and language capacity in the left, we are now aware that music composition, performance, and appreciation are complex processes regulated by expansive regions of cortical and subcortical systems. As previously discussed, data suggests pitch perception and relational tone awareness arise from the primary auditory cortex and its inputs from the thalamus and cochlea. Neuroimaging data shows that the other major component of music, rhythm, is perceived and produced in regions within the cerebellum, basal ganglia, and higher motor circuits [17]. However, how and where do the unity of such primary features create the emotional and cognitive experiences of music? Of this, Nietzsche said, “All possible efforts, excitements, and manifestations of the will, all those processes inside human beings, which reason subsumes under the broad negative concept of feelings, can be expressed through the infinite number of possible melodies” [18].

If one has ever experienced the strength of music, its chills and its joy, it is intuitively evident that music and emotion can be inextricably linked. Physical changes such as thrills, shivers, and alterations of heart rate can occur when listening to music, and neuroimaging data documents activation of the orbitofrontal and cingulate cortices, commonly thought to mediate physiological emotional response, during these physical changes [19]. When listening to music, dopamine is released onto the nucleus accumbens, an area classically thought to mediate reward perception and addiction [20]. Moreover, both “joyful” and “fearful” music resulted in stronger signal changes in the amygdala over emotionally neutral auditory controls, suggesting a dual role in an area once thought of simply as a fear center [21]. In fact, studies have demonstrated differential activation among the amygdala’s individual nuclei and of the entire limbic system during emotionally suggestive, paired visual
and auditory stimuli, respectively [22,23]. Despite this evidence, a melody’s affect on emotion is not thought to be limited to neural circuitry. Prolactin concentration increased in the tears of patients listening to “sorrowful music” in one study, a hypothesis based on the findings that concentrations of the hormone are usually low in tears except during the immense emotional experiences of childbirth and orgasm [24]. The authors suggest the possibility that this property is part of an evolutionary mechanism for encoding memory during powerful emotional experiences. These discoveries beg the image of an orchestra activating an audience’s prolactin concentration (in addition to its limbic, accumbens, and cingulate circuits) at will through executed melodic organization. Indeed, the fact that music activates such primitive and evolutionarily preserved emotional systems provides for interesting consideration as to its importance in the human experience.

MUSIC AND MEMORY

Just as we all have at one time or another remembered the words to an advertising jingle, music also can serve as a thread in the tapestry of a memory. In a study of recovery of cognitive function (verbal memory and attentional focus) and mood in stroke patients, those who listened to their favorite music daily had significant improvement in measures of higher cortical function, as compared to those who listened to audio books or nothing at all [25]. The role of music on implicit and explicit memory in patients with Alzheimer’s disease (AD) has been investigated [26]. Interestingly, while explicit memory (song naming and judging a melody’s familiarity) is impaired in AD, implicit procedural memory for playing a musical instrument was shown to be preserved in several patients with AD, one of whom had not played a particular instrument (xylophone) for more than a decade [27]. Apraxia (shoe tying) and ideomotor apraxia (hand waving) was even present in a few patients [27,28]. Finally, listening to background music has been shown to improve explicit memory retrieval on a semantic autobiographical memory task in AD, possibly through attention modulation and associative cuing [29]. This data is indeed exciting in its implications for music’s effect on memory. Could the activation of music on the limbic system be mediating these effects? As we move further in our exploration, in what other ways will music serve as a preservative of the thoughts and experiences of our lives?

Antonin Dvorak, in his 1879 composition Czech Suite, used music to transcend the individual memory and perception and worked to encompass the pulse and tradition of an entire people [30]. Born from an intense love of the Slavic people and his homeland of Bohemia, Dvorak’s ambition was fueled by the idea that “an artist has his country in which he must have firm faith and an ardent heart” [31]. The style now known as “Czech,” exemplified by this five-movement work chosen by the Yale Symphony Orchestra, incorporated unique patterns of modulation and rhythm influenced by Slavic folk music. In Czech Suite, a conversation between flutes and clarinets heralds a brilliant introduction and an uplifting melody of violins in the second or “Polka” movement, compelling me to “feel” the revival that overpowered Dvorak upon his return to his homeland. It is evident that the love he felt for the Slavic people, and the influences they had on his life, were truly inseparable elements of his work, firmly tying an entire tradition to a melody. It was indeed as described “the people's own music” [31].

MUSICAL THERAPY

With influence over so much that defines our humanity, it is not surprising that many have looked at the means by which music can heal us. Indeed, music can be an inexpensive, powerful tool of medical care that is free of adverse effects and has a broad range of potential applications. Data showing stronger vocabularies and reading capabilities in children studying music (hypothesized to be caused by similarities in hierarchical syntax, tonal properties, and temporal qualities [32])
has led to music therapy becoming an adjunctive means to facilitate language acquisition in patients with learning difficulties and dyslexia [17,33,34]. In the field of developmental psychology, data suggests a medium to large effect of music on clinically relevant outcomes in children with developmental delay and behavioral disorders [35]. In adult psychiatry, a meta analysis of active music-making, improvisation, and listening to music in an interactive environment with a trained therapist showed improvements in emotional expression, motivation, global state, general mood, and negative symptoms, all of which followed a dose response correlation [36].

Pre-operatively, listening to a choice of different music showed decreased blood pressure, heart rate, respiratory rate, and State-Trait Anxiety Inventory scores, as compared to controls [37,38,39]. Post-operatively, patients given music therapy used less analgesia, reported up to a 50 percent reduction in subjective pain, had lower serum cortisol levels, and had decreased blood pressure, data that is consistent across a number of studies [40,41,42]. In patients with traumatic brain injury, rhythmic auditory stimulation increased gait velocity by 14.32 meters per minute, increased stride length by 0.23 meters, and led to greater gait symmetry than in standard treatment groups [43]. Post-stroke patients with a mean aphasia duration of 11.5 years who used specialized music therapy that focused on vocalization improved articulation, repetition, and comprehension to statistically significant effect sizes of 2.12, 1.29, and 1.36, respectively [43]. In a meta-analysis of five studies of insomnia (n = 170 patients), music-assisted relaxation before bed showed a standard mean difference of -0.74 (95 percent CI -0.96 to -0.52) for measures of sleep complaints vs. controls [44]. COPD patients who participated in 24 weeks of singing therapy had increases in maximal expiratory pressure vs. controls in one study (+3 mmH2O vs. -11 mmH2O) [45]. The authors credited this improvement to “a practical and pleasant way of training expiratory muscles.” Finally, back to developmental influences, 31 stable infants in the neonatal intensive care unit were exposed to either live, recorded, or no music for 30 minutes in an otherwise controlled-noise environment [46]. Thirty minutes after the end of the treatment, the live music group had a lower heart rate and an improvement in behavioral scores as compared to both the other groups.

Overall, these data show evidence for music’s influence over a variety of domains in our practice ranging from patient mood, pain perception, language capacity, and sleep function, generally, on an overall sense of well-being. In our roles as healers, it is our duty to utilize all available means to treat our patients as effectively as we can. If an intervention as simple as providing them with music speeds their recovery or minimizes their discomfort in any way, even if only by placebo effect, then why would we not participate in this endeavor?

The final treat of the bicentennial celebration was the world premiere of an original work composed by Professor Thomas C. Duffy of the Yale School of Music, entitled Heart-Throb. This unique work was led by the beat of a drum that mimicked a pulse transitioning from a physiological to a pathological cardiac rhythm. The piece starts with a resting heart rate that is “shocked” by the sound of a wooden percussion instrument called a kokiriko. As additional beats and murmurs crowd the sound, the accompanying melody becomes increasingly dissonant, to a point where a sharp siren rises from the orchestra. The piece ends dramatically, and its inventiveness truly amazed the audience.

CONCLUSION

Music seems to permeate our experience as it intertwines with our thoughts and emotions. Nietzsche said that music “addresses itself symbolically to the primordial contradiction and pain in the heart of the original oneness, and thus presents in symbolic form a sphere which is above all appearances and prior to them” [18]. A so-called Mozart effect was first demonstrated in 1993 by Rauscher et al. showing that after 10 minutes of listening to Mozart’s
double piano sonata K448, a highly structured and ambitious composition, subjects improved their mean spatial IQ scores by 8 to 9 points [47]. The effect did not last beyond 10 to 15 minutes, but this finding correlated with EEG data that showed enhanced synchrony in the left temporoparietal and right frontal brain regions for a mean of 12 minutes in healthy subjects after Mozart’s K448 [48]. EEG data even shows a 50 percent reduction in bilateral spike and wave complexes in patients with status epilepticus who listened to K448 for 5 minutes [49]. The effects do not appear to be limited to short-term exposure. Children who were given keyboard lessons for 6 months showed 30 percent higher scores on a spatial-temporal reasoning task compared to children who were given computer lessons or no training [50]. Finally, a large prospective study showed that cognitive leisure activities, which include the demanding yet graceful task of playing a musical instrument, could in fact reduce the risk of dementia [51].

It is hypothesized that the ordered structure of aesthetic sensory patterns can focus behavior and guide cognition, by which sound energy can manifest itself as physical changes modulating our perceptual experience of the world. Bringing such a modality to medicine is a noble endeavor, ever expanding a physician’s repertoire to promote patients’ health. If indeed it does work, its only limiting factor is the will by any member of the team to make it happen. The composer Virgil Thomson once said, “[w]hatever deceptions life may have in store for you, music itself is not going to let you down.”

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