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NIH/Kennedy Center Workshop on Music and the Brain: Finding Harmony

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The National Institutes of Health and John F. Kennedy Center for the Performing Arts convened a panel of experts to discuss the current state of research on music and the brain. The panel generated research recommendations to accelerate the study of music's effects on the brain and the implications for human health.

Introduction

"Perhaps the most important problem in neuroscience is understanding what it means to be human, and music is an essential part of this." This observation was how Robert Zatorre began his plenary presentation at a workshop entitled "Music and the Brain: Research Across the Lifespan." The meeting, hosted by National Institutes of Health (NIH) Director Francis Collins, soprano Renée Fleming, and Kennedy Center (KC) President Deborah Rutter, is an early step in a larger KC/NIH collaboration, in association with the National Endowment for the Arts (NEA), called the "Sound Health" initiative. The workshop was organized around the three life stages—childhood, adulthood, and aging. In each session, a panel of 25 experts (listed in Table 1) discussed recent breakthroughs in research and their potential therapeutic applications. Over the course of a day and a half, the panelists recommended basic and applied research that will: (1) increase our understanding of how the brain processes music; (2) lead to scientifically based strategies to enhance normal brain development and function; and (3) result in evidence-based music interventions for brain diseases. In the sections that follow, we will review the discussions from the workshop and highlight the major recommendations that emerged. Finally, we will discuss how funding agencies, scientists, clinicians, and supporters of the arts can work together to catalyze further progress.

"Building": Music and the Child's Brain

From an early age, children are remarkably responsive to music and its elemental components (e.g., melody, harmony, rhythm, and dynamics). The childhood session began by framing questions such as "how might musical experience enhance individual development," "how can music be used to promote health," and "how can interventions be customized to an individual's abilities and needs." As noted by John Iversen, there is a growing body of evidence suggesting that musical training has the capacity to foster the development of non-musical skills across a host of domains, including language development, attention, visuospatial perception, and executive function. One goal for future research is the development of rational approaches for music-based programs and interventions guided by an understanding of how music affects brain development.

The panelists also discussed the concept of active versus passive learning and the potential benefits associated with active engagement in music. Infants begin passively processing and engaging with sound at birth, behaviors believed to contribute significantly to language acquisition. Active engagement with music later in life was noted to involve multiple neural networks thought to contribute to "agency" or self-control over one's environment, which may be helpful for certain conditions, such as depression. The conversation also focused on a particular aspect of music, rhythm, and how musical training to enhance the brain's temporal precision in its response to sound may serve as a scaffold for the development of language skills. Panelists discussed how this may foster the development of areas of the brain involved in processing the rhythms of both music and speech.

A challenge noted by participants was that studies aimed at assessing the effects of music engagement in childhood on long-term health or educational outcomes must take into account individual

Table 1. Workshop Panelists

Name	Affiliation
Aniruddh Patel	Tufts University
Brenda Hanna-Pladdy	University of Maryland School of Medicine
Charles Limb	University of California, San Francisco
Christian Gold	Uni Research
Concetta Tomaino	Institute for Music and Neurologic Function
Deforia Lane	University Hospitals Cleveland Medical Center
Edward Roth	Western Michigan University
Elizabeth Stegemoller	Iowa State University
Gay Hanna	Grantmakers in the Arts
Gottfried Schlaug	Beth Israel Deaconess Medical Center, Harvard University Medical School
Isabelle Peretz	University of Montreal
John Iversen	University of California, San Diego
Joke Bradt	Drexel University
Josh McDermott	Massachusetts Institute of Technology
Julene Johnson	University of California, San Francisco
Kevin LaBar	Duke University
Laurel Trainor	McMaster University
Michael Thaut	University of Toronto
Nim Tottenham	Columbia University
Nina Kraus	Northwestern University
Psyche Loui	Wesleyan University
Robert Zatorre	McGill University
Sheri Robb	Indiana University
Steven Holochwost	WolfBrown, Johns Hopkins University
Xiaoqin Wang	Johns Hopkins University

differences, with respect to both biological and environmental factors. Additional discussion involved questions about determining the optimal "dosing" of musical training. How much and what kind of training is necessary to confer benefits later in life? What kind of musical training is most beneficial for what outcomes, and how can we better predict who might need more and who might need less? Rigorously designed longitudinal studies were identified as one way to address such questions. It was noted that ancillary studies to ongoing observational projects (e.g., the NIH-funded Adolescent Brain and Cognitive Development [ABCD] study) or to interventional clinical trials could be a practical, lower-cost way to tackle these questions in the near term.

Music as a Therapeutic Intervention in Children

Workshop participants discussed the therapeutic applications of music during childhood, focusing particularly on autism and pediatric cancer. This session was motivated by the frequent clinical observation that music may have privileged access to the child's brain, which could overcome common therapeutic obstacles to treating pediatric populations. Data were presented showing how exposure to music early in life can have long-term anxiolytic effects. One example presented involved group guitar playing, which appears to promote emotional well-being and focused attention in children and teens.

A consistent challenge identified in this session was how to assess target engagement and outcomes in music therapy interventions. One example described was how "body sway" can be used as a surrogate for engagement with music. The need for such surrogate or clinical endpoints, as well as a better understanding of the underlying biology and mechanism of musical interventions, will become increasingly important as the field moves toward more randomized, controlled clinical trials with music as the intervention. Results of trials using music therapy approaches to treat mental health indications in children and adolescents have been mixed, while other studies focused on using music therapy to help pediatric cancer patients cope with the distress of acute treatment, procedural pain, anxiety, and the maintenance of cognitive function have had more positive results.

Ultimately, the panel agreed that trials designed to test hypothesized mechanisms, as well as a better understanding of the relationship between these mechanisms and endpoints, are needed to advance the application of music therapy in pediatric populations. Various viewpoints were presented on the extent to which music therapy interventions could be standardized. Some believed that such standardization will be essential for detecting meaningful therapeutic effects. Others maintained that interventions may need to be tailored to the individual and that it was more important to develop standardized principles for how such trials should be conducted.

"Engaging": Music and the Adult Brain

The panelists in this session began by discussing the neurological specificity of music and whether this specificity also applies to pitch. A recent neuroimaging study of non-musicians identified regions of the non-primary auditory cortex that respond selectively to music (as opposed to speech and other sounds), suggesting music-specific neural processing (Norman-Haignere et al., 2015). Another study described "harmonic template" neurons in the auditory cortex of the marmoset monkey. These neurons showed a facilitated response to harmonic complex tones, which are common in music and speech (Feng and Wang, 2017). This finding raised the possibility of using animal models to explore certain aspects of musical pitch processing.

When considering the impact of musical training on brain structure and function, the panel discussed neuroimaging evidence supporting structural brain differences between musicians and non-musicians. One study, for example, described how differences in

the thickness of specific cortical regions associated with musically relevant capacities (such as auditory-motor synchronization) correlate with the age at which individuals started musical training (Bailey et al., 2014). Despite the growing evidence for selectivity in the neural processing of certain components of music, there are certainly some overlapping circuits involved in music and language processing. According to one theoretical framework known as the OPERA (overlap, precision, emotion, repetition, and attention) hypothesis (Patel, 2014), the high demands that music places on such shared circuits, combined with music's strong links to the brain's reward systems, make musical training a strong driver of adaptive neural plasticity in circuits involved in speech processing. In terms of creativity, neuroimaging studies suggest that improvising, as opposed to performing a memorized piece of music, results in different patterns of activation and deactivation in the prefrontal cortex (Limb and Braun, 2008). A better understanding of musical creativity could be helpful in recognizing and promoting creativity in other domains.

Challenges and future questions identified in this session mirrored many of those identified earlier, particularly the need for better understanding of the fundamental pathways that underlie the brain's interaction with music. This dialog, in turn, raised the question of whether these pathways could be modulated to enhance function or outcomes in music or other cognitive domains. The panelists also believed that it was important to comprehend the mechanisms underlying the pleasure that listening to or playing music can induce. Since music is (usually) non-addictive, such understanding could potentially be used to modulate the strong physical/emotional responses induced by addiction.

Music as a Therapeutic Intervention in Adults: Overlapping Circuits Suggest Potential Mechanisms

This session focused primarily on the therapeutic promise of music for adults suffering from depression, anxiety, or chronic pain. The panelists described the findings of several recent clinical studies and used them to highlight obstacles that must be overcome to permit more rigorous and informative trials. For example, one study showed that, for adults with depression, improvisational music therapy was more effective than standard of care (Erkkilä et al., 2011). Another study showed that group singing reduces stress and arousal as measured by adrenocorticotropic hormone levels, though the effects on oxytocin were less clear. (Keeler et al., 2015). These studies suggest that music therapy affects brain networks mediating emotion, but the mechanism of such effects remains unclear.

In contrast, more is known about the neural mechanisms underlying pain and the impact that music therapy may have on pain-associated brain circuits and pathways. For example, the panel discussed data demonstrating that the neural signature of pain, which includes concurrent activity in the anterior cingulate cortex, insula, and somatosensory areas, overlaps with areas consistently modulated by music, as shown in a meta-analysis of fMRI data. Panelists hypothesized that this neural signature could serve as a biomarker in music therapy studies for chronic pain. They also presented evidence suggesting mechanisms through which music could ameliorate pain, including its impact on the mesolimbic system, cortical and limbic/paralimbic brain structures involved in the affective and cognitive modulation of pain, and the hypothalamic-pituitary-adrenal (HPA) axis.

The panelists agreed that it will be critical to apply rigorous clinical trial methodologies when designing therapeutic interventions. Particularly needed are tools to measure individual differences in affective processing more effectively, as well as biomarkers (e.g., EEG, fMRI, neurochemical markers) and clinical endpoints to measure the effectiveness of interventions, clarify mechanistic effects, and assess structural and functional changes in the brain. It will also be important to apply music therapy techniques in more advanced imaging settings. The panelists agreed that future progress will require a more multidisciplinary approach involving collaboration among music therapists, psychologists, musicians, and neuroscientists.

"Sustaining": Music and the Aging Brain

During this session, the panelists examined the hypotheses that early musical training confers long-term health benefits in older individuals and that musical engagement can contribute to the wellness of older adults. One study presented suggests that older adults with 10 or more years of musical experience throughout their lifetime perform better on tests of executive function and nonverbal memory than those without musical experience (Hanna-Pladdy and MacKay, 2011), supporting the idea that musical training can confer a cognitive reserve during the aging process. Perhaps fortunately, for those without earlier musical training, recent studies demonstrated the benefits of participation in choir singing on the health and well-being of older adults (Johnson et al., 2017). In addition, the panel discussed the role music might play in the development of hearing loss therapies and that participation in creative musical activities (such as improvisation) may protect against age-related cognitive decline. Overall, there is accumulating evidence that engagement with music confers benefits across multiple functional domains of the aging brain. However, further work, including longitudinal studies, will be needed to strengthen this evidence base.

Music as a Tool for Restoring Function in the Aging Brain

In this discussion, the panel focused on examples of promising applications of music therapy for the treatment of disorders such as stroke, Parkinson's disease, and dementia. One promising application of music therapy was highlighted by a video showing an aphasic individual whose speaking ability improved substantially following Melodic Intonation Therapy (MIT), which involves conferring melody to otherwise spoken language. In addition to the therapeutic benefits seen following MIT intervention, changes in connectivity were observed by MRI between the frontal and temporal regions of the brain, suggesting a potential neural mechanism for speech improvement. Other music therapy interventions in older populations (including those with Parkinson's disease) have demonstrated potential improvements to respiratory control, quality of life, and muscle control associated with swallowing and gait. The panel discussed a randomized controlled trial (RCT) performed in Finland in which individuals with dementia (and their caregivers) were assigned to 10 weeks of group singing, group music,

Table 2. Workshop Recommendations Summary

Topic	Recommendations
Basic and Mechanistic Research	● Establish what neural circuits are involved in the interaction between music and the brain ● Investigate which neural pathways are enhanced by musical training ● Examine to what extent music and language processing overlap ● Explore the possible evolutionary benefit of music to *Homo sapiens*
Translational and Clinical Research	● Better integrate mechanistic understanding with music therapy approaches ● Develop and validate biomarkers for music interventions ● Investigate the question of "dosing" in music interventions ● Explore how music is "special" and develop methods to better understand and predict individual differences in responses to music interventions
Methods and Outcomes	● Develop methods to integrate brain-based measurements with musical activities ● Conduct longitudinal and ancillary studies to assess outcomes of music interventions on timescales matching developmental trajectories ● Promote more rigorous reporting of interventions, methodologies, and results ● Establish standardized and/or personalized outcome measures
Capacity Building and Infrastructure	● Promote multidisciplinary research and capacity building through networks and collaborative studies involving neuroscientists, music therapists, musicians, and biomedical, behavioral, or social scientists ● Support the training of neuroscientists and music therapists interested in basic or clinical research on music and the brain ● Establish evidence-based best practices for music interventions intended to enhance wellness or treat/ameliorate specific health conditions

or standard care. The music interventions resulted in considerable improvement in both cognitive function and quality of life (Särkämö et al., 2016).

Panelists also commented that case studies and small pilot studies can be highly beneficial for the development of new hypotheses. However, as in previous sessions, the participants believed that a major limitation to more widespread application of music interventions in aging populations is the scarcity of data from rigorous, well-powered RCTs.

Conclusions: Seizing the Opportunity

In summarizing the workshop, Gottfried Schlaug emphasized that there is a growing body of research showing that listening to or making music profoundly changes the brain by modulating cognition, emotion, multisensory, and motor networks. He described highly trained musicians as auditory-motor athletes and suggested that changes in their brains offer insight into functional and structural adaptations to music. The diverse studies described in the workshop are dramatically increasing our understanding of how the brain interacts with music, and this understanding is providing a foundation for promoting health and treating disease. Table 2 summarizes, in broad strokes, the recommendations made during the workshop, which are categorized into four domains: (1) Basic and Mechanistic Research, (2) Translational and Clinical Research, (3) Methods and Outcomes, and (4) Capacity Building and Infrastructure.

Funders of biomedical and behavioral research and the arts are poised to capitalize on the momentum in this field. The NIH, Department of Veteran Affairs (VA), and the NEA currently have funding opportunities and active programs supporting the study and application of music in health settings. Based on the recommendations from this workshop and other input, the NIH is developing a comprehensive research agenda and promoting collaborations among the agencies mentioned above, as well as the National Science Foundation (NSF) and the Department of Defense (DoD). With recent progress has come new opportunities and challenges. We believe that enhanced collaboration among basic scientists, clinical researchers, musicians, educators, music therapists, and funding agencies provides an exciting path forward.

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DECLARATION OF INTERESTS

Dr. Charles J. Limb has received funding from cochlear implant manufacturers for research and serves on the advisory board of both professional organizations and private companies, but none of these activities have any relationship to the article here. In addition to her role as president of the John F. Kennedy Center for the Performing Arts, Deborah Rutter is a member of the Advisory Board of The Rodham Institute, a non-profit dedicated to health equity in DC, which has no relationship to this article.

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