



Published in final edited form as:

Hear Res. 2014 February ; 308: 109–121. doi:10.1016/j.heares.2013.08.004.

Biological impact of auditory expertise across the life span: musicians as a model of auditory learning

Dana L. Strait^{1,2,*} and Nina Kraus^{1,2,3,4,5}

¹Auditory Neuroscience Laboratory, Northwestern University, Evanston, Illinois 60208

²Institute for Neuroscience, Northwestern University, Evanston, Illinois 60208

³Departments of Communication Sciences, Northwestern University, Evanston, Illinois 60208

⁴Neurobiology & Physiology, Northwestern University, Evanston, Illinois 60208

⁵Otolaryngology, Northwestern University, Evanston, Illinois 60208

Abstract

Experience-dependent characteristics of auditory function, especially with regard to speech-evoked auditory neurophysiology, have garnered increasing attention in recent years. This interest stems from both pragmatic and theoretical concerns as it bears implications for the prevention and remediation of language-based learning impairment in addition to providing insight into mechanisms engendering experience-dependent changes in human sensory function. Musicians provide an attractive model for studying the experience-dependency of auditory processing in humans due to their distinctive neural enhancements compared to nonmusicians. We have only recently begun to address whether these enhancements are observable early in life, during the initial years of music training when the auditory system is under rapid development, as well as later in life, after the onset of the aging process. Here we review neural enhancements in musically trained individuals across the life span in the context of cellular mechanisms that underlie learning, identified in animal models. Musicians' subcortical physiologic enhancements are interpreted according to a cognitive framework for auditory learning, providing a model by which to study mechanisms of experience-dependent changes in auditory function in humans.

INTRODUCTION

Learning is a fundamental human capacity; not only does it underlie the gradual development of basic skills from infancy (e.g., language) but it also accounts for our attraction to new experiences, the resources we invest in educational opportunities and the effort we put into maintaining a dynamic nervous system in hopes of keeping aging's cognitive detriments at bay. In light of our continuous reliance on learning, it is surprising how much of its neurobiological underpinnings—especially within the auditory system—still eludes us. We have made considerable headway toward defining neuronal correlates of

© 2013 Elsevier B.V. All rights reserved.

CORRESPONDING AUTHOR. Nina Kraus, Ph.D., Auditory Neuroscience Laboratory, Northwestern University, 2240 Campus Drive, Evanston, IL 60208, Ph: (847) 491-3181, Fx: (847) 467-1464, nkraus@northwestern.edu, <http://www.brainvolts.northwestern.edu>.

*Dana L. Strait is now at the Neural Systems Laboratory, Institute for Systems Research, Department of Electrical and Computer Engineering, University of Maryland, College Park, MD, USA

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

learning, in addition to identifying the characteristics that contribute to an organism's readiness to learn. The bulk of this work has been cellular in nature, carried out in animal models; we have only recently begun to apply principles derived from this research to outcomes of learning in humans (e.g., Zatorre et al., 2012). The study of musicians' auditory processing provides a window into auditory learning, not only shedding light on neural mechanisms underlying learning in humans but further contributing to a definition of what makes a good learner.

Investigations into human learning through the study of musicians profit from an almost infinite variety of auditory experts. Musicians' auditory learning approaches vary not only according to instrument, style and level of expertise but also according to their reliance on memory, improvisation, aural learning/mimicry and engagement of the visual modality. Furthermore, music is an inherently rewarding auditory activity, in part due to its activation of the brain's mesolimbic reward network (Koelsch, et al., 2006; Menon and Levitin, 2005; Salimpoor, et al., 2011; Salimpoor, et al., 2013). This may account for why humans view music as one of the top ten most pleasurable things, sometimes even ranking music above the notable rewards of money and food (Dube and Lebel, 2003). This property of music confers emotional benefits that promote its practice and performance and, by co-activating mesolimbic neuromodulatory control centers, promotes long-term learning success (for review see Puschmann, et al., 2012).

Here we interpret principles derived from cellular studies of learning in the context of how auditory experience in the form of music training shapes the structure and function of the human brain. By considering cellular approaches for studying learning alongside the biological evidence of lifelong, interactive auditory enrichment in musicians, we can infer the processes by which the human brain is shaped by the development of expertise and test their boundaries. The parallel consideration of cellular and far-field approaches may encourage further investigations into the capacity of interactive, acoustically rich and cognitively engaging auditory activities, such as that provided through musical training, to shape basic auditory mechanisms. We begin by reviewing progress toward identifying neuronal substrates of learning in animal models and the potential for musicians to provide further conceptual advances as a model of auditory learning in humans.

BIOLOGICAL MECHANISMS OF AUDITORY LEARNING

Neurobiological approaches have uncovered a variety of neuronal substrates of learning, the activity of which is modified by development, experience, gene expression and the neuromodulatory system, among others. We herein discuss major themes in this line of research and their application to musicians, comprising neurogenesis, synaptic plasticity, gene expression and factors guiding metaplasticity (i.e., the potential for plastic changes to take place).

Neurogenesis

Joseph Altman was one of the first to recommend adult neurogenesis as a neural substrate of learning (Altman, 1967). Since then, the birth of new neurons has been associated with environmental enrichment and learning (Deng, et al., 2009; Gould, Beylin, et al., 1999; Nilsson, et al., 1999; Patel, et al., 1997) but it is possible that this relationship reflects covariance with alternate neuronal changes (e.g., synaptic plasticity; see Leuner et al., 2006, for discussion). Neurogenesis has been observed throughout life (Curtis, et al., 2007; Eriksson, et al., 1998; cf. Sanai, et al., 2007), although it is more significant during the prenatal period and decreases with age (Kuhn, et al., 1996). Furthermore, neurogenesis in adults is largely constrained to the dentate gyrus of the hippocampus and the lateral ventricles that supply the olfactory cortex (cf. Gould, 2007; Gould, Reeves, et al., 1999).

Without evidence for the experience-related post-natal birth of new neurons in sensory cortices, local neurogenesis is an unlikely candidate to account for the extent of experience-related changes in neural structure with music training (for further discussion see Zatorre, et al., 2012). It is possible, however, that experience-related changes in sensory cortices are mediated, at least in part, by structural and functional changes in hippocampus that are known to accompany music training (Groussard, et al., 2010; Herdener, et al., 2010; Hutchinson, et al., 2003) and which may reflect neurogenesis. Still, music training, especially during developmental years, may have a more significant impact on the survival and connectivity of existing neurons by increasing the activation of neural circuits involved in auditory processing, stabilizing and sustaining those circuits into adulthood (Alladi, et al., 2005; Ben-Ari, 2001; Katz and Shatz, 1996).

Synaptic plasticity and inhibitory networks

Synaptic plasticity is the experience-dependent change in the connectivity between two neurons, which can comprise synaptogenesis or the strengthening of previously-existing connections. It can be evidenced by the growth and redirection of axonal branching (Galimberti, et al., 2006; Holahan, et al., 2006; Ramirez-Amaya, et al., 2001) and morphological changes in dendritic spine heads that, when enlarged, increase synaptic efficacy. While spines have significant structural diversity, their size correlates with synaptic strength (Matsuzaki, et al., 2004) and the long-term stability of the synapse (Holtmaat, et al., 2005). Their morphological stability appears to underlie long-term learning (Xu, Yu, Perlik, et al., 2009) and is dependent on changes in gene expression and protein synthesis (e.g., Tanaka, et al., 2008). While it is generally accepted that synaptic plasticity underlies learning, the complexity of interactions among ion channels, enzymes and genes that contribute to synaptic plasticity has prevented its thorough characterization (for review see Caroni et al., 2012, and Ho et al., 2011).

Axonal sprouting and the expansion, generation and relocation of dendritic spines occur throughout life but are regulated by development and sensory experience. Specifically, synaptic plasticity decreases with development (Grutzendler, et al., 2002; Pestronk, et al., 1980; Trachtenberg, et al., 2002) but can be augmented by enriched sensory experiences (Bednarek and Caroni, 2011; Bose, et al., 2010; Globus, et al., 1973). Developmental and experience-related changes are underscored by shifts in the balance of inhibitory and excitatory networks: while inhibitory networks generally strengthen from childhood to adulthood, the application of agents that weaken them prevent decreased synaptic plasticity in the adult brain, resetting synaptic plasticity to childhood levels (Bavelier, et al., 2010; Morishita, et al., 2010). Exposure to sensory experiences during development mediates this excitatory-inhibitory balance (Takesian, et al., 2010); in fact, enriched sensory environments reduce inhibition even when this experience is not initiated until adulthood (Sale, et al., 2007). Because of this, the enriched acoustic environment provided by music training may preserve synaptic plasticity within musicians. Music experience early in life is likely to bear even more significant effects on synaptic plasticity than that reported in adults, with the potential to contribute to an increased potential for synaptic remodeling throughout life (see *Gene expression and Metaplasticity: musicians as a model of auditory learning*, below).

Although synaptic remodeling occurs both with environmental enrichment and the learning of specific tasks, their effects can be differentiated. Whereas exposure to enriched sensory environments increases dendritic spine count throughout the exercised sensory domain (Bednarek and Caroni, 2011; Bose, et al., 2010; Globus, et al., 1973), task-learning induces changes in synaptic structure that are specific to the circuitry involved in the task's execution. Synaptic changes with task-learning can be lasting if sufficient task repetition triggers memory consolidation and, given this, might be considered a procedural memory

trace (Hofer, et al., 2009; Xu, Yu, Perlik, et al., 2009; Yang, et al., 2009). Although the generalization of task learning-induced synaptic plasticity to other behaviors has not been determined, it may be reasonable to assume minimal-to-no advantages for behaviors, even within the same sensory domain, that do not call on sufficiently overlapping circuitry. The variety of auditory, visual and tactile experiences provided by music training may engender outcomes more similar to environmental enrichment than procedural learning by contributing to synaptic remodeling within and across sensory systems that enhances the diversity of synaptic connections and promotes the generalization of expertise.

Gene expression

Dendritic morphology and, thus, synaptic transmission are largely regulated by gene expression, which is in turn controlled by a host of proteins called transcription factors. Given that we have identified over 2000 transcription factors and that they tend to work in combination to influence gene expression, investigations into their relationships to sensory experience and development have only scratched the surface. Here we touch on two well-known topics related to gene expression that bear consequences for the brain's readiness to learn from the perspective that they, among others, have the capacity to contribute to music training's impact on brain structure and its development: the expression of N-Methyl-aspartate receptor (NMDAR) subunits and tyrosine kinase receptor B (TrkB), which has a high affinity for brain-derived neurotrophic factor (BDNF), a neurotrophic factor implicated in learning and memory.

NMDA glutamate receptors facilitate the experience-dependent synaptic plasticity that undergirds learning by increasing synaptic efficacy (for review see Lau and Zukin, 2007). Enriched auditory experiences during childhood, such as that engendered by music training, have the potential to increase the NMDAR population throughout the auditory system (and, potentially, throughout the nervous system). Within the auditory brainstem, NMDARs mediate the malleability of neuronal responses with new auditory experiences during development (Feldman, et al., 1996). Within the auditory cortex, NMDARs have been specifically linked to enriched auditory exposure early in life: young music-exposed rats demonstrate more populous NMDAR subunit protein expression than rats raised in a typical laboratory environment. These outcomes stand in contrast to observations in post-pubescent music-exposed rats, who show no measurable change with enrichment (Xu, Yu, Cai, et al., 2009). NMDAR subunit population has a clear impact on learning potential, relating to enhanced auditory perceptual acuity (i.e., signal detection and duration discrimination) and more proficient learning performance, even outside the auditory domain (Tang, et al., 1999) and augmented neurobiological benefits of environmental enrichment (Tang, et al., 2001). If, as in rodents, children who regularly engage in musical activities have more populous NMDAR subunits, they may similarly demonstrate an increased capacity to benefit from learning opportunities and further enriched sensory experiences. These effects are doubtfully exclusive to music, however: auditory enrichment by means of music exposure has not yet been compared to other approaches that can be initiated during early childhood and may yield similar effects (e.g., increased language exposure).

The expression of neurotrophic factor BDNF and its receptor, TrkB, relates to experience-related neuroplasticity akin to NMDARs by promoting synaptic plasticity but with a focus on increasing synapto- and neurogenesis (for review see Cunha, et al., 2010) and enhancing the survival of existing cells (Acheson, et al., 1995). Like NMDARs, enriched auditory stimulation during early developmental stages regulates BDNF and TrkB expression (Chaudhury and Wadhwa, 2009; Chikahisa, et al., 2006), concurrent with enhanced learning performance even outside the auditory domain (Chikahisa, et al., 2006). Studies such as these indicate that early exposure to auditory-rich, interactive and engaging environments during initial development, such that facilitated by music training, sets the stage for later

auditory learning success by promoting gene expression that enhances immediate synaptic plasticity and cell survival. NMDAR subunit and BDNF/TrkB expression may account for musicians' enhanced learning performance, including foreign and novel language learning (Schon and Francois, 2011; Shook, et al., 2013), and increased sensitivity to statistical regularities in ongoing sound streams (Herholz, et al., 2011).

Metaplasticity: musicians as a model of auditory learning

The term “metaplasticity” describes experience-dependent neural changes that shape the brain's capacity for subsequent synaptic plasticity—“the plasticity of synaptic plasticity.” Initially coined by Abraham and Bear (1996), this term has provided a framework for the study of cellular mechanisms that prime the nervous system for experience-related neuronal and synaptic restructuring. This priming can be contrasted with the effects of intercellular signaling molecules, such as neuromodulators, catecholamines and hormones, which regulate plasticity online; instead, metaplasticity brings about lasting physiological or biochemical neuronal changes that increase an organism's later learning potential. Many metaplastic mechanisms overlap with mechanisms of plasticity themselves, a number of which are introduced above. These include the concentration of NMDARs and TrkB/BDNF but also comprise the activation of other metabotropic glutamate receptors and the priming of plastic changes through potentiation at neighboring synapses (i.e., “heterosynaptic metaplasticity”), all of which promote lasting changes in synaptic transmission (for review see Abraham, 2008). Although we have identified a number of biological mechanisms that underlie the brain's readiness to learn, their practical implications for everyday performance remain poorly understood. The study of musicians may yield insights into the practical implications of metaplasticity by providing an example of improved learning and memory in humans, above and beyond their advantaged sensory skills (Boh, et al., 2011; Chan, et al., 1998; George and Coch, 2011; Herholz, et al., 2011; Ho, et al., 2003; Jakobson, et al., 2008; Parbery-Clark, Skoe, Lam, et al., 2009; Parbery-Clark, Strait, Anderson, et al., 2011; Ragert, et al., 2004; Schon and Francois, 2011; Shook, et al., 2013; Strait, et al., 2013; Strait, Parbery-Clark, et al., 2012).

AUDITORY LEARNING IN MUSICIANS: WHAT CAN MUSIC TEACH US?

Despite our progress toward identifying neuronal mechanisms that underscore experience-related plasticity and subsequent learning potential, the complexity of interactions among these mechanisms and their different relationships to development and environmental factors make it difficult to determine how they work in concert to shape system-wide behavior. Furthermore, the bulk of this work has taken place in animal models, challenging its generalization to everyday learning in humans. Here we discuss our research in musicians from ages three to sixty-five as an example of the physiological outcomes that are possible with auditory learning, *in situ*.

Overview of auditory enhancements in musicians

Music training has been associated with significant physiological enhancements throughout the auditory system that underscore general (i.e., not music-specific) auditory processing. For example, adult musicians have heightened auditory perception (Kishon-Rabin, et al., 2001; Micheyl, et al., 2006; Parbery-Clark, Skoe, Lam, et al., 2009; Parbery-Clark, Strait, Anderson, et al., 2011; Rammsayer and Altenmuller, 2006; Strait, et al., 2010; Zendel and Alain, 2009) and more differentiated cortical evoked potentials to slight acoustic distinctions compared to nonmusicians (Chobert, et al., 2011; Marie, et al., 2010; Marques, et al., 2007; Schon, et al., 2004; Tervaniemi, et al., 1997; van Zuijen, et al., 2005). Functional cortical distinctions between musicians and nonmusicians are accompanied by structural differences: musicians have more gray matter within auditory and sensorimotor cortices (Bermudez, et

al., 2009; Gaser and Schlaug, 2003a; Schneider, et al., 2002) in addition to more voluminous white matter tracts that underscore cortical connectivity (Bengtsson, et al., 2005; Halwani, et al., 2011; Lee, et al., 2003; Schlaug, 2001; Schlaug, Forgeard, et al., 2009; Schlaug, et al., 1995; Schmithorst and Wilke, 2002). Cortical distinctions that stem from training rather than innate predispositions are sometimes greater in musicians who received auditory enrichment in the form of music training during early childhood, a sensitive developmental period (e.g., Steele, et al., 2013). This could account for correlations that are often observed between structural and functional musician-distinctions and years of music training or age of training onset (e.g., Gaser and Schlaug, 2003b; Hutchinson, et al., 2003; Pantev, et al., 1998).

Work from our lab and others has extended what we know about musicians' neural responses to the neural encoding of specific sound characteristics by means of the auditory brainstem response to complex sounds (cABR). Because it can be elicited in humans from infancy to adulthood and is measurable in both humans and animal models, the cABR provides a promising avenue for unifying cellular and far-field approaches across both developmental stages and model organisms. Furthermore, the cABR can provide a meaningful marker of an individual's auditory processing characteristics, with signatures that indicate good and poor speech-in-noise perception, auditory working memory, or reading ability and that segregate musicians from nonmusicians, language-impaired from typically-developing, and older from younger adults (Kraus and Nicol, in press). By means of the cABR we have been able to determine the driving characteristics distinguishing musicians' auditory brainstem function, which bears a distinct signature compared to nonmusicians. This is because cABRs permit the selective assessment of the neural encoding of specific acoustic features (e.g., the neural encoding of fundamental frequency versus harmonics) and over distinct acoustic regions within a single stimulus, even very short speech stimuli (e.g., the onset, formant transition and vowel portions of a 170-ms speech syllable; Fig. 1). The fine temporal precision and high-frequency phase-locking capacity of the auditory brainstem and midbrain nuclei that generate cABRs result in neural responses that can be reliably measured on the order of fractions of a millisecond and that acoustically resemble evoking stimuli (for review, see the cABR tutorial provided by Skoe and Kraus, 2010). Rather than demonstrating overall enhanced cABRs, musicians have selectively enhanced neural encoding of specific acoustic features (e.g., speech sound harmonics but not fundamental frequency; Fig. 1). Musicians also have faster cABRs and more precise response timing compared to nonmusicians but only in response to the most spectrotemporally dynamic and informationally salient regions of speech stimuli. Whereas musicians and nonmusicians have equivalent response timing in response to the sustained vowel region of speech syllables, musicians have faster and more precise timing in response to the onset and formant transition regions of these same syllables that reflect the encoding of consonants (Figs. 2 and 3). While general cABR signature enhancements have been identified in musicians, it is important to note that musicians' enhancements change as a function of stimulus context: although musicians typically do not demonstrate enhanced encoding of an invariant fundamental frequency, for example, their responses become enhanced when sounds are presented with differing statistical probability (Parbery-Clark, Strait, & Kraus, 2011) or acoustic complexity (Strait, et al., 2009; Wong, et al., 2007).

Musicians' cABR enhancements are especially apparent to spectrotemporally rich signals (i.e., speech or music but not click stimuli; Musacchia, et al., 2007; Strait, et al., 2009; Wong, et al., 2007). They are most consistently observed in challenging listening environments, such as in the presence of background noise (Parbery-Clark, Skoe, & Kraus, 2009) or reverberation (Bidelman and Krishnan, 2010), and between responses to sounds that are difficult to differentiate, such as for the similar speech sounds "ba" and "ga" (Parbery-Clark, Tierney, et al., 2012; Strait, et al., 2013). Whereas musician and nonmusician young adults have equivalent response timing and neural encoding of speech

harmonics in quiet, for example, young adult musicians have faster responses and more robust encoding of speech harmonics in the presence of background noise or acoustic complexity (Figs. 1 and 2; Parbery-Clark, Skoe, & Kraus, 2009; Strait, et al., 2009). These neural enhancements appear to undergird musicians' better performance on auditory tasks, such as hearing speech in noise (Parbery-Clark, Skoe, & Kraus, 2009; Parbery-Clark, Strait, & Kraus, 2011; Zendel and Alain, 2011), and correspond to better auditory but not visual cognitive performance in musicians (Strait, et al., 2013). While music training may impact visual cognitive performance to some degree (e.g., Jakobson, et al., 2008), relationships between cABR properties and cognitive behavior have been most strongly observed in the auditory domain.

Musicians' enhanced cABRs across the life span

We have since compared speech-evoked cABRs in musicians and nonmusicians over different developmental stages, from early childhood to late adulthood. This work has revealed that enhanced speech-evoked auditory brainstem function in musicians can be observed in school-aged children and preschoolers as young as age three and with as little as one year of music training (Strait, et al., 2013; Strait, Parbery-Clark, et al., 2012; Strait, et al., in press). Investigations in older adult musicians and nonmusicians further reveal that young adults' cABR advantages persist into older adulthood (Parbery-Clark, Anderson, et al., 2012a, 2012b), even, despite some degree of modification, through the onset of hearing loss (Parbery-Clark, et al., 2013). Together, this work reveals that some aspects of musicians' auditory brainstem function emerge (and fade) with development prior to others. That is, musicians' signature cABR characteristics reflect development and aging and are not identical across the life span. It is notable that these musician-enhancements are observed in the absence of advantages for concurrently recorded cortical-evoked responses (i.e., P1, P2, N1 and N2): cortical evoked responses can be extracted from the same passively-collected EEG recordings from which cABRs are generated by re-filtering according to cortical response characteristics, from 0.1–30 Hz. Musician and nonmusician children and adults have equivalent passively-recorded cortical onset peak timing and amplitudes in response to these same stimuli (Strait et al., unpublished data). In light of the exquisite temporal tuning of auditory brainstem nuclei, with precision on the order of milliseconds, it is possible that experience-dependent plasticity in the form of fine-grained changes in acoustic processing is primarily expressed subcortically, even if its evolution is cortically induced by means of descending cortico-collicular projections. This could account for short-term changes in frequency tuning within primary auditory cortex with training despite perseverant changes in behavior (Reed, et al., 2011). Musicians' cortical onset responses can, however, differ in response to different stimuli (e.g., Musacchia, et al., 2008; Pantev, et al., 1998; Shahin, et al., 2003) or, as we have observed, even to the same stimuli under different recording parameters (i.e., with attention: Strait and Kraus, 2011a). Their absence here indicates that enhancements in musicians' cortical onset responses are not always observed but depend on the stimulus employed and its presentation parameters; while many aspects of musicians' auditory processing are advantaged, this is not a pan-effect.

Even with their differences, musicians across the life span do share a number of cABR characteristics: for example, young adults, school-aged children and preschoolers all have more precise cABR timing to the contrasting syllables /ba/ and /ga/, resulting in more differentiated responses to these commonly confused speech sounds (Fig. 3; this has not yet been explored in older adults). Similarly, young adults, preschoolers, school-aged children and older adults involved in music training all have faster cABR timing than nonmusicians in response to the spectrotemporally dynamic formant transition of speech in the context of background noise but not in response to the sustained vowel. In contrast to young adults,

however, older adult and child musicians have faster timing to the formant transition of speech not only in noise but also in quiet (Fig. 2). This observation in children may indicate that music training steepens the neurodevelopmental trajectory of subcortical timing mechanisms irrespective of the listening environment. Although the musician advantage in quiet fades with increasing development, musicians' faster neural timing in the presence of noise persists through young adulthood and into the middle-aged years. Distinctions between older and younger adult musicians' cABR enhancements have been interpreted in the context of music training's interactions with the aging process: older adult musicians experience less detrimental effects of aging on auditory processing than nonmusicians (Parbery-Clark, Anderson, et al., 2012a; Parbery-Clark, Strait, Anderson, et al., 2011; Zendel and Alain, 2011). This may account for why the musician advantage for processing speech in quiet re-emerges with aging, reflecting less age-related delays in musicians' cABRs compared to nonmusicians'.

The developmental interpretation of cABR distinctions between musician and nonmusician children and young adults may be further supported by their encoding of speech harmonics: as with timing, adult musicians only demonstrate more robust encoding of harmonics in the context of background noise but school-aged musician children have more robust harmonics encoding in both noise and quiet, relative to nonmusicians (Fig. 1). In contrast to our formant transition timing results, however, musicians' enhanced cABRs to speech harmonics are not observed in musically trained preschoolers (Strait, et al., in press); this may indicate the emergence of this musician-enhancement with more years of music training and development. The neural encoding of speech harmonics is not only the last to emerge with music training during childhood but also the first to fade in the aging process as hearing becomes compromised (Parbery-Clark, et al., 2013). The later emergence of musicians' enhanced encoding of speech harmonics may reflect better-honed subcortical timing mechanisms with more years of music training. Its disappearance in older adult musicians with compromised hearing, in contrast, may reflect the delayed timing and decreased neural response variability known to accompany the aging process (Anderson, et al., 2012; Schmiedt, et al., 1996; Turner, et al., 2005).

Although up to now we have interpreted these outcomes to reflect training rather than innate differences predistinguishing musicians from nonmusicians, it is not only possible but *likely* that innate differences contribute in part to the effects observed. While we discuss this point in depth below, more work, especially longitudinal work, is necessary to isolate training-related contributions of musicians' neural enhancements. Still, in light of cellular evidence for long-term effects of experience-related plasticity setting the stage for later learning success, we propose that neural enhancements in musically-trained children during early developmental years may optimize child development by strengthening learning facility.

Processes underlying musicians' auditory enhancements: cognitive- sensory reciprocity

Although we cannot directly access the cellular mechanisms that drive musicians' auditory advantages, we can make inferences by interpreting outcomes from research focusing on different brain regions in the context of what we know about cellular mechanisms of learning. Recently, we have argued that musicians' speech-evoked ABR enhancements reflect strengthened top-down control over sensory processing (Kraus and Chandrasekaran, 2010; Strait and Kraus, 2011b; Strait, et al., 2013; see also Patel, 2011 for discussion) by means of descending cortico-thalamic, -collicular and -cochlear nuclear projections (Bauerle, et al., 2011; Luo, et al., 2008; Yan, et al., 2005). These descending connections are crucial for engendering behavioral learning and its cellular correlates (e.g., descending innervations to the inferior colliculus and medial geniculate body: Bajo, et al., 2010; Bauerle, et al., 2011). Here we evaluate data in musician and nonmusician children and

adults that corroborate this claim, reflecting strengthened corticofugal systems with auditory expertise.

Increasing evidence indicates that adult musicians more heavily recruit extra-sensory and association cortices that underlie cognitive involvement associated with attention and memory for auditory task performance than nonmusicians (Baumann, et al., 2008; Gaab and Schlaug, 2003; Haslinger, et al., 2005; Pallesen, et al., 2010; Stewart, et al., 2003). Musicians' frequent exercising of higher-order brain regions during sensory processing may induce long-range synaptic plasticity that facilitates strengthened top-down control over basic auditory response properties (e.g., sharpened frequency tuning, faster response timing, heightened neuronal recruitment). Strengthened cognitive-sensory connectivity would bear implications for both passive and active sound processing: much like a muscle, once the circuitry has been strengthened it retains its capacity even during the most basic auditory activities. This strengthened circuitry may account for musicians' increased neural sensitivity to acoustic regularities (Francois and Schon, 2011; Schon and Francois, 2011) and more robust cortical indices of memory and attention performance (George and Coch, 2011; Strait and Kraus, 2011a), evident even in passive recording paradigms (Boh, et al., 2011; Herholz, et al., 2011; Seppanen, Hamalainen, et al., 2012; Seppanen, Pesonen, et al., 2012; van Zuijen, et al., 2005).

Scalp-recorded speech-evoked ABRs provide insight into musicians' cognitive-sensory circuitry; even when recorded passively, while participants watch unrelated movies, cABRs reflect auditory cognitive performance (i.e., performance on auditory working memory and attention tasks). Correlations between cABR properties and auditory attention and working memory have recently been reported across development, in school-aged children (Kraus, et al., 2012; Strait, et al., 2011; Strait, et al., 2013; Strait, Parbery-Clark, et al., 2012), adolescents (Krizman, et al., 2012), young adults (Strait, et al., 2013) and older adults (Anderson et al. *Hear Res* 2013). Musicians' auditory cognitive advantages persist into older adulthood, potentially offsetting aging-related cognitive declines (Parbery-Clark, Strait, Anderson, et al., 2011). Musicians' consistently enhanced cognitive performance correlates with the degrees of enhancement observed in their cABRs compared to age- and IQ-matched peers. As such, we argue that the cABR provides a window into a fundamental characteristic of auditory learning in musicians: namely, the strengthening of the cognitive-sensory circuitry that brings about better auditory performance.

Musicians' auditory enhancements reflect experience-related neuroplasticity

A thorough treatment of musician-nonmusician distinctions must consider both innate and training-related factors that may underlie the development of auditory expertise. It is well-established that cognitive and neural functions, including cABRs, reflect a confluence of genetic (Blokland, et al., 2008; Blokland, et al., 2011; Hornickel, et al., 2013; O'Connor, et al., 1994; Rust, 1975) and experience-related contributions (e.g., Engineer, et al., 2004; Fujioka, et al., 2006; Hayes, et al., 2003; Hornickel, et al., 2012; Mailloux, et al., 1974; Russo, et al., 2005; Song, et al., 2012; Song, et al., 2008). Shared genetic influences may account for why music and language abilities appear to be inherently connected, even among a nonmusician population (Anvari, et al., 2002; Milovanov, et al., 2009; Milovanov, et al., 2008; Milovanov, et al., 2010; Overy, et al., 2003; Slevc and Miyake, 2006; Strait, et al., 2011). Although innate characteristics may contribute to covariance between language and music skills, cellular and systems studies have established an added impact of sensory experience on neural structure and function that extends beyond innate predispositions (see *Biological mechanisms of auditory learning*, above). Regular engagement with musical sound—both in its production, manipulation and perception—further shapes biological and cognitive foundations of human sound processing.

Evidence from our lab has substantiated relationships between extent of music practice and speech-evoked subcortical and non-passively recorded cortical neural responses, with increased training yielding a greater degree of neural enhancement in both children (Strait, et al., 2013; Strait, Parbery-Clark, et al., 2012) and young adults (Musacchia, et al., 2007; Musacchia, et al., 2008; Parbery-Clark, Strait, & Kraus, 2011; Strait, et al., 2009; Wong, et al., 2007) (Fig. 4). These relationships are not exclusive to musicians who are actively pursuing musical activities at the time of testing but extend to all individuals with any degree of music training. While observed in both children and young adults, relationships between neural metrics and extent of training are most prevalent in children, inconsistently observed in young adults but have not yet been observed in middle-aged adults (Parbery-Clark, Anderson, et al., 2012b). It is possible that these age-related distinctions reflect a plateau in the strengthening of neural function with music training, with more years of training beyond a certain point yielding no additional neural benefit.

A frequent question facing this research reflects a common trend in current-day music education, which often persists throughout childhood but is discontinued in adolescence or early adulthood: what happens to musicians' neural enhancements after music training has ceased? Skoe and Kraus recently demonstrated a lasting impact of music training during childhood on neural function this by recording cABRs to musical tones in adult nonmusicians with zero to eleven years of music training during childhood (on average participants had five years of training; Skoe and Kraus, 2012). In addition to systematic increases in the subcortical encoding of concurrent with less background noise in the neural responses (i.e., smaller responses in the absence of stimulation), these data indicate that neural enhancements associated with even small amounts of music training are preserved into adulthood. Similar results reported by White-Schwoch and colleagues indicate that benefits related to small amounts of prior music training may even persist into early aging: older adults ages 55–70 demonstrate faster cABRs to the formant transitions of consonant-vowel syllables as a function of the extent of music training received during childhood and adolescence, long-since discontinued (White-Schwoch, et al., under review). Still, both of these studies relied on correlational designs: longitudinal studies addressing questions of music training's lasting impact would be enormous undertakings given the time-scales of decades, in the case of Skoe and Kraus, 2012, and generations, in the case of White-Schwoch et al. Taken together, however, these outcomes bear practical implications by indicating a lasting impact of childhood music education on neural function, even when continued training is not feasible or desired. Although we can only speculate as to the cellular origins of these results, they may in part reflect cellular changes stemming from synaptic plasticity or the expression of glutamate/BDNF receptors with increased interactive auditory exposure early in life (see BIOLOGICAL MECHANISMS OF LEARNING). Such effects could account for more efficient auditory processing later in life, years after musical training has ceased.

Although correlational analyses conducted after music training has initiated reveal covariance between the extent of music training and neural outcomes of auditory learning, longitudinal studies that measure within-subject neural changes from pre- to post-music training onset are necessary to directly test how auditory learning with music shapes the nervous system. Few studies have attempted longitudinal approaches, attesting to their enormous practical and financial challenges. The research that has examined longitudinal data, however, has established that music training in school-aged children engenders more robust cortical responses to changes in pitch (Besson, et al., 2007; Moreno, et al., 2009) and voice-onset time (Chobert, et al., 2012) as well as increased growth of primary auditory and motor cortices (Hyde, et al., 2009). We recently demonstrated the first longitudinal evidence of music training's impact on auditory brainstem function in preschoolers already engaged in music training, with preschoolers involved in music classes developing less of an impact

of background noise on cABR timing over the course of one year compared to age- and IQ-matched nonmusician peers (Strait, et al., in press). These data further reveal that cABRs recorded in preschoolers undergoing music training are not differentiated from nonmusicians' to the extent observed in older children and adults. Whereas school-aged, young adult and older adult musicians demonstrate both faster cABR timing and more robust cABRs (i.e., larger spectral harmonic magnitudes) compared to nonmusicians, music-trained preschoolers are only distinguished by faster cABR timing to the formant transitions of consonant-vowel syllables. Although some aspects of auditory brainstem function emerge with as little as one year of training during preschool years (or, alternately, may be more constrained by innate contributors) (Strait, et al., 2013; Strait, et al., in press), continued music training over development is necessary to further distinguish musicians from nonmusicians.

Music as an optimal vehicle for studying auditory learning

In addition to yielding insights into cognitive contributors to sensory malleability and innate versus training-related features of experience-associated neural characteristics, the study of musicians may further our understanding of auditory learning by providing a diverse auditory-trained human population. Music's acoustic, stylistic and educational diversity offers an ideal framework for testing the outcomes of different types of sound exposure or educational strategies on learning and its generalization. While cellular definitions of neural mechanisms that take place with learning give us an exceptional starting point for understanding human learning, the study of musicians may move us toward determining how to optimize training approaches for long-term learning success.

We have only touched the surface of the variety available within musicians but this approach has already advanced the study of human learning. For example, research has determined that musicians' auditory (Margulis, 2009; Pantev, et al., 2001; Strait, Chan, et al., 2012) and sensorimotor enhancements (Bangert and Schlaug, 2006; Elbert, et al., 1995) reflect their instruments of practice; further research should determine the impact of different instruments on nonmusical abilities. For example, we might determine whether musical practice involving certain musical timbres (or a combination of timbres) more easily generalizes to speech processing or if instruments requiring manual opposition (e.g., the piano over the trumpet) more significantly increase inhibitory control. Musicians' training strategies, such as a focus on solo versus ensemble playing or the reliance on written music versus playing "by ear", are also bound to lead to different impacts on neural structure and function. An effect of the latter comparison has been established by cortical evoked potentials to music recorded in musicians who varied in their reliance on aural training strategies (Seppanen, et al., 2007). This work indicates that aurally-focused music practice, which emphasizes "playing by ear," leads to faster neural responses to musical interval and contour changes, concurrent with heightened performance on an auditory discrimination task comprising musical patterns. Future work might define implications of these outcomes for general auditory processing, behavior and learning outside the musical domain.

In addition to providing a diverse population of auditory experts, the application of music as an auditory learning medium has the added benefit of engaging the brain's mesolimbic reward network (Koelsch, et al., 2006; Menon and Levitin, 2005; Salimpoor, et al., 2011; Salimpoor, et al., 2013; for review see Zatorre and Salimpoor, 2013), which promotes long-term learning success (e.g., see Puschmann, et al., 2012). Activation of this network promotes the release of neuromodulators that contribute to synaptic plasticity and gene expression, including acetylcholine, serotonin and the catecholamines dopamine and noradrenaline. Although the cell bodies of neuromodulatory neurons reside within different brainstem, midbrain and forebrain sites, their projections extend throughout the brain and widely impact sensory processing and its experience-dependency (for examples in the

auditory domain, see Bao, et al., 2001; Cardin and Schmidt, 2004; Hurley and Hall, 2011; Kilgard and Merzenich, 1998a; Kilgard and Merzenich, 1998b; Velho, et al., 2012). Music's activation of the reward network also confers a practical advantage for the study of auditory learning, providing an emotionally rewarding and satisfying medium for auditory training.

MOVING FORWARD: WHAT DO MUSICIANS STILL HAVE TO TEACH US ABOUT AUDITORY LEARNING?

The insights provided by basic science give us a strong starting point from which to consider restructuring auditory training approaches and learning strategies, especially with regard to sensitive developmental periods during which they can be most effective (e.g., see Sanes and Woolley, 2011). But how do principles taken from cellular approaches translate into recommendations for human habits that raise one's learning potential? Considering musicians as a model of auditory learning may yield significant advances toward defining the limits of human learning, how they can be stretched by distinct learning strategies over different developmental time points and how they shape later brain and behavioral functions even after training has ceased. Auditory training during developmental years, for example, may impact later auditory performance, as has been observed in rats (Sarro and Sanes, 2011), in addition to enhanced neural response properties, as evidenced by cABRs in adult nonmusicians with some degree of childhood music training (Skoe and Kraus, 2012; White-Schwoch, et al., under review). Furthermore, auditory training early in life may shape later learning facility by strengthening metaplastic mechanisms that underlie learning potential. Moving forward, we might better define the impact of music on learning performance, such as through the comparison of online learning and short-term training outcomes in musically trained and untrained populations.

Principles of music training may be further applied toward optimizing existing auditory training regimens to increase their efficacy. Music training itself, in fact, may be a profitable strategy for improving auditory processing in clinical populations, such as for training the brains of new cochlear implant users to optimally use available acoustic input (Abdi, et al., 2001; Chen, et al., 2010) or for stroke patients struggling to regain language function (Norton, et al., 2009; Schlaug, Marchina, et al., 2009). Although we have determined that music training throughout life prevents or reduces the impact of a number of age-related cognitive, perceptual and neural declines (Hanna-Pladdy and Gajewski, 2012; Parbery-Clark, Anderson, et al., 2012a, 2012b; Parbery-Clark, Strait, Anderson, et al., 2011; Zendel and Alain, 2011), even in the presence of hearing loss (Parbery-Clark, et al., 2013), no studies have yet addressed the extent of training required, how recent it must be nor whether training during advanced adulthood confers immediate benefits.

Furthermore, principles of auditory learning observed in musicians have the potential to shed light on mechanisms of learning and to reinforce their applications in non-auditory domains. Few studies have assessed the impact of music training on neural processes underlying sensory and motor behavior outside the auditory system, although visual and tactile neural and cognitive musician advantages have been observed to some extent (Jakobson, et al., 2008; Musacchia, et al., 2007; Musacchia, et al., 2008; Ragert, et al., 2004). Motor synchronization is also improved in musicians compared to nonmusicians, observed to pairings with auditory or visual cues in the form of beat synchronization (Krause, et al., 2010; Repp, 2010; Repp and Doggett, 2007; Steele, et al., 2013; Watanabe, et al., 2007). The malleability of auditory-motor synchronization with music training may yield insights for mechanisms by which music training affects everyday, non-musical functions given that this ability has been tied to language and cognitive skills. In fact, beat synchronization (and, not surprisingly, rhythm perception) relates to auditory attention and reading abilities (Tierney and Kraus, 2013), is deficient with language-based learning

impairment (Huss, et al., 2010; Strait, et al., 2011; Thomson and Goswami, 2008) and, we propose, may be remediated with music-based training (see Strait and Kraus, 2011b for discussion). The interaction between beat synchronization and language skills may drive the generalization of musicians' perceptual, cognitive and neural enhancements to the language domain, engendered through music's consistent emphasis on auditory-motor synchronization according to a governing beat. Future work should determine musicians' learning potential across sensory domains and define its limits in addition to assessing its generalization to other skills (e.g., reading and executive function).

CONCLUSIONS

Here we have interpreted principles derived from cellular studies alongside evidence for the impact of auditory expertise on human brain structure and function. While the most effective approach would comprise a thorough integration of knowledge gained from cellular work with outcomes from our far-field metric in humans, present knowledge cannot bridge these approaches. Many reports have revealed effects of learning on subcortical physiology using cellular measurements in animal models but to our knowledge no work has yet defined how cellular metrics relate to scalp-recorded cABRs. These effects may reflect mechanisms of learning that involve synaptic plasticity, gene expression or others, especially those involved in metaplasticity, but this knowledge gap could be bridged by concurrent cellular and far-field approaches in animal models such as that reported by Warrier and colleagues (Warrier, et al., 2011), either following auditory training or over the course of the learning process. Together, these approaches may not only lead to a better definition of the musician as a model organism but have the capacity to further our understanding of the potential of human experience to fundamentally shape the biology underlying everyday learning.

Acknowledgments

This research was funded by the National Institutes of Health grant F31DC011457-01 to D.S., the National Science Foundation grants BCS-0921275, 1057556 and 0842376 to N.K., the Grammy Foundation and the Knowles Hearing Center. The authors thank Samantha O'Connell for her contributions to data collection in preschoolers and Alexandra Parbery-Clark, Karen Chan, Trent Nicol and Jennifer Krizman for their comments.

WORKS CITED

- Abdi S, Khalessi MH, Khorsandi M, Gholami B. Introducing music as a means of habilitation for children with cochlear implants. *Int J Ped Otorhinolaryngol*. 2001; 59:105–113.
- Abraham WC. Metaplasticity: tuning synapses and networks for plasticity. *Nat Rev Neurosci*. 2008; 9:387. [PubMed: 18401345]
- Abraham WC, Bear MF. Metaplasticity: the plasticity of synaptic plasticity. *Trends Neurosci*. 1996; 19:126–130. [PubMed: 8658594]
- Acheson A, Conover JC, Fandl JP, DeChiara TM, Russell M, Thadani A, Squinto SP, Yancopoulos GD, Lindsay RM. A BDNF autocrine loop in adult sensory neurons prevents cell death. *Nature*. 1995; 374:450–453. [PubMed: 7700353]
- Alladi PA, Roy T, Singh N, Wadhwa S. Prenatal auditory enrichment with species-specific calls and sitar music modulates expression of Bcl-2 and Bax to alter programmed cell death in developing chick auditory nuclei. *Int J Dev Neurosci*. 2005; 23:363–373. [PubMed: 15927760]
- Altman, J. Postnatal growth and differentiation of the mammalian brain, with implications for a morphological theory of memory. In: Quarten, GC.; Melnechuck, T.; Schmitt, FO., editors. *The Neurosciences, a Study Program*. New York, NY: Rockefeller University Press; 1967.
- Anderson S, Parbery-Clark A, White-Schwoch T, Kraus N. Aging affects neural precision of speech encoding. *J Neurosci*. 2012; 32:14156–14164. [PubMed: 23055485]

- Anvari SH, Trainor LJ, Woodside J, Levy BA. Relations among musical skills, phonological processing, and early reading ability in preschool children. *J Exp Child Psychol.* 2002; 83:111–130. [PubMed: 12408958]
- Bajo VM, Nodal FR, Moore DR, King AJ. The descending corticocollicular pathway mediates learning-induced auditory plasticity. *Nat Neurosci.* 2010; 13:253–260. [PubMed: 20037578]
- Bangert M, Schlaug G. Specialization of the specialized in features of external human brain morphology. *Eur J Neurosci.* 2006; 24:1832–1834. [PubMed: 17004946]
- Bao S, Chan VT, Merzenich MM. Cortical remodelling induced by activity of ventral tegmental dopamine neurons. *Nature.* 2001; 412:79–83. [PubMed: 11452310]
- Bauerle P, von der Behrens W, Kossel M, Gaese BH. Stimulus-specific adaptation in the gerbil primary auditory thalamus is the result of a fast frequency-specific habituation and is regulated by the corticofugal system. *J Neurosci.* 2011; 31:9708–9722. [PubMed: 21715636]
- Baumann S, Meyer M, Jancke L. Enhancement of auditory-evoked potentials in musicians reflects an influence of expertise but not selective attention. *J Cogn Neurosci.* 2008; 20:2238–2249. [PubMed: 18457513]
- Bavelier D, Levi DM, Li RW, Dan Y, Hensch TK. Removing brakes on adult brain plasticity: from molecular to behavioral interventions. *J Neurosci.* 2010; 30:14964–14971. [PubMed: 21068299]
- Bednarek E, Caroni P. beta-Adducin is required for stable assembly of new synapses and improved memory upon environmental enrichment. *Neuron.* 2011; 69:1132–1146. [PubMed: 21435558]
- Ben-Ari Y. Developing networks play a similar melody. *Trends Neurosci.* 2001; 24:353–360. [PubMed: 11356508]
- Bengtsson SL, Nagy Z, Skare S, Forsman L, Forssberg H, Ullen F. Extensive piano practicing has regionally specific effects on white matter development. *Nat Neurosci.* 2005; 8:1148–1150. [PubMed: 16116456]
- Bermudez P, Lerch JP, Evans AC, Zatorre RJ. Neuroanatomical correlates of musicianship as revealed by cortical thickness and voxel-based morphometry. *Cereb Cortex.* 2009; 19:1583–1596. [PubMed: 19073623]
- Besson M, Schon D, Moreno S, Santos A, Magne C. Influence of musical expertise and musical training on pitch processing in music and language. *Restor Neurol Neurosci.* 2007; 25:399–410. [PubMed: 17943015]
- Bidelman GM, Krishnan A. Effects of reverberation on brainstem representation of speech in musicians and non-musicians. *Brain Res.* 2010; 1355:112–125. [PubMed: 20691672]
- Blokland GA, McMahon KL, Hoffman J, Zhu G, Meredith M, Martin NG, Thompson PM, de Zubicaray GI, Wright MJ. Quantifying the heritability of task-related brain activation and performance during the N-back working memory task: a twin fMRI study. *Biol Psychol.* 2008; 79:70–79. [PubMed: 18423837]
- Blokland GA, McMahon KL, Thompson PM, Martin NG, de Zubicaray GI, Wright MJ. Heritability of working memory brain activation. *J Neurosci.* 2011; 31:10882–10890. [PubMed: 21795540]
- Boh B, Herholz SC, Lappe C, Pantev C. Processing of complex auditory patterns in musicians and nonmusicians. *PLoS ONE.* 2011; 6:e21458. [PubMed: 21750713]
- Bose M, Munoz-Llanca P, Roychowdhury S, Nichols JA, Jakkamsetti V, Porter B, Byrapureddy R, Salgado H, Kilgard MP, Aboitiz F, Dagnino-Subiabre A, Atzori M. Effect of the environment on the dendritic morphology of the rat auditory cortex. *Synapse.* 2010; 64:97–110. [PubMed: 19771593]
- Cardin JA, Schmidt MF. Noradrenergic inputs mediate state dependence of auditory responses in the avian song system. *J Neurosci.* 2004; 24:7745–7753. [PubMed: 15342742]
- Caroni P, Donato F, Muller D. Structural plasticity upon learning: regulation and functions. *Nat Rev Neurosci.* 2012; 13:478–490. [PubMed: 22714019]
- Chan AS, Ho YC, Cheung MC. Music training improves verbal memory. *Nature.* 1998; 396:128. [PubMed: 9823892]
- Chaudhury S, Wadhwa S. Prenatal auditory stimulation alters the levels of CREB mRNA, p-CREB and BDNF expression in chick hippocampus. *Int J Dev Neurosci.* 2009; 27:583–590. [PubMed: 19559781]

- Chen JK, Chuang AY, McMahon C, Hsieh JC, Tung TH, Li LP. Music training improves pitch perception in prelingually deafened children with cochlear implants. *Pediatrics*. 2010; 125:e793–e800. [PubMed: 20211951]
- Chikahisa S, Sei H, Morishima M, Sano A, Kitaoka K, Nakaya Y, Morita Y. Exposure to music in the perinatal period enhances learning performance and alters BDNF/TrkB signaling in mice as adults. *Behav Brain Res*. 2006; 169:312–319. [PubMed: 16530277]
- Chobert J, Francois C, Velay JL, Besson M. Twelve Months of Active Musical Training in 8- to 10-Year-Old Children Enhances the Preattentive Processing of Syllabic Duration and Voice Onset Time. *Cereb Cortex*. 2012
- Chobert J, Marie C, Francois C, Schon D, Besson M. Enhanced passive and active processing of syllables in musician children. *J Cogn Neurosci*. 2011; 23:3874–3887. [PubMed: 21736456]
- Cunha C, Brambilla R, Thomas KL. A simple role for BDNF in learning and memory? *Front Mol Neurosci*. 2010; 3:1. [PubMed: 20162032]
- Curtis MA, Kam M, Nannmark U, Anderson MF, Axell MZ, Wikkelsø C, Holtas S, van Roon-Mom WM, Bjork-Eriksson T, Nordborg C, Frisen J, Dragunow M, Faull RL, Eriksson PS. Human neuroblasts migrate to the olfactory bulb via a lateral ventricular extension. *Science*. 2007; 315:1243–1249. [PubMed: 17303719]
- Deng W, Saxe MD, Gallina IS, Gage FH. Adult-born hippocampal dentate granule cells undergoing maturation modulate learning and memory in the brain. *J Neurosci*. 2009; 29:13532–13542. [PubMed: 19864566]
- Dube L, Lebel J. The categorical structure of pleasure. *Cognition and Emotion*. 2003; 17:263–297.
- Elbert T, Pantev C, Wienbruch C, Rockstroh B, Taub E. Increased cortical representation of the fingers of the left hand in string players. *Science*. 1995; 270:305–307. [PubMed: 7569982]
- Engineer ND, Percaccio CR, Pandya PK, Moucha R, Rathbun DL, Kilgard MP. Environmental enrichment improves response strength, threshold, selectivity, and latency of auditory cortex neurons. *J Neurophysiol*. 2004; 92:73–82. [PubMed: 15014105]
- Eriksson PS, Perfilieva E, Bjork-Eriksson T, Alborn AM, Nordborg C, Peterson DA, Gage FH. Neurogenesis in the adult human hippocampus. *Nat Med*. 1998; 4:1313–1317. [PubMed: 9809557]
- Feldman DE, Brainard MS, Knudsen EI. Newly learned auditory responses mediated by NMDA receptors in the owl inferior colliculus. *Science*. 1996; 271:525–528. [PubMed: 8560271]
- Francois C, Schon D. Musical expertise boosts implicit learning of both musical and linguistic structures. *Cereb Cortex*. 2011; 21:2357–2365. [PubMed: 21383236]
- Fujioka T, Ross B, Kakigi R, Pantev C, Trainor LJ. One year of musical training affects development of auditory cortical-evoked fields in young children. *Brain*. 2006; 129:2593–2608. [PubMed: 16959812]
- Gaab N, Schlaug G. The effect of musicianship on pitch memory in performance matched groups. *Neuroreport*. 2003; 14:2291–2295. [PubMed: 14663178]
- Galimberti I, Gogolla N, Alberi S, Santos AF, Muller D, Caroni P. Long-term rearrangements of hippocampal mossy fiber terminal connectivity in the adult regulated by experience. *Neuron*. 2006; 50:749–763. [PubMed: 16731513]
- Gaser C, Schlaug G. Brain structure differs between musicians and non-musicians. *Journal of Neuroscience*. 2003a; 23:9240–9245. [PubMed: 14534258]
- Gaser C, Schlaug G. Brain structures differ between musicians and non-musicians. *J Neurosci*. 2003b; 23:9240–9245. [PubMed: 14534258]
- George EM, Coch D. Music training and working memory: an ERP study. *Neuropsychologia*. 2011; 49:1083–1094. [PubMed: 21315092]
- Globus A, Rosenzweig MR, Bennett EL, Diamond MC. Effects of differential experience on dendritic spine counts in rat cerebral cortex. *J Comp Physiol Psychol*. 1973; 82:175–181. [PubMed: 4571892]
- Gould E. How widespread is adult neurogenesis in mammals? *Nat Rev Neurosci*. 2007; 8:481–488. [PubMed: 17514200]
- Gould E, Beylin A, Tanapat P, Reeves A, Shors TJ. Learning enhances adult neurogenesis in the hippocampal formation. *Nat Neurosci*. 1999; 2:260–265. [PubMed: 10195219]

- Gould E, Reeves AJ, Graziano MS, Gross CG. Neurogenesis in the neocortex of adult primates. *Science*. 1999; 286:548–552. [PubMed: 10521353]
- Groussard M, La Joie R, Rauchs G, Landeau B, Chetelat G, Viader F, Desgranges B, Eustache F, Platel H. When music and long-term memory interact: effects of musical expertise on functional and structural plasticity in the hippocampus. *PLoS ONE*. 2010; 5
- Grutzendler J, Kasthuri N, Gan WB. Long-term dendritic spine stability in the adult cortex. *Nature*. 2002; 420:812–816. [PubMed: 12490949]
- Halwani GF, Loui P, Ruber T, Schlaug G. Effects of practice and experience on the arcuate fasciculus: comparing singers, instrumentalists, and non-musicians. *Front Psychol*. 2011; 2:156. [PubMed: 21779271]
- Hanna-Pladdy B, Gajewski B. Recent and past musical activity predicts cognitive aging variability: direct comparison with general lifestyle activities. *Front Hum Neurosci*. 2012; 6:198. [PubMed: 22833722]
- Haslinger B, Erhard P, Altenmüller E, Schroeder U, Boecker H, Ceballos-Baumann AO. Transmodal sensorimotor networks during action observation in professional pianists. *J Cogn Neurosci*. 2005; 17:282–293. [PubMed: 15811240]
- Hayes EA, Warrier CM, Nicol TG, Zecker SG, Kraus N. Neural plasticity following auditory training in children with learning problems. *Clin Neurophysiol*. 2003; 114:673–684. [PubMed: 12686276]
- Herdener M, Esposito F, di Salle F, Boller C, Hilti CC, Habermeyer B, Scheffler K, Wetzel S, Seifritz E, Cattapan-Ludewig K. Musical training induces functional plasticity in human hippocampus. *J Neurosci*. 2010; 30:1377–1384. [PubMed: 20107063]
- Herholz SC, Boh B, Pantev C. Musical training modulates encoding of higher-order regularities in the auditory cortex. *Eur J Neurosci*. 2011; 34:524–529. [PubMed: 21801242]
- Ho VM, Lee JA, Martin KC. The cell biology of synaptic plasticity. *Science*. 2011; 334:623–628. [PubMed: 22053042]
- Ho YC, Cheung MC, Chan AS. Music training improves verbal but not visual memory: cross-sectional and longitudinal explorations in children. *Neuropsycholog*. 2003; 17:439–450.
- Hofer SB, Mrsic-Flogel TD, Bonhoeffer T, Hubener M. Experience leaves a lasting structural trace in cortical circuits. *Nature*. 2009; 457:313–317. [PubMed: 19005470]
- Holahan MR, Rekart JL, Sandoval J, Routtenberg A. Spatial learning induces presynaptic structural remodeling in the hippocampal mossy fiber system of two rat strains. *Hippocampus*. 2006; 16:560–570. [PubMed: 16685708]
- Holtmaat AJ, Trachtenberg JT, Wilbrecht L, Shepherd GM, Zhang X, Knott GW, Svoboda K. Transient and persistent dendritic spines in the neocortex in vivo. *Neuron*. 2005; 45:279–291. [PubMed: 15664179]
- Hornickel J, Lin D, Kraus N. Speech-evoked auditory brainstem responses reflect familial and cognitive influences. *Dev Sci*. 2013; 16:101–110. [PubMed: 23278931]
- Hornickel J, Zecker SG, Bradlow AR, Kraus N. Assistive listening devices drive neuroplasticity in children with dyslexia. *Proc Natl Acad Sci U S A*. 2012; 109:16731–16736. [PubMed: 22949632]
- Hurley LM, Hall IC. Context-dependent modulation of auditory processing by serotonin. *Hear Res*. 2011; 279:74–84. [PubMed: 21187135]
- Huss M, Verney JP, Fosker T, Mead N, Goswami U. Music, rhythm, rise time perception and developmental dyslexia: perception of musical meter predicts reading and phonology. *Cortex*. 2010; 47:674–689. [PubMed: 20843509]
- Hutchinson S, Lee LH, Gaab N, Schlaug G. Cerebellar volume of musicians. *Cereb Cortex*. 2003; 13:943–949. [PubMed: 12902393]
- Hyde KL, Lerch J, Norton A, Forgeard M, Winner E, Evans AC, Schlaug G. Musical training shapes structural brain development. *Journal of Neuroscience*. 2009; 29:3019–3025. [PubMed: 19279238]
- Jakobson LS, Lewycky ST, Kilgour AR, Stoesz BM. Memory for verbal and visual material in highly trained musicians. *Music Perception*. 2008; 26:41–55.
- Katz LC, Shatz CJ. Synaptic activity and the construction of cortical circuits. *Science*. 1996; 274:1133–1138. [PubMed: 8895456]

- Kilgard MP, Merzenich MM. Cortical map reorganization enabled by nucleus basalis activity. *Science*. 1998a; 279:1714–1718. [PubMed: 9497289]
- Kilgard MP, Merzenich MM. Plasticity of temporal information processing in the primary auditory cortex. *Nat Neurosci*. 1998b; 1:727–731. [PubMed: 10196590]
- Kishon-Rabin L, Amir O, Vexler Y, Zaltz Y. Pitch discrimination: are professional musicians better than non-musicians? *J Basic Clin Physiol Pharmacol*. 2001; 12:125–143. [PubMed: 11605682]
- Koelsch S, Fritz T, DY VC, Muller K, Friederici AD. Investigating emotion with music: an fMRI study. *Hum Brain Mapp*. 2006; 27:239–250. [PubMed: 16078183]
- Kraus N, Chandrasekaran B. Music training for the development of auditory skills. *Nat Rev Neurosci*. 2010; 11:599–605. [PubMed: 20648064]
- Kraus N, Nicol T. The cognitive auditory system. (in press).
- Kraus N, Strait DL, Parbery-Clark A. Cognitive factors shape brain networks for auditory skills: spotlight on auditory working memory. *Ann N Y Acad Sci*. 2012; 1252:100–107. [PubMed: 22524346]
- Krause V, Pollok B, Schnitzler A. Perception in action: the impact of sensory information on sensorimotor synchronization in musicians and non-musicians. *Acta Psychol (Amst)*. 2010; 133:28–37. [PubMed: 19751937]
- Krizman J, Marian V, Shook A, Skoe E, Kraus N. Subcortical encoding of sound is enhanced in bilinguals and relates to executive function advantages. *Proc Natl Acad Sci U S A*. 2012; 109:7877–7881. [PubMed: 22547804]
- Kuhn HG, Dickinson-Anson H, Gage FH. Neurogenesis in the dentate gyrus of the adult rat: age-related decrease of neuronal progenitor proliferation. *J Neurosci*. 1996; 16:2027–2033. [PubMed: 8604047]
- Lau CG, Zukin RS. NMDA receptor trafficking in synaptic plasticity and neuropsychiatric disorders. *Nat Rev Neurosci*. 2007; 8:413–426. [PubMed: 17514195]
- Lee DJ, Chen Y, Schlaug G. Corpus callosum: musician and gender effects. *Neuroreport*. 2003; 14:205–209. [PubMed: 12598730]
- Leuner B, Gould E, Shors TJ. Is there a link between adult neurogenesis and learning? *Hippocampus*. 2006; 16:216–224. [PubMed: 16421862]
- Luo F, Wang Q, Kashani A, Yan J. Corticofugal modulation of initial sound processing in the brain. *J Neurosci*. 2008; 28:11615–11621. [PubMed: 18987197]
- Mailloux JG, Edwards HP, Barry WF, Rowsell HC, Achorn EG. Effects of differential rearing on cortical evoked potentials of the albino rat. *J Comp Physiol Psychol*. 1974; 87:475–480. [PubMed: 4413130]
- Margulis E, Mlsna LM, Uppunda AK, Parrish TB, Wong PCM. Selective Neurophysiologic Responses to Music in Instrumentalists with Different Listening Biographies. *Hum Brain Mapp*. 2009; 30:267–275. [PubMed: 18072277]
- Marie C, Magne C, Besson M. Musicians and the metric structure of words. *J Cogn Neurosci*. 2010; 23:294–305. [PubMed: 20044890]
- Marques C, Moreno S, Castro SL, Besson M. Musicians detect pitch violation in a foreign language better than nonmusicians: behavioral and electrophysiological evidence. *J Cogn Neurosci*. 2007; 19:1453–1463. [PubMed: 17714007]
- Matsuzaki M, Honkura N, Ellis-Davies GC, Kasai H. Structural basis of long-term potentiation in single dendritic spines. *Nature*. 2004; 429:761–766. [PubMed: 15190253]
- Menon V, Levitin DJ. The rewards of music listening: response and physiological connectivity of the mesolimbic system. *Neuroimage*. 2005; 28:175–184. [PubMed: 16023376]
- Micheyl C, Delhommeau K, Perrot X, Oxenham AJ. Influence of musical and psychoacoustical training on pitch discrimination. *Hear Res*. 2006; 219:36–47. [PubMed: 16839723]
- Milovanov R, Huotilainen M, Esquef PA, Alku P, Valimaki V, Tervaniemi M. The role of musical aptitude and language skills in preattentive duration processing in school-aged children. *Neurosci Lett*. 2009; 460:161–165. [PubMed: 19481587]

- Milovanov R, Huotilainen M, Valimaki V, Esquef PA, Tervaniemi M. Musical aptitude and second language pronunciation skills in school-aged children: neural and behavioral evidence. *Brain Res.* 2008; 1194:81–89. [PubMed: 18182165]
- Milovanov R, Pietila P, Tervaniemi M, Esquef PA. Foreign language pronunciation skills and musical aptitude: A study of Finnish adults with higher education. *Learn Individ Diff.* 2010; 20:56–60.
- Moreno S, Marques C, Santos A, Santos M, Castro SL, Besson M. Musical training influences linguistic abilities in 8-year-old children: More evidence for brain plasticity. *Cerebral Cortex.* 2009; 19:712–723. [PubMed: 18832336]
- Morishita H, Miwa JM, Heintz N, Hensch TK. Lynx1, a cholinergic brake, limits plasticity in adult visual cortex. *Science.* 2010; 330:1238–1240. [PubMed: 21071629]
- Musacchia G, Sams M, Skoe E, Kraus N. Musicians have enhanced subcortical auditory and audiovisual processing of speech and music. *Proc Natl Acad Sci USA.* 2007; 104:15894–15898. [PubMed: 17898180]
- Musacchia G, Strait D, Kraus N. Relationships between behavior, brainstem and cortical encoding of seen and heard speech in musicians and non-musicians. *Hear Res.* 2008; 241:34–42. [PubMed: 18562137]
- Nilsson M, Perfilieva E, Johansson U, Orwar O, Eriksson PS. Enriched environment increases neurogenesis in the adult rat dentate gyrus and improves spatial memory. *J Neurobiol.* 1999; 39:569–578. [PubMed: 10380078]
- Norton A, Zipse L, Marchina S, Schlaug G. Melodic intonation therapy: shared insights on how it is done and why it might help. *Ann N Y Acad Sci.* 2009; 1169:431–436. [PubMed: 19673819]
- O'Connor S, Morzorati S, Christian JC, Li TK. Heritable features of the auditory oddball event-related potential: peaks, latencies, morphology and topography. *Electroencephalogr Clin Neurophysiol.* 1994; 92:115–125. [PubMed: 7511509]
- Overy K, Nicolson RI, Fawcett AJ, Clarke EF. Dyslexia and music: measuring musical timing skills. *Dyslexia.* 2003; 9:18–36. [PubMed: 12625374]
- Pallesen KJ, Brattico E, Bailey CJ, Korvenoja A, Koivisto J, Gjedde A, Carlson S. Cognitive control in auditory working memory is enhanced in musicians. *PLoS ONE.* 2010; 5:e11120. [PubMed: 20559545]
- Pantev C, Oostenveld R, Engelien A, Ross B, Roberts LE, Hoke M. Increased auditory cortical representation in musicians. *Nature.* 1998; 392:811–814. [PubMed: 9572139]
- Pantev C, Roberts LE, Schulz M, Engelien A, Ross B. Timbre-specific enhancement of auditory cortical representations in musicians. *Neuroreport.* 2001; 12:169–174. [PubMed: 11201080]
- Parbery-Clark A, Anderson S, Hittner E, Kraus N. Musical experience offsets age-related delays in neural timing. *Neurobiol Aging.* 2012a; 33:1483, e1481–e1484. [PubMed: 22227006]
- Parbery-Clark A, Anderson S, Hittner E, Kraus N. Musical experience strengthens the neural representation of sounds important for communication in middle-aged adults. *Front Aging Neurosci.* 2012b; 4:1–12. [PubMed: 22514534]
- Parbery-Clark A, Anderson S, Kraus N. Musicians change their tune: how hearing loss alters the neural code. *Hear Res.* 2013; 302:121–131. [PubMed: 23566981]
- Parbery-Clark A, Skoe E, Kraus N. Musical experience limits the degradative effects of background noise on the neural processing of sound. *J Neurosci.* 2009; 29:14100–14107. [PubMed: 19906958]
- Parbery-Clark A, Skoe E, Lam C, Kraus N. Musician enhancement for speech-in-noise. *Ear Hear.* 2009; 30:653–661. [PubMed: 19734788]
- Parbery-Clark A, Strait DL, Anderson S, Hittner E, Kraus N. Musical experience and the aging auditory system: implications for cognitive abilities and hearing speech in noise. *PLoS ONE.* 2011; 6:e18082. [PubMed: 21589653]
- Parbery-Clark A, Strait DL, Kraus N. Context-dependent encoding in the auditory brainstem subserves enhanced speech-in-noise perception in musicians. *Neuropsychologia.* 2011; 49:3338–3345. [PubMed: 21864552]
- Parbery-Clark A, Tierney A, Strait DL, Kraus N. Musicians have fine-tuned neural distinction of speech syllables. *Neuroscience.* 2012; 219:111–119. [PubMed: 22634507]

- Patel AD. Why would musical training benefit the neural encoding of speech? The OPERA hypothesis. *Front Psychol.* 2011; 2:142. [PubMed: 21747773]
- Patel SN, Clayton NS, Krebs JR. Spatial learning induces neurogenesis in the avian brain. *Behav Brain Res.* 1997; 89:115–128. [PubMed: 9475620]
- Pestronk A, Drachman DB, Griffin JW. Effects of aging on nerve sprouting and regeneration. *Exp Neurol.* 1980; 70:65–82. [PubMed: 7418774]
- Puschmann S, Brechmann A, Thiel CM. Learning-dependent plasticity in human auditory cortex during appetitive operant conditioning. *Hum Brain Mapp.* 2012
- Ragert P, Schmidt A, Altenmüller E, Dinse HR. Superior tactile performance and learning in professional pianists: evidence for meta-plasticity in musicians. *Eur J Neurosci.* 2004; 19:473–478. [PubMed: 14725642]
- Ramirez-Amaya V, Balderas I, Sandoval J, Escobar ML, Bermudez-Rattoni F. Spatial long-term memory is related to mossy fiber synaptogenesis. *J Neurosci.* 2001; 21:7340–7348. [PubMed: 11549744]
- Rammsayer T, Altenmüller E. Temporal Information Processing in Musicians and Nonmusicians. *Music Perception.* 2006; 24:37–48.
- Reed A, Riley J, Carraway R, Carrasco A, Perez C, Jakkamsetti V, Kilgard MP. Cortical map plasticity improves learning but is not necessary for improved performance. *Neuron.* 2011; 70:121–131. [PubMed: 21482361]
- Repp BH. Sensorimotor synchronization and perception of timing: effects of music training and task experience. *Hum Mov Sci.* 2010; 29:200–213. [PubMed: 20074825]
- Repp BH, Doggett R. Tapping to a very slow beat: A comparison of musicians and non-musicians. *Music Percept.* 2007; 24:367–376.
- Russo NM, Nicol TG, Zecker SG, Hayes EA, Kraus N. Auditory training improves neural timing in the human brainstem. *Behav Brain Res.* 2005; 156:95–103. [PubMed: 15474654]
- Rust J. Genetic effects in the cortical auditory evoked potential: a twin study. *Electroencephalogr Clin Neurophysiol.* 1975; 39:321–327. [PubMed: 51715]
- Sale A, Maya Vetencourt JF, Medini P, Cenni MC, Baroncelli L, De Pasquale R, Maffei L. Environmental enrichment in adulthood promotes amblyopia recovery through a reduction of intracortical inhibition. *Nat Neurosci.* 2007; 10:679–681. [PubMed: 17468749]
- Salimpoor VN, Benovoy M, Larcher K, Dagher A, Zatorre RJ. Anatomically distinct dopamine release during anticipation and experience of peak emotion to music. *Nat Neurosci.* 2011; 14:257–262. [PubMed: 21217764]
- Salimpoor VN, van den Bosch I, Kovacevic N, McIntosh AR, Dagher A, Zatorre RJ. Interactions between the nucleus accumbens and auditory cortices predict music reward value. *Science.* 2013; 340:216–219. [PubMed: 23580531]
- Sanai N, Berger MS, Garcia-Verdugo JM, Alvarez-Buylla A. Comment on "Human neuroblasts migrate to the olfactory bulb via a lateral ventricular extension". *Science.* 2007; 318:393. author reply 393. [PubMed: 17947566]
- Sanes DH, Woolley SM. A behavioral framework to guide research on central auditory development and plasticity. *Neuron.* 2011; 72:912–929. [PubMed: 22196328]
- Sarro EC, Sanes DH. The cost and benefit of juvenile training on adult perceptual skill. *J Neurosci.* 2011; 31:5383–5391. [PubMed: 21471373]
- Schlaug G. The brain of musicians. A model for functional and structural adaptation. *Ann NY Acad Sci.* 2001; 930:281–299. [PubMed: 11458836]
- Schlaug G, Forgeard M, Zhu L, Norton A, Winner E. Training-induced neuroplasticity in young children. *Ann N Y Acad Sci.* 2009; 1169:205–208. [PubMed: 19673782]
- Schlaug G, Jancke L, Huang Y, Staiger JF, Steinmetz H. Increased corpus callosum size in musicians. *Neuropsychologia.* 1995; 33:1047–1055. [PubMed: 8524453]
- Schlaug G, Marchina S, Norton A. Evidence for plasticity in white-matter tracts of patients with chronic Broca's aphasia undergoing intense intonation-based speech therapy. *Ann N Y Acad Sci.* 2009; 1169:385–394. [PubMed: 19673813]

- Schmiedt RA, Mills JH, Boettcher FA. Age-related loss of activity of auditory-nerve fibers. *J Neurophysiol.* 1996; 76:2799–2803. [PubMed: 8899648]
- Schmithorst VJ, Wilke M. Differences in white matter architecture between musicians and non-musicians: a diffusion tensor imaging study. *Neurosci Lett.* 2002; 321:57–60. [PubMed: 11872256]
- Schneider P, Scherg M, Dosch HG, Specht HJ, Gutschalk A, Rupp A. Morphology of Heschl's gyrus reflects enhanced activation in the auditory cortex of musicians. *Nat Neurosci.* 2002; 5:688–694. [PubMed: 12068300]
- Schon D, Francois C. Musical expertise and statistical learning of musical and linguistic structures. *Front Psychol.* 2011; 2:167. [PubMed: 21811482]
- Schon D, Magne C, Besson M. The music of speech: music training facilitates pitch processing in both music and language. *Psychophysiology.* 2004; 41:341–349. [PubMed: 15102118]
- Seppanen M, Brattico E, Tervaniemi M. Practice strategies of musicians modulate neural processing and the learning of sound-patterns. *Neurobiol Learn Mem.* 2007; 87:236–247. [PubMed: 17046293]
- Seppanen M, Hamalainen J, Pesonen AK, Tervaniemi M. Music training enhances rapid neural plasticity of n1 and p2 source activation for unattended sounds. *Front Hum Neurosci.* 2012; 6:43. [PubMed: 22435057]
- Seppanen M, Pesonen AK, Tervaniemi M. Music training enhances the rapid plasticity of P3a/P3b event-related brain potentials for unattended and attended target sounds. *Atten Percept Psychophys.* 2012; 74:600–612. [PubMed: 22222306]
- Shahin A, Bosnyak DJ, Trainor LJ, Roberts LE. Enhancement of neuroplastic P2 and N1c auditory evoked potentials in musicians. *J Neurosci.* 2003; 23:5545–5552. [PubMed: 12843255]
- Shook A, Marian V, Bartolotti J, Schroeder S. Musical experience influences novel language learning. *Amer J Psychol.* 2013; 126:95–104.
- Skoe E, Kraus N. Auditory brain stem response to complex sounds: a tutorial. *Ear Hear.* 2010; 31:302–324. [PubMed: 20084007]
- Skoe E, Kraus N. A little goes a long way: how the adult brain is shaped by musical training in childhood. *J Neurosci.* 2012; 32:11507–11510. [PubMed: 22915097]
- Slevc LR, Miyake A. Individual differences in second-language proficiency: does musical ability matter? *Psychological Science.* 2006; 17:675–681. [PubMed: 16913949]
- Song JH, Skoe E, Banai K, Kraus N. Training to improve hearing speech in noise: biological mechanisms. *Cereb Cortex.* 2012; 22:1180–1190. [PubMed: 21799207]
- Song JH, Skoe E, Wong PC, Kraus N. Plasticity in the adult human auditory brainstem following short-term linguistic training. *J Cogn Neurosci.* 2008; 20:1892–1902. [PubMed: 18370594]
- Steele CJ, Bailey JA, Zatorre RJ, Penhune VB. Early musical training and white-matter plasticity in the corpus callosum: evidence for a sensitive period. *J Neurosci.* 2013; 33:1282–1290. [PubMed: 23325263]
- Stewart L, Henson R, Kampe K, Walsh V, Turner R, Frith U. Brain changes after learning to read and play music. *Neuroimage.* 2003; 20:71–83. [PubMed: 14527571]
- Strait DL, Chan K, Ashley R, Kraus N. Specialization among the specialized: Auditory brainstem function is tuned in to timbre. *Cortex.* 2012; 48:360–362. [PubMed: 21536264]
- Strait DL, Hornickel J, Kraus N. Subcortical processing of speech regularities underlies reading and music aptitude in children. *Behav Brain Funct.* 2011; 7:44. [PubMed: 22005291]
- Strait DL, Kraus N. Can you hear me now? Musical training shapes functional brain networks for selective auditory attention and hearing speech in noise. *Front Psychology.* 2011a; 2:113.
- Strait DL, Kraus N. Playing music for a smarter ear: cognitive, perceptual and neurobiological evidence. *Music Perception.* 2011b; 29:133–147. [PubMed: 22993456]
- Strait DL, Kraus N, Parbery-Clark A, Ashley R. Musical experience shapes top-down auditory mechanisms: evidence from masking and auditory attention performance. *Hear Res.* 2010; 261:22–29. [PubMed: 20018234]

- Strait DL, Kraus N, Skoe E, Ashley R. Musical experience and neural efficiency: effects of training on subcortical processing of vocal expressions of emotion. *Eur J Neurosci*. 2009; 29:661–668. [PubMed: 19222564]
- Strait DL, O'Connell S, Parbery-Clark A, Kraus N. Musicians' enhanced neural differentiation of speech sounds arises early in life: developmental evidence from ages three to thirty. *Cereb Cortex*. 2013
- Strait DL, Parbery-Clark A, Hittner E, Kraus N. Musical training during early childhood enhances the neural encoding of speech in noise. *Brain Lang*. 2012; 123:191–201. [PubMed: 23102977]
- Strait DL, Parbery-Clark A, O'Connell S, Kraus N. Biological impact of preschool music classes on processing speech in noise. *J Dev Cogn Neurosci*. (in press).
- Takesian AE, Kotak VC, Sanes DH. Presynaptic GABA(B) receptors regulate experience-dependent development of inhibitory short-term plasticity. *J Neurosci*. 2010; 30:2716–2727. [PubMed: 20164356]
- Tanaka J, Horiike Y, Matsuzaki M, Miyazaki T, Ellis-Davies GC, Kasai H. Protein synthesis and neurotrophin-dependent structural plasticity of single dendritic spines. *Science*. 2008; 319:1683–1687. [PubMed: 18309046]
- Tang YP, Shimizu E, Dube GR, Rampon C, Kerchner GA, Zhuo M, Liu G, Tsien JZ. Genetic enhancement of learning and memory in mice. *Nature*. 1999; 401:63–69. [PubMed: 10485705]
- Tang YP, Wang H, Feng R, Kyin M, Tsien JZ. Differential effects of enrichment on learning and memory function in NR2B transgenic mice. *Neuropharmacology*. 2001; 41:779–790. [PubMed: 11640933]
- Tervaniemi M, Ilvonen T, Karma K, Alho K, Naatanen R. The musical brain: brain waves reveal the neurophysiological basis of musicality in human subjects. *Neurosci Lett*. 1997; 226:1–4. [PubMed: 9153627]
- Thomson JM, Goswami U. Rhythmic processing in children with developmental dyslexia: auditory and motor rhythms link to reading and spelling. *J Physiol Paris*. 2008; 102:120–129. [PubMed: 18448317]
- Tierney AT, Kraus N. The ability to tap to a beat relates to cognitive, linguistic, and perceptual skills. *Brain Lang*. 2013; 124:225–231. [PubMed: 23400117]
- Trachtenberg JT, Chen BE, Knott GW, Feng G, Sanes JR, Welker E, Svoboda K. Long-term in vivo imaging of experience-dependent synaptic plasticity in adult cortex. *Nature*. 2002; 420:788–794. [PubMed: 12490942]
- Turner JG, Hughes LF, Caspary DM. Affects of aging on receptive fields in rat primary auditory cortex layer V neurons. *J Neurophysiol*. 2005; 94:2738–2747. [PubMed: 16000522]
- van Zuijen TL, Sussman E, Winkler I, Naatanen R, Tervaniemi M. Auditory organization of sound sequences by a temporal or numerical regularity--a mismatch negativity study comparing musicians and non-musicians. *Brain Res Cogn Brain Res*. 2005; 23:270–276. [PubMed: 15820634]
- Velho TA, Lu K, Ribeiro S, Pinaud R, Vicario D, Mello CV. Noradrenergic control of gene expression and long-term neuronal adaptation evoked by learned vocalizations in songbirds. *PLoS ONE*. 2012; 7:e36276. [PubMed: 22574146]
- Warrier CM, Abrams DA, Nicol TG, Kraus N. Inferior colliculus contributions to phase encoding of stop consonants in an animal model. *Hearing Research*. 2011; 282:108–118. [PubMed: 21945200]
- Watanabe D, Savion-Lemieux T, Penhune VB. The effect of early musical training on adult motor performance: evidence for a sensitive period in motor learning. *Exp Brain Res*. 2007; 176:332–340. [PubMed: 16896980]
- White-Schwoch T, Woodruff Carr K, Anderson S, Strait DL, Kraus N. Older adults benefit from music training early in life: Biological evidence for long-term training-driven plasticity. (under review).
- Wong PC, Skoe E, Russo NM, Dees T, Kraus N. Musical experience shapes human brainstem encoding of linguistic pitch patterns. *Nat Neurosci*. 2007; 10:420–422. [PubMed: 17351633]
- Xu J, Yu L, Cai R, Zhang J, Sun X. Early auditory enrichment with music enhances auditory discrimination learning and alters NR2B protein expression in rat auditory cortex. *Behav Brain Res*. 2009; 196:49–54. [PubMed: 18706452]

- Xu T, Yu X, Perlik AJ, Tobin WF, Zweig JA, Tennant K, Jones T, Zuo Y. Rapid formation and selective stabilization of synapses for enduring motor memories. *Nature*. 2009; 462:915–919. [PubMed: 19946267]
- Yan J, Zhang Y, Ehret G. Corticofugal shaping of frequency tuning curves in the central nucleus of the inferior colliculus of mice. *J Neurophysiol*. 2005; 93:71–83. [PubMed: 15331615]
- Yang G, Pan F, Gan WB. Stably maintained dendritic spines are associated with lifelong memories. *Nature*. 2009; 462:920–924. [PubMed: 19946265]
- Zatorre RJ, Fields RD, Johansen-Berg H. Plasticity in gray and white: neuroimaging changes in brain structure during learning. *Nat Neurosci*. 2012; 15:528–536. [PubMed: 22426254]
- Zatorre RJ, Salimpoor VN. From perception to pleasure: Music and its neural substrates. *Proc Natl Acad Sci U S A*. 2013
- Zendel BR, Alain C. Concurrent sound segregation is enhanced in musicians. *J Cogn Neurosci*. 2009; 21:1488–1498. [PubMed: 18823227]
- Zendel BR, Alain C. Musicians experience less age-related decline in central auditory processing. *Psychol Aging*. 2011; 27:410–417. [PubMed: 21910546]

- Musicians provide a model of experience-dependency in human auditory processing.
- We review neural markers of musicianship and cellular learning mechanisms identified in animal models.
- Interactive auditory enrichment during early development may prime musicians for auditory learning.

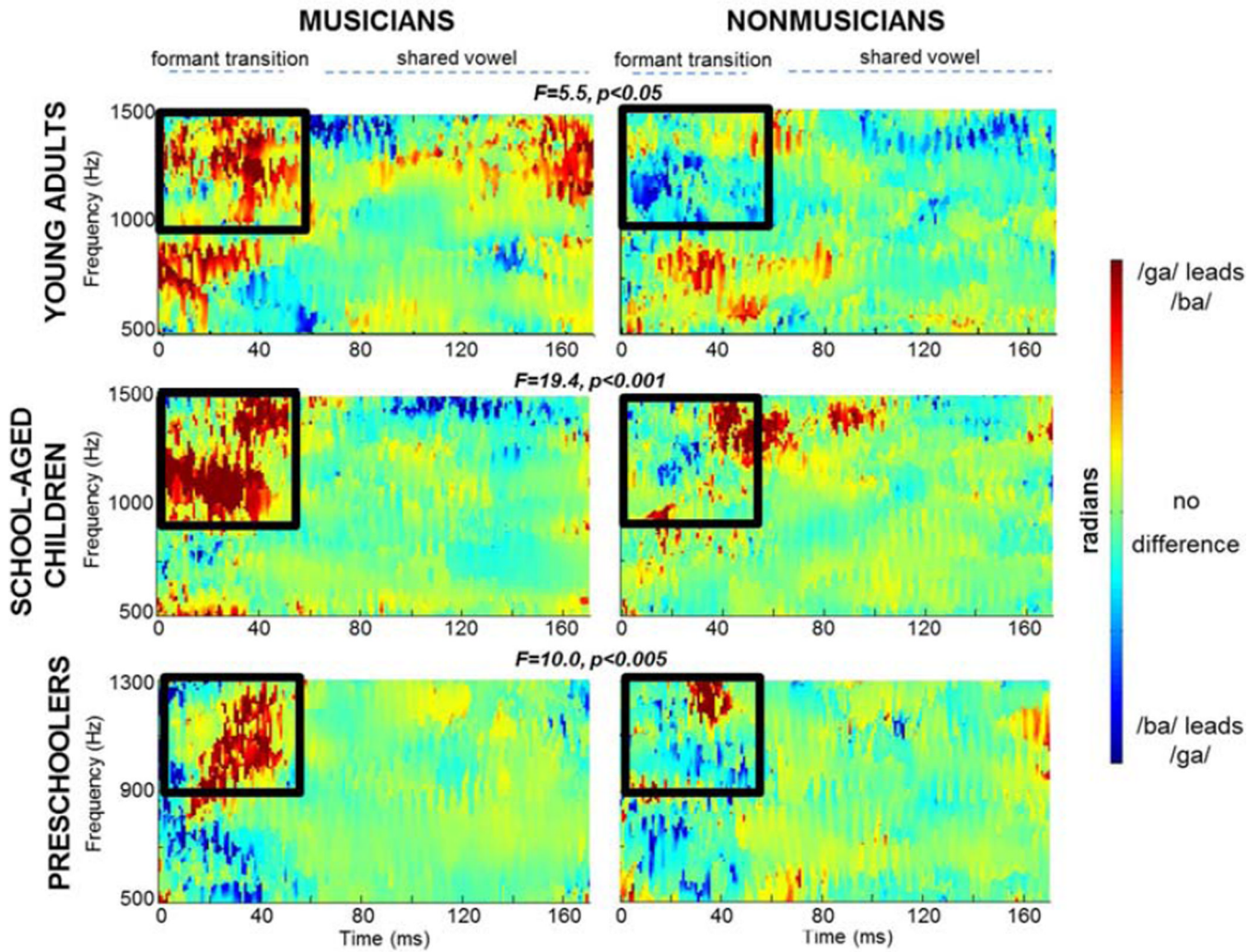


Figure 1. Musicians’ neural enhancements to speech build up over the life span
 Average auditory brainstem responses to the speech sound /da/ in musicians and nonmusicians in each of four age groups. Responses were recorded using three scalp-electrodes (A) in quiet and noise and are presented in both temporal and spectral domains (B). ** $p < 0.01$ Adapted from Parbery-Clark, et al., 2012; Parbery-Clark, Skoe, Lam, et al., 2009; Strait, Parbery-Clark, et al., 2012; and Strait, et al., in press.

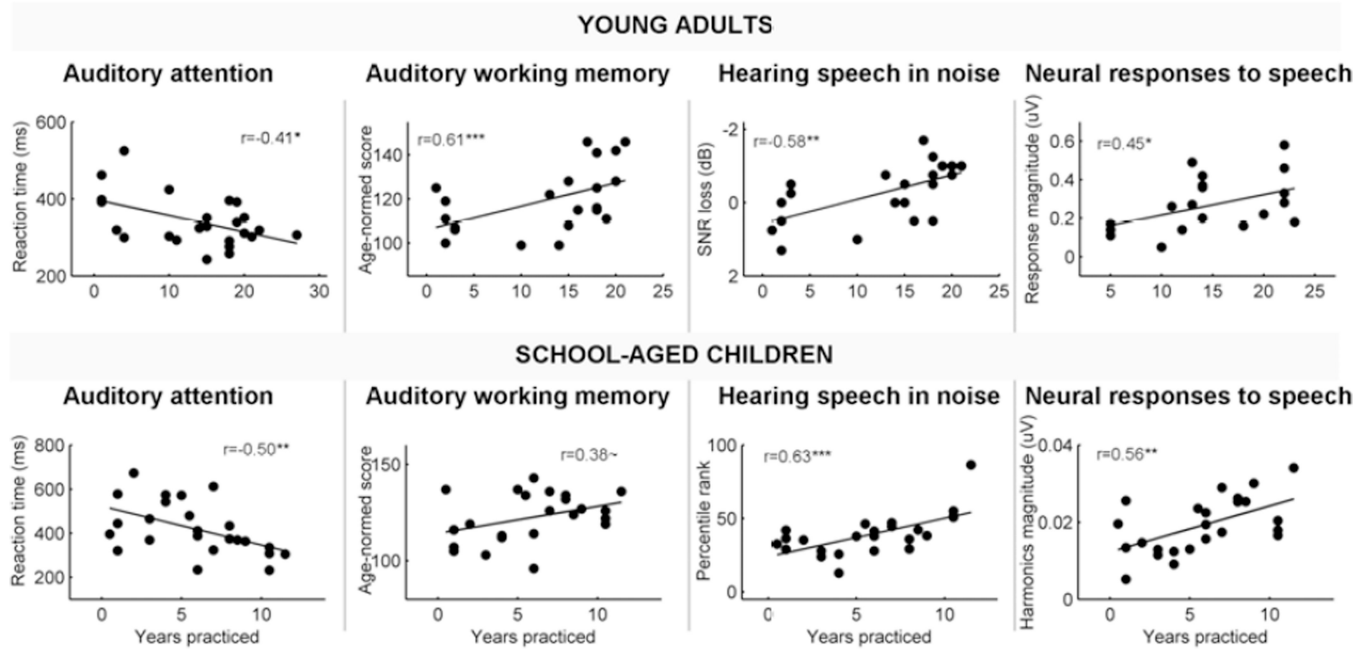


Figure 2. Musicians across the life span have faster neural responses than nonmusicians to the formant transition of the speech syllable /da/
 Bar graphs depict average latencies for the first consistent peak in the response to the formant transition region of /da/ in quiet and noise conditions (occurring at ~43 ms post-stimulus onset). Error bars depict one standard error. *Adapted from* Parbery-Clark, et al., 2012; Parbery-Clark, Skoe, Lam, et al., 2009; Strait, Parbery-Clark, et al., 2012; and Strait, et al., in press. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

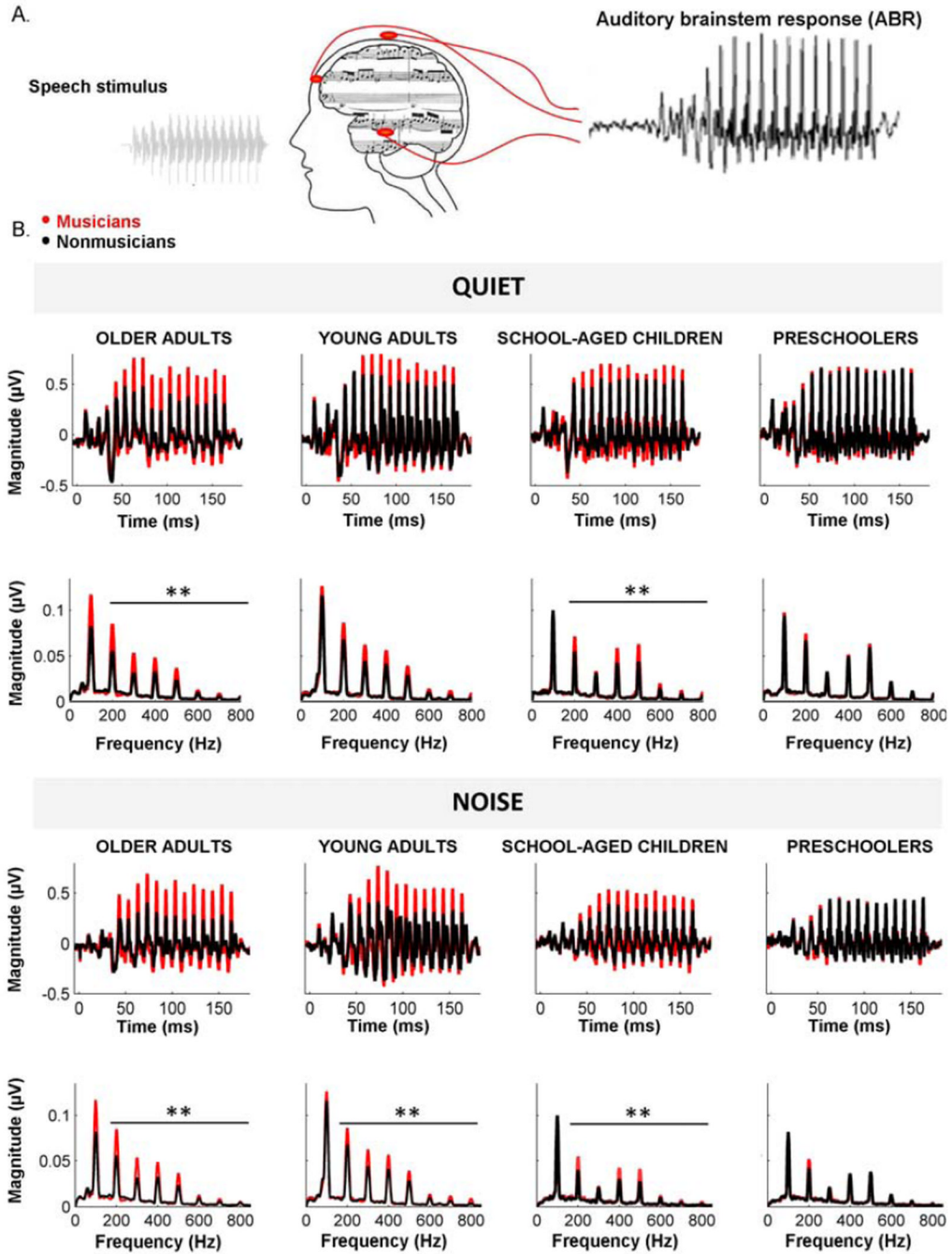


Figure 3. Musicians have more distinct neural responses to contrasting speech sounds than nonmusicians across the life span

Cross-phaseograms indicate phase differences between responses to /ga/ and /ba/ as a function of frequency over time. Phase shift in radians is indicated by color, with warm colors indicating phase-lead and cool colors indicating phase-lag. Musicians have greater phase shifts than nonmusicians in response to the formant transition, indicating a phase-lead in the response to /ga/. The acoustics of the sustained vowel are identical between stimuli and responses show an appropriate lack of phase shift. *Adapted from Strait, et al, 2013.*

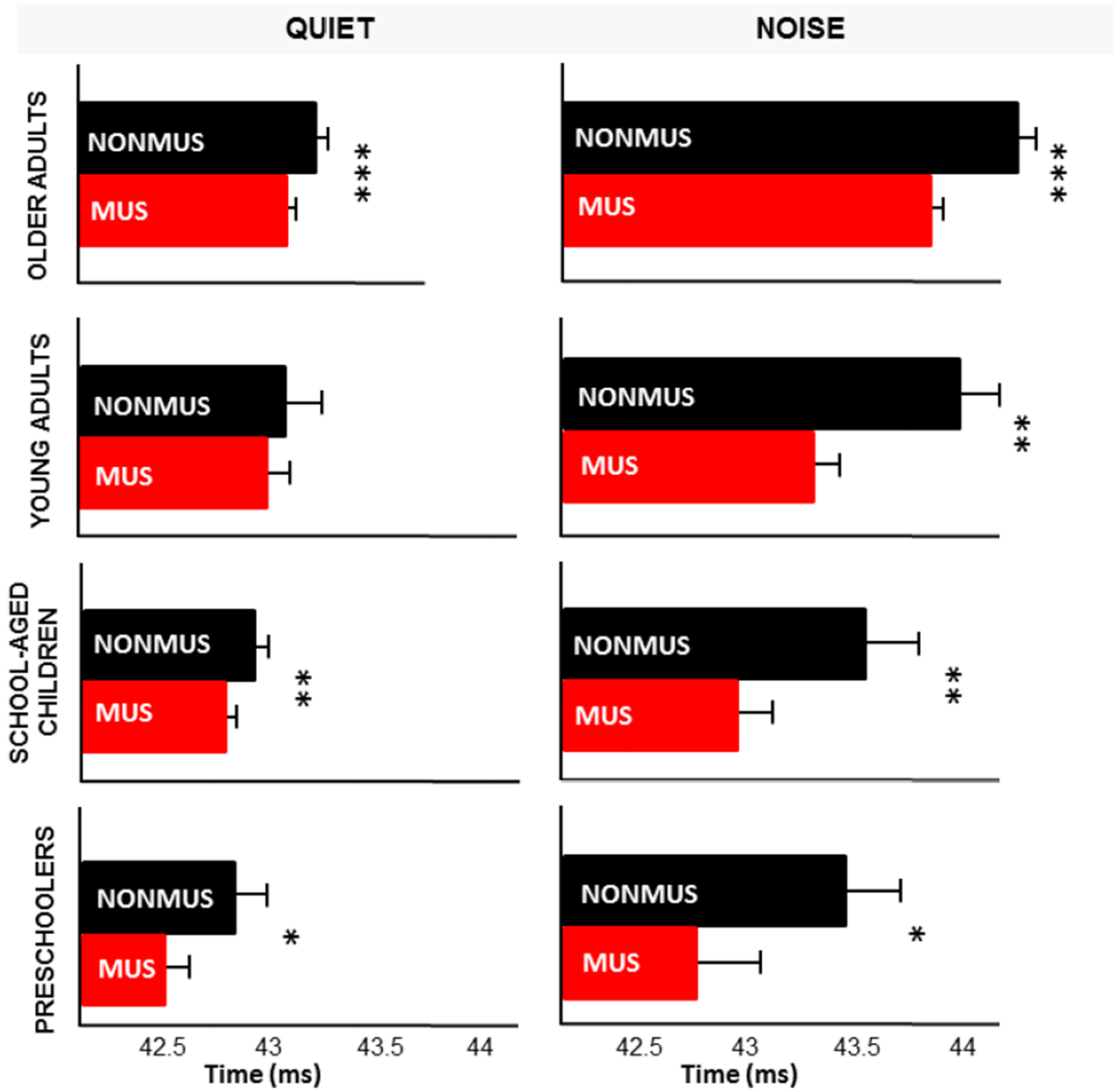


Figure 4. Auditory abilities and neural responses to speech relate to extent of music training in young adults and children
 ~p<0.1, *p<0.05, **p<0.01, ***p<0.001