



Contents lists available at ScienceDirect

Hearing Research

journal homepage: www.elsevier.com/locate/heares

The layering of auditory experiences in driving experience-dependent subcortical plasticity

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ARTICLE INFO

Article history:

Received 30 September 2013

Received in revised form

26 December 2013

Accepted 7 January 2014

Available online xxx

ABSTRACT

In this review article, we focus on recent studies of experiential influences on brainstem function. Using these studies as scaffolding, we then lay the initial groundwork for the *Layering Hypothesis*, which explicates how experiences combine to shape subcortical auditory function. Our hypothesis builds on the idea that the subcortical auditory system reflects the collective auditory experiences of an individual, including interactions with sound that occurred in the distant past. Our goal for this article is to begin to shift the field away from examining the effect of single experiences to examining how different auditory experiences layer or superimpose on each other.

This article is part of a Special Issue entitled <Annual Reviews 2014>.

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1. Introduction

The human auditory brainstem is sensitive to many different experiences, ranging from long-term musical training (reviewed in [Kraus and Chandrasekaran, 2010](#)) to more limited experiences occurring over the course of a few hours ([Skoe and Kraus, 2010a](#)). However, less is known about how different types of experiences interact to influence sensory processing in the auditory brainstem. Following a review of the current literature on experience-dependent auditory brainstem plasticity in Sections 3–13, we present the *Layering Hypothesis*. Our hypothesis diverges from previous models ([Kraus and Chandrasekaran, 2010](#); [Krishnan and Gandour, 2009](#); [Patel, 2011](#)) by seeking to explain how multiple experiences, occurring concurrently or consecutively, combine to guide the manner and mechanisms by which the auditory brainstem represents sound. We posit that auditory function is informed

by the collective set of auditory experiences that an individual is exposed to or partakes in throughout life, resulting in a ‘fingerprint’ that reflects an individual’s unique set of experiences. This fingerprint captures not only the extent and nature of each type of experience but also the age and the overall metaplasticity of the system. The layering of experiences may explain individual differences in auditory function that can be seen even in typically-developing populations ([Chandrasekaran et al., 2012](#); [Hairston et al., 2013](#); [Skoe et al., 2013b](#)). Understanding how experiences combine to shape auditory function is an important first step in designing optimal and individualized training programs ([Chandrasekaran et al., 2013a](#); [Perrachione et al., 2011](#)). This approach can be likened to the concept of ‘personalized medicine’, which is considered one of the most important goals in the medical sciences ([Hamburg and Collins, 2010](#)).

This article focuses on experience-dependent plasticity observed in the human auditory brainstem. Until recently, the auditory brainstem had been viewed as a nonplastic site of sensory processing that unlike the auditory cortex did not undergo experience-dependent changes. However, more recent studies focusing on these evolutionarily older structures have revealed that subcortical auditory structures, like cortical ones, are malleable throughout life. Although our spotlight here is on subcortical

Abbreviations: ABR, auditory brainstem response; BOLD, blood-oxygen level dependent; FFR, frequency following) response; IC, inferior colliculus; MOC, medial olivary cochlear; RCT, randomized control training

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<http://dx.doi.org/10.1016/j.heares.2014.01.002>

Please cite this article in press as: Skoe, E., Chandrasekaran, B., The layering of auditory experiences in driving experience-dependent subcortical plasticity, *Hearing Research* (2014), <http://dx.doi.org/10.1016/j.heares.2014.01.002>

structures, the central tenets of the *Layering Hypothesis* can be applied to the auditory system as a whole, not just the subcortical branch. Indeed, there is evidence for the layering of experiences from cortical neuroimaging techniques and also behavioral paradigms (e.g., Bregman et al., 2012; Engel de Abreu et al., 2012; Slevc and Miyake, 2006; Wong et al., 2011b). However, because of the fideliu s manner in which specific sound features are captured by the auditory brainstem, this affords greater transparency (compared to cortical responses) into how different auditory experiences have selectively altered the way in which different components of the auditory signal are encoded in the brain.

2. Definition of experience-dependent plasticity

In crafting our operational definition of experience-dependent plasticity, we begin with the notion that our environment is composed of a series of auditory events that have varying durations and behavioral relevance, with some occurring transiently and others occurring on a more regular basis. We then define auditory experience, simply, as the exposure to an auditory event. By this definition, auditory experience could either be the result of passive exposure to sound or it could involve more active (behaviorally-relevant) interactions with sound that engage other modalities, such as vision and somatosensation. This article will survey what we currently know about how the auditory brainstem is changed by *repeated* experience with sound in both unimodal and multimodal settings. This is, however, not to downplay the role of transient events, such as an intense noise or head trauma, and their potential to change auditory brain function. We use the term ‘experience-dependent plasticity’ to refer to changes in neural circuits and synapses occurring throughout life that result from the environment and the specific ways in which the individual interacts with that environment.

Examinations of experience-dependent plasticity in the auditory system have often examined auditory system development under radically altered environmental conditions (Chang and Merzenich, 2003; Oliver et al., 2011) or described the extent to which the auditory system is modified by sensory deprivation (Tillein et al., 2012) or the reversal of deprivation (Kral and Sharma, 2012). This article instead focuses on human subcortical auditory system plasticity that results from natural variations in language exposure, current and past musical training, and abbreviated yet intensive auditory training.

3. How do we measure experience-dependent plasticity within the subcortical auditory system?

In animal models, experience-dependent plasticity has been examined in the subcortical auditory system using invasive methods (Dean et al., 2005; Luo et al., 2008; Suga et al., 2002). In humans, the two most common (non-invasive) experimental designs for studying experience-dependent plasticity are (1) a descriptive-comparative approach that compares two or more groups of participants who have distinctly different auditory experiences, but are equivalent in other relevant measures. This approach has generally been used to examine lifelong experiences related to language (a cross-language design) or music (reviewed in Krishnan et al., 2009; Strait and Kraus, 2013); and (2) a causality or a causality-descriptive approach that measures subcortical activity before or after the participant undergoes a prescribed auditory experience. In a causality-descriptive approach, a comparison is made to a group that does not undergo the auditory experience or undergoes a different type of auditory experience. For the experimental group, the prescribed experience could be a laboratory-designed training protocol where participants learn a new sound

contrast or artificial language (Carcagno and Plack, 2011; Chandrasekaran et al., 2012; Song et al., 2012), it could involve auditory remediation/training performed in school (Hornickel et al., 2012; Tierney et al., 2013) or at home (Anderson et al., 2013a; Song et al., 2012), and/or it could involve augmenting the acoustic input in a specific manner (Hornickel et al., 2013; Munro et al., 2007).

In humans, there are a variety of methods for measuring subcortical function and the plasticity that results from different types of auditory experiences. For example, the efferent pathway between the auditory brainstem and cochlea, called the medial olivocochlear (MOC) system, can be targeted by presenting broadband noise to the contralateral ear. The activation of the MOC bundle is then registered as a change in the otoacoustic emission (reviewed in Guinan, 2010). Using this methodology, de Boer and Thornton reported increases in MOCB activity following a consonant–vowel phoneme-in-noise discrimination task (de Boer and Thornton, 2008; de Boer et al., 2012), lending further support to the idea that efferent function undergoes experience-dependent plasticity (Perrot et al., 1999). Positron emission tomography and functional magnetic resonance imaging are other approaches for studying changes in auditory midbrain (inferior colliculus) function (Rinne et al., 2008; Yu et al., 2009; Zatorre and Halpern, 1996), and recent advances in high resolution imaging and network analysis (Deshpande et al., 2009; Ress and Chandrasekaran, 2013) may lead to greater use of these method for studying experience-dependent subcortical plasticity in humans.

Subcortical auditory function can also be appraised using scalp-electrodes that detect electrical potentials generated by ensembles of intricately-connected subcortical nuclei belonging to the efferent and afferent auditory systems, including the cochlear nucleus, superior olive, lateral lemniscus, and inferior colliculus. Synchronous activity from these populations of neurons is responsive to transient and sustained features of auditory stimuli (Chandrasekaran and Kraus, 2010; Marsh et al., 1975; Moushegian et al., 1973; Skoe and Kraus, 2010b). This response, known as the auditory brainstem response (ABR), provides a means for objectively and non-invasively studying the neural encoding of sound. This review will spotlight experience-dependent plasticity as indexed by the ABR to speech or other sounds commonly encountered in the natural world. For the purposes of this review, we use ‘ABR’ to refer to both transient and phase-locked responses produced within the upper brainstem (lateral lemniscus, inferior colliculus).

One of the remarkable features of the ABR is that it captures the acoustic features of the sound stimulus (Fig. 1), making it possible to observe how the neural representation of specific sound features, such as the fundamental frequency, harmonics, and temporal envelope, change as a function of experience (Krishnan et al., 2005; Marmel et al., 2011; Parbery-Clark et al., 2009; Strait et al., 2012a). By comparison, functional magnetic resonance imaging (due to the temporal limitations of the hemodynamic response) and cortical-evoked electrophysiological responses (due to the more abstract response function of auditory cortical neurons) provide a more abstract representation of the evoking stimulus.

4. Experience is the engine that guides auditory function

The experience-dependent nature of the auditory brainstem and midbrain are not surprising given that these structures are always ‘on’. Whether we are asleep, zoned out in front of the television, or under anesthesia, the auditory soundscape continues to be processed. Not surprisingly, subcortical auditory structures show some of the highest metabolic activity in the brain (Sokoloff, 1977). This steadfast quality has made the ABR (in its many variants) so attractive to medical professionals in the business of

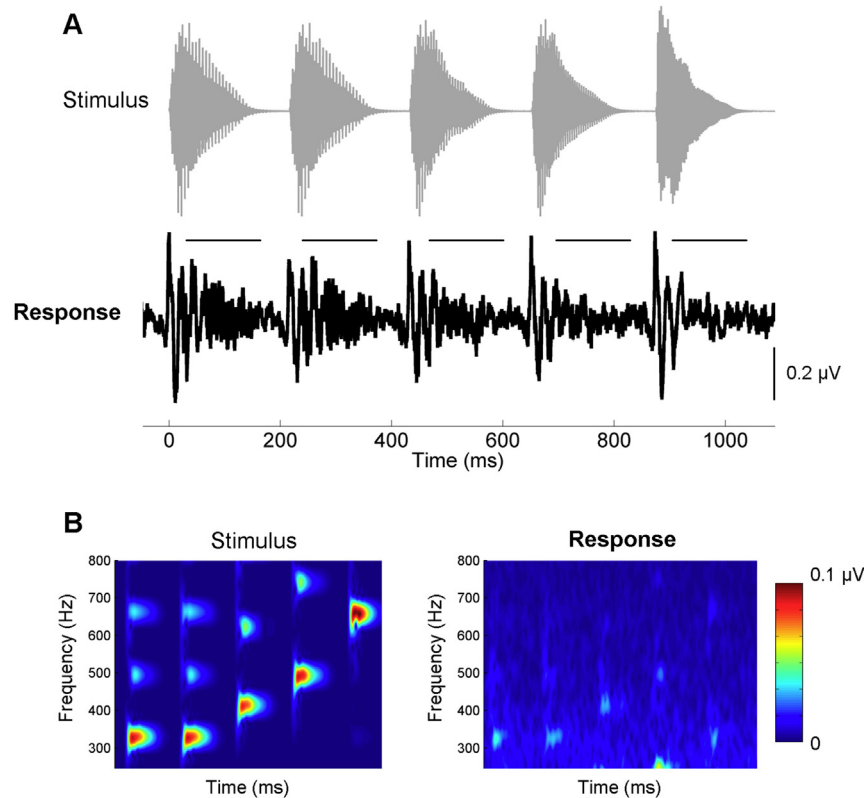


Fig. 1. The auditory brainstem response captures many of the temporal (A) and spectral (B) features of the stimulus (top). For illustration, the response to a 5-note melody is plotted (E3-E3-G#3-B3-E4). (A) The time-domain rendering of the stimulus (top) and response (bottom). Horizontal bars identify the frequency following response (FFR), the neural synchronization to the periodic aspects of each note. (B) The precision of this synchronization is more clearly seen in panel B, where the stimulus (left) and response (right) are plotted as spectrograms. Phaselocking is observed to each note at 330, 330, 416, 494, 660 Hz, respectively. Modified from Skoe and Kraus, *PLoS ONE* 2010.

measuring the health and function of the auditory system (audiologists, otolaryngologists). This quality, we argue, is also what makes the auditory brainstem and midbrain so susceptible to experiential effects, including being highly sensitive to the context in which and the frequency with which a sound is presented (Chandrasekaran et al., 2009; Gnanateja et al., 2013; Skoe et al., 2013b,c; Slabu et al., 2012). Auditory experience can, change both how the brainstem indexes the physical features of sounds (e.g., Song et al., 2012) and how stimulus probability is encoded (Skoe et al., 2013c), with the outcome thought to be either facilitative or detrimental to auditory learning/processing. In some cases, lifelong experience appears to be a heuristic that the brain uses to spotlight important sounds in the environment (Kraus and Chandrasekaran, 2010; Krizman et al., 2012). In extreme cases, altered experiences due to dysfunctional cochlear function, or auditory impoverishment, can result in hyperactivity within the auditory system that interferes with signal transmission (Anderson et al., 2013b; Engineer et al., 2013; Gu et al., 2012; Skoe et al., 2013a).

5. Mechanisms of experience-dependent plasticity within the subcortical auditory system

The neural mechanisms of experience-dependent plasticity are difficult to study in humans and generally require more invasive techniques that can only be achieved in animal models. As revealed through animal models, experience-dependent plasticity can arise through a number of avenues as the result of either (1) feedback from the cortex (top-down corticofugal modulation), (2) changes initiated locally within brainstem circuitry, or (3) through a

combination of the two (reviewed in Chandrasekaran et al., 2013b; Krishnan et al., 2012).

The corticofugal pathway serves as the messenger, or conduit, through which the primary and secondary auditory cortices can issue instructions to subcortical regions. Depending on the stimulus conditions, and the demands of the situation, the message may be to either increase or reduce the gain of the response to the target sound or inhibit the background noise (Luo et al., 2008). When encountering a highly-repetitive soundscape (Dean et al., 2008; Malmierca et al., 2009; Perez-Gonzalez et al., 2005), the initial message may be to turn down the gain (i.e., adapt). However, through continued exposure or by virtue of having prior experiences where the repeating sound was behaviorally-relevant, the cortex may egocentrically boost the subcortical response (Skoe et al., 2013b; Suga et al., 2002). Also, because the same conditions may not be equally taxing or familiar for all individuals, this might lead to idiosyncratic differences in the message issued by the cortex and/or idiosyncratic differences in how top-down modulation is expressed (Perrot et al., 1999; Skoe et al., 2013b).

We currently do not have the ability to effectively isolate local- from top-down mechanisms. That is, we are lacking the ability to isolate the activity of the corticofugal activity or to measure the ABR in the complete absence of corticofugal effects. The advent of such technology would greatly expand our ability to understand the genesis of experience-dependent plasticity in humans.

6. Auditory enrichment: the gateway to expertise

Much of what we know about experience-dependent auditory brainstem plasticity is based on populations considered as 'experts'.

We define an auditory expert to be someone who through his/her experience is able to discern details in the acoustics of sound that others (who have the same level of audibility) would not register. In this way, we view auditory experience as the necessary gateway through which auditory expertise is acquired. Expertise is also something that by definition cannot be acquired instantly but requires time to develop and mature. With respect to auditory subcortical plasticity, the expert systems that have received the most attention thus far are musicians (Fig. 2), tonal language speakers (processing tonal sounds or non-speech sounds that approximate tones), and bilinguals. Recently, this set of auditory expert systems has been expanded to include the congenitally blind (Jafari and Asadmalayeri, 2013). However, there are other populations of highly-skilled listeners who have not been studied by auditory neuroscientists but who have likewise developed expertise through repeated and continued exposure to, and interaction with, specific sound sets. These include the car mechanic who can tell whether a car is out of alignment by how all of the parts harmonize together and also the naturalist who hears the cracking and booming of the ice on the lake in late spring and recognizes instantly whether it is a sign of danger or the normal dynamics of ice.

Because there have been several recent comprehensive reviews devoted specifically to experience-dependent auditory subcortical changes (Chandrasekaran et al., 2013b; Krishnan et al., 2009; Strait and Kraus, 2013), we keep this section brief and cover what we consider to be the highlights.

6.1. Musicians

Through routine musical practice, often over the course of many years, musicians gain extensive experience manipulating sound, fine-tuning auditory output based on multisensory cues, and hearing a variety of sounds and sound combinations (Patel, 2013). This is the case for classically-trained musicians as well as those trained through less traditional methods, and it applies no matter what the primary instrument might be. Because of the time commitment involved in mastering an instrument, and the ways in which music activates the neural reward system, it is perhaps not surprising that musical training produces such widespread plasticity across sensory, motor, and cognitive domains (Herholz and Zatorre, 2012).

The first studies of auditory subcortical plasticity in musicians were published in 2007 (Musacchia et al., 2007; Wong et al.,

2007b). In the short time since then, this area has grown exponentially. By our count, the number of publications in this area now numbers upwards of 50 (including review articles), with more studies continuing to emerge each month. From this ever-growing body of research we have learned that musical-training (1) intensifies audiovisual processing of speech and music (Musacchia et al., 2007) (Fig. 2), (2) fine tunes the response to the instrument of specialization (Strait et al., 2012a), (3) produces more efficient representation of sounds with a high emotional valence (Strait et al., 2009), (4) heightens the contrast between speech sounds (Parbery-Clark et al., 2012a; Strait et al., 2013b), (5) enhances the representation of highly-predictable sounds (Parbery-Clark et al., 2012a; Strait et al., 2013b), (6) augments how musical intervals are represented (Bidelman and Krishnan, 2009; Lee et al., 2009), (7) enhances the representation of continuous pitch contours (Bidelman et al., 2011b; Wong et al., 2007b), (8) leads to more resilient neural processing in reverberant and noisy conditions (Bidelman and Krishnan, 2010; Parbery-Clark et al., 2009; Strait et al., 2013a), (9) shapes binaural processing (Parbery-Clark et al., 2013b), and (10) interacts with developmental and aging processes (Parbery-Clark et al., 2012b; Skoe and Kraus, 2013). The effects of musical training have been shown to take effect with just a few years of lessons (Skoe and Kraus, 2012; Tierney et al., 2013; White-Schwoch et al., 2013) and are evident in very young musicians (3 year olds) (Skoe and Kraus, 2013; Strait et al., 2012b, 2013a,b). In addition, middle-aged musicians show less age-related changes in ABR latency compared to age-matched peers, suggesting that musical training might counteract the effects of aging (Anderson and Kraus, 2013; Parbery-Clark et al., 2012b). It has been argued that lifelong musical experience may serve to fortify inhibitory neural networks, which based on animal models are known to decline with age (Caspary et al., 2008) but can be recovered through auditory training (de Villiers-Sidani et al., 2010).

While our understanding of music-related auditory subcortical plasticity has grown in recent years, currently all of the published work has focused on musicians who started as children or adolescents. Whether these same effects are observed when musical training begins later in life is unknown. Given that music is a skill that can be acquired at any age (although to varying levels of success) and that it may offset aging processes (Anderson and Kraus, 2013; Parbery-Clark et al., 2012b), we view this as an important area for future investigation.

6.2. Native language

Through the process of learning one's native language, each of us becomes an expert of our mother tongue, allowing us to hear acoustic contrasts that speakers of other languages overlook. Krishnan and colleagues were the first to demonstrate that this kind of auditory expertise imprints upon auditory subcortical processing (Krishnan et al., 2005). This observation emerged from their work in speakers of tonal language. In tonal languages, pitch changes within a syllable can change the meaning of a word. For example, in Thai, which has five lexical tones, when 'mai' is spoken with a low tone it means 'to burn' but with a falling tone it denotes 'to be modern or fresh', a completely different word. Acoustically, these pitch changes are primarily conveyed by changes in the fundamental frequency of the utterance (Howie, 1976). Through a series of studies in young adults, Krishnan and colleagues have demonstrated that ABRs from tonal language speakers follow the tonal contour of native-contours more faithfully than non-native speakers. In addition, this increased sensitivity has been shown to generalize to non-native speech and musical contours that include native-like features (Bidelman et al., 2011a; Krishnan et al., 2009; Swaminathan et al., 2008), and to be preserved even when the

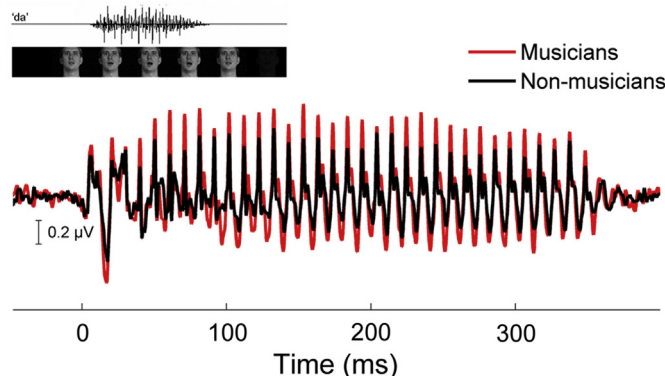


Fig. 2. Example of experience-dependent plasticity in musicians. Grand average auditory brainstem responses to an audiovisual presentation of a 350-ms speech syllable (top) for young adult musician (red) and non-musician (black) groups. Amplitude differences between the groups are evident over the entire response waveform. Modified from Musacchia, Sams, Skoe, and Kraus, Proceedings of the National Academy of Sciences of the USA 2007.

stimulus acoustics are presented in a non-speech context (e.g., by using iterative-ripple noise homologs of Mandarin tone categories) (Krishnan et al., 2010b; Swaminathan et al., 2008).

These enhancements to subcortical auditory function are theorized to be the outcome of tonal language speaker's extensive experience with curvilinear pitch contours within their native language. To begin to understand the developmental timeline over which such experience-dependent enhancements emerge, Jeng and colleagues compared ABRs from neonates and adults in China and the United States (Jeng et al., 2011). Consistent with Krishnan and colleague's work, they found that pitch tracking differed between Chinese- and English-speaking adults. However, neonates from these two countries did not differ in their ABR pitch tracking, suggesting that language-dependent changes emerge over time, presumably requiring sufficient input from and interaction with one's native language. Because discrimination of non-native contrasts declines between 9 and 12 months of age in full-term infants (Rivera-Gaxiola et al., 2005), this raises the possibility that ABR differences between adult tonal and non-tonal languages reflect the enhancement of complex pitch features in the native speakers *but* potentially *also* a decrease in sensitivity in the non-native speakers.

Although the literature on speech-ABRs has included speakers of different languages, including English (e.g., Chandrasekaran et al., 2009), French (Akhoun et al., 2008), Catalan (Slabu et al., 2012), Spanish (Krizman et al., 2012; Slabu et al., 2012), Greek (Kouni et al., 2013), Persian (Jafari and Asadmalayeri, 2013) and Hindi (Gnanateja et al., 2013), to the best of our knowledge the only cross-language comparisons outside of English vs. tonal languages (Thai, Vietnamese, Mandarin, Cantonese) has been Hebrew vs. Arabic (Karawani and Banai, 2010). For native speakers of these two Semitic languages, Karawani and Banai found no brainstem processing differences for a short syllable /da/ (Karawani and Banai, 2010). However, the lack of difference may have been because the two languages are related or because, more likely, this stimulus did not tap into underlying differences in ABRs between speakers of Hebrew and Arabic. Thus, in addition to having an incomplete understanding of how these language-specific effects emerge and change throughout development, very little is currently known about how different languages and different language features affect auditory subcortical processes. How phonemic categories might influence subcortical processing of speech is also currently unclear (Bidelman et al., 2013; Slabu et al., 2012). There is, therefore, a distinct need to study responses to phonetic inventories from a wide variety of languages.

6.3. Bilinguals

If one's native language can affect sound processing in the auditory brainstem, then what is the effect of growing up speaking two languages or learning a second language later in life? To date, this question has only been addressed by comparing Spanish–English adolescent bilinguals to age- and demographically-matched English monolinguals (Krizman et al., 2014, 2012). Based on this sample population, it appears that early exposure to multiple languages strengthens how the brainstem represents auditory signals. Krizman et al. (2014) report that speech-evoked ABRs are more stable in Spanish–English bilinguals relative to their monolingual peers who show more fluctuations in ABR morphology over the course of the recording. This enhanced stability may allow bilinguals to more effectively extract the acoustic features of the auditory signal in both quiet and noisy backgrounds (Krizman et al., in 2014, 2012). Among the bilinguals, those with greater language proficiency have higher ABR stability, which supports the argument that sensory processing is being changed over the course of

acquiring and mastering two languages. In addition, the link between attentional abilities and ABRs in the bilingual group but not the monolinguals, also suggests that bilingual experience binds together sensory and cognitive circuits. However, whether or not these findings generalize to all bilinguals, or are specific to Spanish–English bilinguals, remains an unanswered question.

7. Multimodal experiences with sound

In natural environments, auditory signals are often synched with other sensory cues, such as the movement of the lips during speech production or the rhythmic timekeeping of the orchestra conductor's arm movements. There is escalating evidence from animal models (reviewed in Gruters and Groh, 2012) and a small yet growing body of evidence from humans (Musacchia et al., 2006, 2007; Tierney and Kraus, 2013), that the inferior colliculus, a primary generator of the ABR to complex sounds, is involved in multisensory processing. For example, Musacchia and colleagues showed that concurrent visual information modulates ABRs to complex sounds, but that visual information when presented without auditory input does not produce an ABR (Musacchia et al., 2006, 2007). More recent research in humans is also further suggesting that the auditory subcortex is linked to other sensory modalities, as seen by (1) correlations between ABRs and visual (Krizman et al., 2012) and motor abilities (Tierney and Kraus, 2013) and (2) by evidence that the lack of audiovisual information changes how auditory system represents sound subcortically (Jafari and Asadmalayeri, 2013). It has also been argued that repeated engagement of multisensory processes, through musical training for example, may drive experience-dependent subcortical auditory plasticity to levels beyond what might occur if multisensory information were decoupled or if auditory information were presented in isolation (Barrett et al., 2013; Musacchia et al., 2007; Patel, 2011). However, more work in this area is needed — including expanding beyond musicians to other populations such as dancers or stutters — to appreciate the full extent to which the human subcortical auditory system might be influenced by different multimodal experiences.

8. All experiences are not created equal

Auditory experience comes in many forms, those that can be construed as positive, and others that are pose more negative for the auditory system. The research we have reviewed thus far has examined the impact of beneficial experiences, using musicians and bilinguals, as models for environmental enrichment. Now we turn to the question of how auditory impoverishment — a reduction in quality and quantity of auditory input — affects auditory subcortical processing. In this section we focus on two populations: hearing impaired older adults and socioeconomically-impoverished adolescents.

8.1. Hearing loss

In the United States, roughly 1 in 5 individuals 12 years and older have some level of hearing loss, with the incidence increasing with age (Lin et al., 2011). This deprivation of auditory input, resulting from loss of peripheral auditory function, induces changes in central auditory processing in both subcortical and cortical auditory structures that emerge over time (Anderson et al., 2013b; Bledsoe et al., 1995). In cases of unilateral deafness, the effects of deprivation on the ABR are not specific to the deaf ear but also emerge when probing the unaffected ear (Gordon et al., 2011; Musser, 2010).

Anderson and Kraus (2013) recently reported that presbycusis (age-related hearing loss) affects how speech cues are represented, leading to an over representation, i.e., an enhancement, of envelope cues (Anderson et al., 2013b). As a consequence of presbycusis, fine structure cues in the speech signal become dwarfed by the augmentation of these envelope cues. This distortion of the speech signal is argued to play a part in reduced perceptual abilities in noise and changes in loudness experienced by individuals with sensorineural hearing loss.

The Anderson et al. study emphasizes an important point: neural enhancements, as reflected by ABRs, are not necessarily beneficial to an individual. In some cases, even in cases of hearing loss (Parbery-Clark et al., 2013a), experience-dependent enhancements of the envelope may promote auditory processing, as seen in lifelong musicians (Parbery-Clark et al., 2013a; Strait et al., 2012a; Wong et al., 2007b) and in individuals who have undergone intensive auditory training (Chandrasekaran et al., 2012; Song et al., 2008, 2012). However, especially in the case of auditory impoverishment (occurring in the absence of other forms of auditory enrichment), the same kind of change to the ABR may be maladaptive or be potentially indicative of a disordered system (Gu et al., 2012). In addition, there is evidence to suggest that aging may shift which features of the ABR are most closely connected to cognitive abilities (Shinn-Cunningham et al., 2013). Thus, because the ABR captures, within a single snapshot, many simultaneously-occurring neural processes (Kraus and Nicol, 2014), examining a single component of the response in isolation may lead to false conclusions, especially if a comprehensive subject history is not obtained and other measures of auditory and cognitive function are not administered. Also, because the ABR is a far-field response, two studies may give superficially-similar results, but in fact reflect very different underlying mechanisms that just happen to manifest similarly in the ABR. The outcomes of the Anderson et al., study thus underscore the importance of factoring in how neuroplastic changes affect how other auditory cues are being represented and it also emphasizes the need to develop techniques to disambiguate different neural mechanisms and underlying pathologies via non-invasive methods.

8.2. Low socioeconomic status (SES)

In humans, studies of auditory impoverishment have historically focused on the effects of deafness. However, auditory impoverishment can occur even when peripheral auditory function is normal if the auditory environment is lacking structured, complex auditory input. For a classic example of this from the animal literature, see Chang and Merzenich 2003, in which animals who were exposed in a controlled laboratory environment to only white noise from birth showed abnormal auditory development (Chang and Merzenich, 2003). Examples of auditory impoverishment can also be found in the natural world. Children from socioeconomically-disadvantaged families are one such example. Compared to their more privileged peers, low-SES children tend to hear fewer words and less complex linguistic stimulation from their caregivers, in addition to facing greater exposure to background noise and other toxins that can impede auditory development (reviewed in Bradley and Corwyn, 2002; Evans, 2004). Skoe and colleagues have recently shown that the cocktail of environmental impoverishment associated with low-SES negatively affects how the auditory system represents sound, as seen by ABRs that are noisier, more variable, and in which the input signal is represented less faithfully (Skoe et al., 2013a). This increased variability in how the brain captures auditory information from the environment is hypothesized to compromise the interaction between sensory and cognitive systems, leading to the disparities in cognitive abilities

that exist between high- and low-SES children (reviewed in Lipina and Posner, 2012).

9. Limitations of the descriptive comparative approach

The major limitation of the descriptive comparative approach is that directional causality cannot be established. So while lifelong experience, in the form of auditory enrichment or auditory impoverishment, may in fact be driving subcortical plasticity, because measurements are not taken before the experience begins, this raises the possibility that differences reflect in-born or pre-existing differences. In addition, the groups being compared may differ in other ways other than the experience. For example, musicians differ from non-musicians on a number of other domains unrelated to music (Merrett et al., 2013). Therefore, longitudinal and randomized control-training (RCT) approaches provide the best evidence for experience-dependent plasticity. A handful of studies of subcortical plasticity have taken this approach (Anderson et al., 2013a; Carcagno and Plack, 2011; Skoe et al., 2013c; Song et al., 2012).

Carcagno and Plack were the first to use an RCT approach to demonstrate that brainstem pitch-tracking can improve with experience (Carcagno and Plack, 2011). In this study, participants were randomly assigned to either a trained or control group. Baseline ABR measurements were taken at the outset of the experiment. When re-tested after roughly 4 weeks, ABR pitch tracking was more precise in the group who underwent pitch discrimination training, whereas pitch tracking was unchanged from baseline in the control group. This study, combined with Skoe et al. (2013c), help to validate the idea that that heightened pitch tracking abilities in native tonal language speakers result from language experience and not genetic factors.

Longitudinal designs have also proven useful in studying the emergence of music-related neuroplasticity in the developing auditory system (Strait et al., 2013a; Tierney et al., 2013). It is well known that background noise has a disruptive effect on auditory processing, as seen by delayed response latencies and reduced amplitudes in the ABR and other auditory evoked potentials (e.g., Burkard and Sims, 2002). However, in highly-trained musicians the effect is less pronounced (Parbery-Clark et al., 2009, 2012b; Strait et al., 2012b). To examine whether the same effects can be brought about in a controlled longitudinal design, Tierney and colleagues tested teenagers before they began group musical instruction in a high school setting and then again after two years of training (Tierney et al., 2013). Compared to an active control group who underwent physical fitness training over the same period, the musically-trained group had earlier ABR latencies in noise after 2 years, despite the groups being matched initially. The differences that emerged between the active control and trained groups, while not as large as those seen in highly-trained musicians and untrained peers, suggests that musical training, like other forms of auditory training (Anderson et al., 2013a; Song et al., 2012), can change the auditory system and lead to improved sensory processing in noise.

10. From dawn till dusk: the interaction between age-dependent and experience-dependent processes

Experience-dependent auditory plasticity has been observed across the lifespan, in immature, mature, and aging auditory systems (reviewed in Skoe and Kraus, 2013; Strait and Kraus, 2013). But how do these experience-dependent processes interact with changes to auditory subcortical function that occur naturally with age? Are experience-dependent effects constant throughout life, or might there be privileged windows, i.e., sensitive periods, when the subcortical auditory system may be most open to change by

environmental factors? More generally, how does the auditory subcortical system balance the need for homeostasis while retaining the flexibility to adapt to new environments and auditory challenges?

To understand these competing forces in the auditory system, Skoe and colleagues tracked ABR changes from infancy to old age in a large dataset that included large samples of children and adolescents, two age groups that have been generally overlooked in previous investigations of subcortical auditory development (Skoe and Kraus, 2013; Skoe et al., in press). The outcomes of these studies provide three important insights into auditory brainstem development and experience-dependent plasticity: First, they indicate that developmental plasticity continues well into the second decade of life, a finding that challenges conventional wisdom that the auditory brainstem is mature in early infancy. This protracted development of the subcortical auditory system may create greater opportunities for the sensory environment to influence neural function (Johnson, 2001). Second, they reveal that brainstem function is heightened during school-age years (e.g., earlier latencies and larger amplitudes during this age period compared to younger and older ages). And third, they suggest that experience-dependent processes likely piggyback on age-related changes, such that experience-dependent changes are greatest when the developmental trajectory is most in flux. Skoe and Kraus (2013) theorized that sensitive periods in auditory brainstem function are the byproduct of how brainstem circuitry changes with age, such that sensitive periods emerge when developmental changes are underway and close when age-dependent processes have stabilized. Given that age-dependent processes slow between adolescence and young adulthood but emerge again in the fifth or sixth decade of life, this theory suggests that the plastic nature of the aging auditory system may set the stage for a second privileged window that can be re-opened or triggered later in life by repeated auditory tasks/training. As evidence of this, Skoe and Kraus (2013) show that the differences between highly-trained musicians and non-musicians are greatest in children and older adults, yet minimized in young adults. The notion that sensitive/critical periods can be reinstated is supported by recent evidence in animal models of experienced-dependent plasticity (Gervain et al., 2013; Hensch, 2003; Yang et al., 2012; Zhou et al., 2011). The existence of a sensitive period or periods does not mean that experience-dependent changes do not occur outside these windows, but instead that it may be more difficult to drive such changes or that the amount of change may be more greatly constrained by homeostatic processes. To gain insight into how developmental plasticity constrains or promotes experience-dependent plasticity, future planned experiments will address how auditory impoverishment such as low-SES, and different auditory disorders, alter the developmental trajectory of the ABR at different points in life.

11. How long does an experience stick?

Once experience-dependent plasticity has occurred, what is the *half-life* of that experience? In other words, once the experience has terminated, does the plasticity stick or does it fade away over time? There are multiple ways of addressing this question from tracking subjects longitudinally to observe the after effects of short-term auditory training (Song et al., 2012) or by retrospectively studying a group of individuals who underwent an intensive experience earlier in life (Skoe and Kraus, 2012; White-Schwoch et al., 2013).

In the Song et al. (2012) study, normal-hearing young adults were trained using an adaptive computer-based training program designed to target communication in noise (Sweetow and Sabes, 2006) (LACE: Listening and Communication Enhancement Program). After 20 sessions of training, over the course of roughly 2

months, the trained subjects demonstrated improved perceptual and cognitive abilities, as seen by better speech recognition in noise. This improved speech perception was accompanied by larger speech-evoked ABRs after training but only in the condition where the stimulus was embedded in noise. The same changes were not seen in the age- and demographically-matched control group. To test the persistence of the effect, a large subset of the participants returned for testing 6 months later. Across the board, the behavioral and neurophysiological effects were retained, suggesting that once experience-dependent plasticity has occurred, it will stick, even if the experience occurred after the ABR has reached a point of maturity.

But how long does it stick? This was the question addressed by Skoe and Kraus (2012) in a young adult population and White-Schwoch et al. (2013) in an older adult population. In the Skoe and Kraus study, ABRs were collected from young adults who had a few years of music lessons as children, beginning on average around age 9, and lasting between 1 to 5 years. This study revealed that adults who played a musical instrument as children, but then quit a few years into it, still showed a benefit of that experience. This benefit took the form of enhanced ABRs relative to peers who had never taken any musical classes. Notably, similar enhancements were seen between those with limited musical training and the group who continued with musical training for a longer period (6–11 years) (Fig. 3). One possible interpretation of this and other musician-related work is that the musically-trained participants were different from the untrained group *from the get go*, that is, that group differences existed before musical training even began. However, arguing against that possibility is evidence that the enhancement decreased as a function of how long it had been since training occurred (Fig. 3) (Skoe and Kraus, 2012). That is, the further away the experience, the less of an effect it still had. Yet, the lingering effect of childhood musical experience into old age, reported by White-Schwoch et al. (2013), suggests that the effect of past musical experience on the ABR may not ever completely fade away.

These two recent studies of former musicians raise the rather provocative idea that it may be possible to build up a sensory reserve of positive experiences that can be capitalized upon later in life. New work in hearing-impaired musicians is helping to support that idea (Parbery-Clark et al., 2013a). While the timeline over which this building of experience occurs is undoubtedly determined by the duration of the experience and the valence of that experience, many questions still remain: Do other types of enrichment have similar residuals (e.g., former bilinguals)? Is the persistence greater for auditory impoverishment? Under what conditions, and time-constraints, do the effects of experience fade away? As has been demonstrated in the auditory cortex (Reed et al., 2011), this fading may be a normal part of the cycle of experience-dependent plasticity. That is, learning a new auditory skill may induce a temporary change that is a necessary part of the learning process, but once the skill has been mastered the circuitry returns to its baseline level.

Another way to evaluate fading effects is to use a short-term training approach to test whether the effects of prior experience can be *washed out* by more recent experience. There have been several demonstrations that the ABR is affected by implicit learning of auditory information. The learning-dependent effects emerge as a sensitivity to familiar speech sounds (Galbraith et al., 2004) as well as a sensitivity to the statistical probability with which sounds co-occur within one's daily environment (Marmel et al., 2011). For example, Marmel and colleagues demonstrated that a listener's knowledge of musical syntax (i.e., implicit knowledge of which sounds are commonly combined) affects how the ABR represents music stimuli. But we wonder what might happen if listeners heard

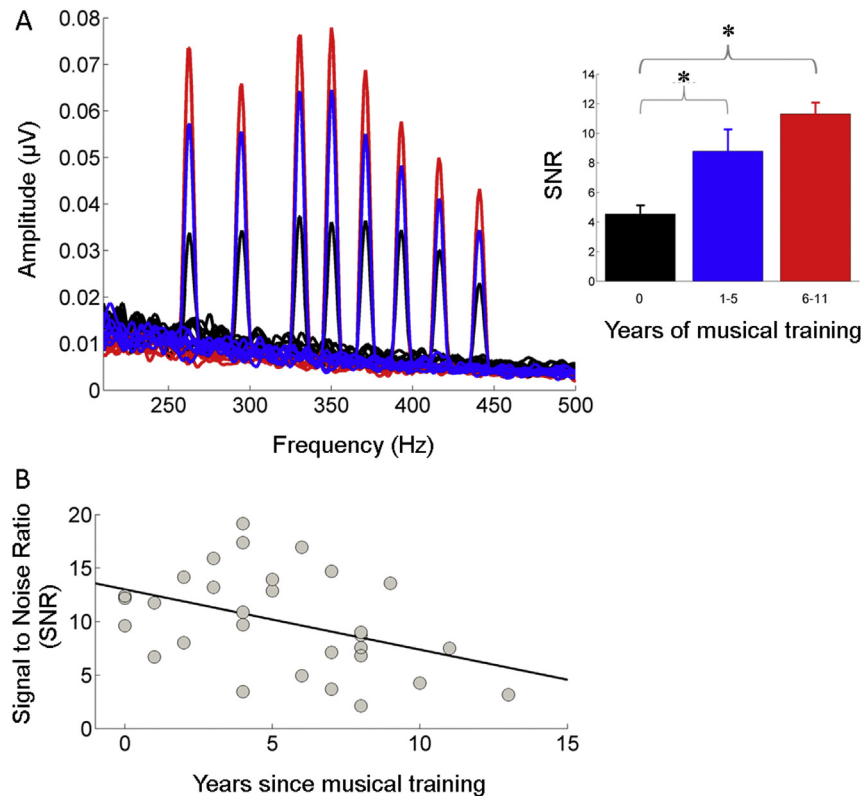


Fig. 3. Persistence of experience-dependent plasticity. (A) Adults who played a musical instrument during childhood have more robust neural responses to sound in adulthood. For adults with no past musical experience (black), the brainstem frequency-following response (FFR) is diminished in amplitude (smaller signal to noise ratios (SNRs)) relative to adults who started playing a musical instrument around age nine and continued to play for either 1–5 (blue) or 6–11 (red) years. FFRs to eight sounds of varying frequency (left). Bar graphs (right) represent the average SNR for each group. Asterisks represent significance levels of $p < 0.001$. (B) In the musically trained subjects, there is an inverse correlation between how recently training occurred ($r = -0.41$, $p = 0.02$) and the magnitude of the enhancement, suggesting that the effect of musical experience may fade as the experience moves further into the past.

Modified from Skoe and Kraus, *Journal of Neuroscience* 2012.

non-Western music for a sufficient amount of time. Might this rewrite how musical stimuli are processed? After all, with sufficient listening experience even the most ingrained musical categories can be overwritten (Hedger et al., 2013). Might there, however, be a point where the two experiences act competitively? Understanding what experience can trump another is not only interesting from a theoretical perspective but it will greatly inform intervention strategies.

12. Training and rehabilitation: retuning of the auditory brainstem through short-term, intensive interactions with sound

Experiences early in life shape auditory brainstem function later in life (Sarro and Sanes, 2011; Skoe and Kraus, 2012); however, as we have hopefully made clear at this point, this does not mean that the auditory brain is a prisoner of its past or immutable later in life. To the contrary, experience-dependent plasticity within subcortical systems can be observed in both children and adults after just a few weeks of intensive auditory training (Anderson et al., 2013, 2013a; Carcagno and Plack, 2011; Chandrasekaran et al., 2012; de Boer and Thornton, 2008; Hornickel et al., 2012; Russo et al., 2005; Schochat et al., 2010; Song et al., 2008, 2012). For example, Anderson and colleagues found that 8-weeks of in-home computerized training on cognitive and auditory skills leads to systematic changes in ABR timing in an older-adult population resulting in earlier response latencies after training (Anderson et al., 2013a). Other cognitive-based auditory training approaches have offered similar benefit in

young adults (Song et al., 2012). However, the question remains whether cognitive training alone, without auditory input, might produce similar outcomes (Oba et al., 2013).

Short-term training-related changes in the ABR have also been observed in impaired systems, including hearing-impaired older adults (Anderson et al., 2013) and children with language-based disorders (Hornickel et al., 2012; Russo et al., 2005). In a recent demonstration of this, Hornickel and colleagues compared two groups of dyslexic children: the students in the experimental group were taught in acoustically-augmented classrooms where the teacher wore a microphone and the children wore a personalized receiver, which piped the teacher's voice directly into the student's ear. The assistive listening device did not actively manipulate the teacher's voice, but instead allowed his/her voice to reach the student's ear at a more favorable signal-to-noise ratio thereby helping to overcome classroom acoustics (Crandell and Smaldino, 1999). Unlike the short-term training studies described to this point, the participants in the experimental group were not given explicit training; instead they received an acoustically-enhanced academic environment during the school day. The control group, on the other hand, attended the same schools but did not wear an assistive listening device. Hornickel et al. (2012) found that the children who wore the listening devices had more stable ABRs after 1 year of use, compared to the control group whose ABRs were essentially unchanged over that same time period. This finding suggests that modifying the auditory world, even if just for a portion of the day, can improve academic performance and fine tune how sound is automatically encoded in the brain, a finding

that also has implications for the potential remediation of socio-economically disadvantaged populations. Similar to the Hornickel et al. study, Munro et al. (2007) have shown that hearing aids, which likewise serve to augment auditory input, can induce changes in the auditory brainstem that persist after the hearing aid is removed (Munro et al., 2007).

13. The Layering Hypothesis

Most studies of experience-dependent brainstem plasticity have taken a reductionist approach by considering only one type of experience, using a more or less binary group definition or an extreme grouping approach. That is, generally one group has a specific set of experiences and a second group is matched relative to the other group with the exception of not having had that same set of experiences (+ experience, – experience). Typically there is also an attempt to create groups that are as homogenous as possible, controlling for other variables or experience, and recruiting individuals who have had an intense form of an experience (in the sense that the experience lasted many years or was condensed within a short time period). This kind of approach is often necessary for passing the rigors of peer review. However, this experimental paradigm by its very design puts one type of experience in the foreground thereby overshadowing the ability to observe the layering of experience that we believe occurs. While in some cases there might be one dominating force that has shaped or continues to shape the auditory system (e.g., lifelong musician, lifelong bilinguals, tonal language speakers, growing up in a low-SES household), within these populations we would still expect to see a layering of experiences. For example, a tonal language speaker who plays the bassoon, we predict would show auditory brainstem tuning to pitch cues of speech (by virtue of their language experience) and also enhanced responses to the acoustic features that give the bassoon its characteristic sound.

We hypothesize that our auditory systems are continuously modulated in small and incremental ways by new (unimodal and multimodal) auditory experiences, and that the effects of new experiences combine with the effects of previous experiences to create interacting layers of plasticity. This hypothesis leads to two central predictions: The first is that *the past guides future plasticity*; in other words existing 'layers' of plasticity can constrain how new layers are formed. In this way, how the auditory subcortical system responds right now depends on what has happened in the past, back to the earliest days of when the auditory system was first developing (see Section 14). The idea that new experiences both borrow from the past and influence the future has been coined the *Continuity of Experience* by the educational philosopher John Dewey. He wrote that "every experience both takes up something from those which have gone before and modifies in some way the quality of those which come after" (Dewey, 1938). We take Dewey's ideas one step further by theorizing that we can objectively index the layering of experiences by probing the auditory brain. Thus, our second prediction is that each layer makes a unique contribution to the neural response to sounds and that they can, as such, be teased apart with the right experimental techniques.

13.1. The accumulation of experiences: layering in action

Within the subcortical auditory system, the strongest evidence for the layering of experience comes from middle-aged musicians with mild (bilateral) hearing loss (Parbery-Clark et al., 2013a). ABRs recorded from this group reflect both their experience with hearing loss (i.e., reduced encoding of the harmonic complexity of sounds) and their extensive musical experience (i.e., enhanced encoding of the fundamental frequency compared to hearing impaired non-musicians).

As more potential evidence for the *Layering Hypothesis*, we recently found that short-term experiences can overwrite on-line processing of stimulus statistics in the auditory brainstem (Skoe et al., 2013c). Our results suggest that experiences may act hierarchically, with some experiences being dominant over others. Thus each layer of experience may not carry the same weight in terms of its influence on ABR processing. However, at this point, it is unclear whether more extensive experience trumps more transient experience and/or whether active listening experiences prevail over passive experiences.

By virtue of each of us having a different set of experiences throughout our lifetime, our *Layering Hypothesis* makes the prediction that we each have an auditory fingerprint, a unique neural signature of that experience. This auditory fingerprint may explain the individual differences in subcortical auditory function that are evident within a normal young adult population (Chandrasekaran et al., 2012; Hairston et al., 2013; Skoe et al., 2013b). Neuroanatomical and neurophysiological studies, using ABRs and fMRI, have demonstrated the existence of individual differences in auditory regions that are associated with differential learning success on short-term auditory training paradigms (Golestani et al., 2007; Wong et al., 2011a, 2007a). For example, Chandrasekaran et al. (2012) examined inferior colliculus activity, using both fMRI and ABRs, before native English speaking participants underwent auditory training on an artificial tonal language (Chandrasekaran et al., 2012). The artificial language consisted of 24 novel words containing curvilinear pitch contours not found in English. The participants in this study were selected to be as homogenous as possible: young adult monolinguals with little music training and no prior exposure to tone languages. Yet, in this relatively homogenous group, different patterns of IC BOLD activity to the pitch contours emerged even *before training* commenced: one that encoded pitch information more efficiently before training, as measured by BOLD responses, and another group encoded this information less efficiently (Fig. 4). These differences in IC BOLD activity were predictive of how much learning occurred over the course of the training paradigm and also how accurately the pitch contours were tracked in the ABR after training ceased. This finding suggests that the initial IC activity patterns may be affecting future plasticity. Similarly, Skoe et al. (2013b) demonstrated a predictive relationship between ABR and behavioral indices of learning. Their findings suggest that individual differences in rapid auditory learning reflect individual differences in the brainstem's sensitivity to auditory patterns (Skoe et al., 2013b). In most of these studies, although the participants had similar demographics, they most surely had varied auditory experiences leading up to the experiment.

We speculate that these individual differences reflect layered auditory experiences that have accumulated over the lifetime and which combine with genetic characteristics to influence plasticity in a novel learning environment. For some individuals the accumulation of experiences limits future plasticity, whereas other individuals may be able to capitalize on their unique set of experiences. For example, long-term musical training has been shown to facilitate short-term and on-line auditory learning, suggesting that musical training endows a state of metaplasticity (reviewed in Herholz and Zatorre, 2012). We argue that musical training may therefore create a layer of plasticity that enables future plasticity. In contrast, environmental impoverishment associated with low-SES may create a layer of plasticity, which through negative feedback loops reinforces the poverty of input and impose limits on future subcortical auditory plasticity. The idea that disadvantages or advantages accumulate over time, sometimes called the *Mathew Effect* (Merton, 1968; Shaywitz et al., 1995), thus may help to explain how the auditory system is changed by

repeated auditory impoverishment or repeated auditory enrichment.

13.2. Testing the Layering Hypothesis

How can we test this hypothesis? With the right experimental design, can we peel back the layers? This could be achieved by taking more comprehensive and detailed subject histories of not just auditory experience but multisensory experiences and then examining how short-term training differentially affects populations with different histories. A variant of that idea could also involve administering different combinations of auditory training to different groups of participants. Another straightforward approach is to target individuals who have undergone two different types of significant experience, for example, someone who is both a lifelong bilingual and a lifelong musician. Based on some preliminary data in that area, we predict that the effect of the experiences compound but are not necessarily additive, such that the combined experience (especially in cases when they experiences occur simultaneously) creates a non-linear amalgam of the individual experiences. Another approach is to study how two different, perhaps opposing types of experiences compete. In addition to musicians with hearing loss, hearing impaired bilinguals, or low-SES musicians, are other candidate populations to study.

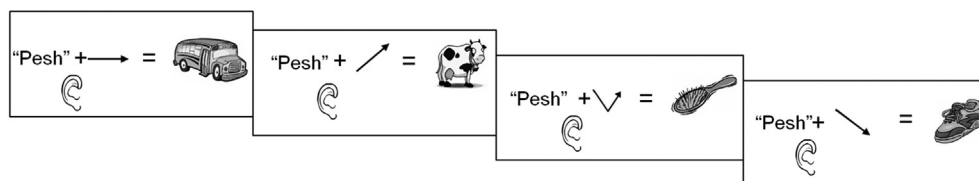
14. The initial layer: when does experience-dependent plasticity first emerge?

The youngest age at which auditory enrichment has been shown to affect auditory subcortical function is age 3 (Skoe and Kraus,

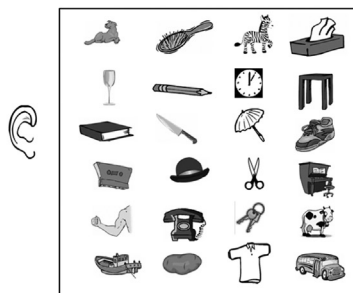
2013; Strait et al., 2013a,b). However, experience-dependent processes may emerge earlier. Indeed, the precocious nature of human hearing may enable experience-dependent auditory plasticity to emerge during the earliest days of hearing, as supported by research in animal models (Lickliter and Stoumbos, 1992). The human fetus, which has been described as having relatively “advanced sensory capabilities” (Bernhardt, 1987), begins to respond to sound around the 22nd–24th gestational week (Birnholtz and Benacerraf, 1983; Hepper and Shahidullah, 1994). During the next few months, the fetus becomes sensitized to the sound of the mother’s voice and other frequent sounds in the environment that are transmitted through the amniotic fluid, as evidenced by behavioral and neurophysiological (cortical) data from newborns (Beauchemin et al., 2011; Fifer and Moon, 1994; Kisilevsky et al., 2003) (reviewed in Fava et al., 2011). In a recent study, Partanen and colleagues, performed a controlled training study, in which one group of fetuses was exposed to non-native speech stimuli and the control group was not (Partanen et al., 2013). The stimuli contained pitch changes that were not common to the language in the environment that both groups shared (Finnish). After birth, the infants exposed to the experimental stimuli were more sensitive to pitch changes, as seen in cortical-evoked potentials. The neural correlates of *in utero* learning were seen for both trained and untrained stimuli, suggesting that learning had generalized.

While we know that early negative auditory experiences – such as exposure to the noisy environment of a neonatal intensive care unit (McMahon et al., 2012) – can compromise ABRs, little is known about how reduced and/or enriched *in utero* auditory worlds can affect human subcortical auditory function. The Jeng et al. (2011) study (described above) suggests that *in utero* linguistic exposure

(A) Sound-to-Meaning Association Training



(B) Test



(C) Learning Differences

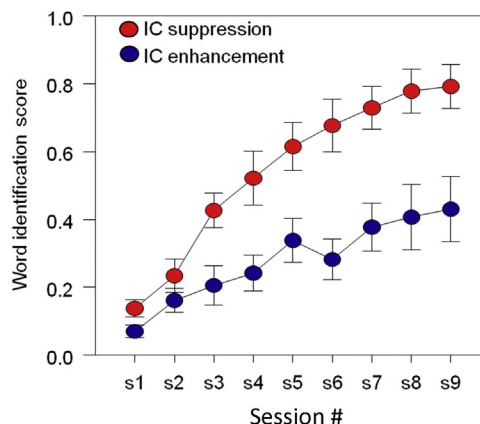


Fig. 4. Human inferior colliculus (IC) activity relates to individual differences in spoken language learning. (A) Participants underwent a 9-session sound-to-meaning association training paradigm during which they learned to differentiate objects based on pseudowords (e.g., ‘pesh’) with superimposed (non-native) pitch patterns (level, rising, dipping, or falling pitch patterns). Pseudowords were paired with visual presentation of a unique object in each training session. (B) Each session ended with a final test in which participants heard a sound (e.g., ‘pesh’ with a falling pitch pattern) and had to pick 1 of 24 objects (e.g., shoe). A final score, representing the proportion of words correctly identified, was calculated for each participant for each session. (C) Based on *pre-training* blood-oxygen level dependent (BOLD) responses from the IC, two groups of participants emerged. The group showing IC suppression, that is, a reduction in BOLD response with repetitive presentation (an indication of neural efficiency) (red) was more successful in the sound-to-meaning training program, relative to the group in which IC responses were enhanced (blue). The groups showed a clear separation after the second session (s2) of training. This finding suggests that IC encoding of nonnative time-varying pitch patterns is related to future learning of linguistic pitch patterns.

Modified from Chandrasekaran, Wong, Kraus, *Journal of Neurophysiology* 2012.

is not sufficient for driving the kind of language-dependent brainstem plasticity that has been robustly documented in adults across a variety of studies (Jeng et al., 2011; Krishnan et al., 2010a, 2005). However, far more work is needed in this nascent area of study to understand how the earliest of auditory experiences, including formal and informal language and music activities (Fava et al., 2011; Putkinen et al., 2013; Trainor et al., 2012), might affect auditory subcortical development and provide the initial layer upon which other experience-dependent changes take root.

15. Conclusion

The studies we reviewed here paint a complex, ever-evolving picture of the experience-dependent nature of the subcortical auditory system. This body of evidence, especially the recent work in fetuses, raises the question of whether the subcortical auditory system has a default state that is independent of auditory experience, and if it does, how do we assess it? Another important consideration that we have largely glossed over is how experience-dependent factors may interact with such things as hormonal fluctuations during development (McFadden, 2002) and genetic processes. Because auditory disorders run in families (e.g., Maziade et al., 2000), and family members appear to have similar ABR fingerprints (Hornickel et al., 2013), this suggests an intricate interaction between genetics and shared-auditory experiences that may be difficult to fully dissociate without large scale epidemiological investigations.

We have provided the initial groundwork for the *Layering Hypothesis*, which we expect will evolve as the research on subcortical plasticity evolves. By understanding the brain's capacity to change throughout the lifespan in response to different experiences, and then maintain those changes, this line of research on subcortical auditory plasticity can potentially inform the development of effective and long-lasting rehabilitative programs. That is, by understanding the combination of experiences that promote auditory plasticity, or impede auditory plasticity, we can optimally train listeners to maximally benefit from their auditory environments and potentially overcome, through the right combination of treatments and/or multimodal stimulation, auditory impairments that arise from peripheral damage, genetic abnormalities, or sensory impoverishment.

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