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Research report

Auditory training improves neural timing in the human brainstem

Nicole M. Russo[a,b,c,*], Trent G. Nicol[a,c], Steven G. Zecker[c], Erin A. Hayes[a,b,c], Nina Kraus[a,b,c,d,e]

[a] *Auditory Neuroscience Laboratory, Northwestern University, 2240 Campus Drive, Evanston, IL 60208, USA*[1]
[b] *Institute for Neuroscience, Northwestern University, 2240 Campus Drive, Evanston, IL 60208, USA*
[c] *Department of Communication Sciences, Northwestern University, 2240 Campus Drive, Evanston, IL 60208, USA*
[d] *Department of Neurobiology and Physiology, Northwestern University, 2240 Campus Drive, Evanston, IL 60208, USA*
[e] *Department of Otolaryngology, Northwestern University, Northwestern University, 2240 Campus Drive, Evanston, IL 60208, USA*

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Abstract

The auditory brainstem response reflects neural encoding of the acoustic characteristic of a speech syllable with remarkable precision. Some children with learning impairments demonstrate abnormalities in this preconscious measure of neural encoding especially in background noise.

This study investigated whether auditory training targeted to remediate perceptually-based learning problems would alter the neural brainstem encoding of the acoustic sound structure of speech in such children. Nine subjects, clinically diagnosed with a language-based learning problem (e.g., dyslexia), worked with auditory perceptual training software. Prior to beginning and within three months after completing the training program, brainstem responses to the syllable /da/ were recorded in quiet and background noise. Subjects underwent additional auditory neurophysiological, perceptual, and cognitive testing. Ten control subjects, who did not participate in any remediation program, underwent the same battery of tests at time intervals equivalent to the trained subjects.

Transient and sustained (frequency-following response) components of the brainstem response were evaluated. The primary pathway afferent volley – neural events occurring earlier than 11 ms after stimulus onset – did not demonstrate plasticity. However, quiet-to-noise inter-response correlations of the sustained response (~11–50 ms) increased significantly in the trained children, reflecting improved stimulus encoding precision, whereas control subjects did not exhibit this change. Thus, auditory training can alter the preconscious neural encoding of complex sounds by improving neural synchrony in the auditory brainstem. Additionally, several measures of brainstem response timing were related to changes in cortical physiology, as well as perceptual, academic, and cognitive measures from pre- to post-training.

Keywords: Auditory brainstem response; Neural timing; Plasticity; Speech; Auditory training; Frequency-following response; Reading disability

1. Introduction

This study addresses several questions: Is there plasticity in the neural encoding of sound in the human auditory brainstem? If so, is this manifested in a way that can be readily measured? Can the brainstem representation of speech-sound structure in children with learning disabilities be altered by work with a commercially available auditory training regimen?

Auditory training has been shown to alter the neural encoding of sound structure at the cortical level. Cortical plasticity has been established in both animals [4,7,11,15,22,31,36,42,43] and humans [25,39]. Cortical changes have accompanied perceptual learning of non-native speech sounds in adults [59] and improved auditory perception in children with learning problems [25,61]. However, neural plasticity is not necessarily restricted to the cortex. The auditory cortex receives sensory input via the thalamocortical loop and there is a precedent for subcortical plasticity from a number of animal studies [3,10,12–14,21,24,27–30,35,45–47,56,62]. In general, it is thought that subcortical plasticity is short-term. However,

* Corresponding author. Tel.: +1 847 491 2465; fax: +1 847 491 2523.
E-mail address: n-russo@northwestern.edu (N.M. Russo).
[1] http://www.communication.northwestern.edu/csd/research/brainvolts.

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once conditioned, the association of a sound with a meaning causes long-term cortical changes. Furthermore, it has been suggested that there is an interaction between ascending auditory pathways and the descending corticofugal system, as well as interactions with the amygdala and basal forebrain [56]. A positive feedback loop involving lateral inhibition modulates subcortical and cortical activity. The extent to which plasticity at subcortical regions directly influences the cortex or vice versa has yet to be determined. Whatever the mechanism, current research supports a relationship between cortical and subcortical plasticity.

Subcortical plasticity in the medial geniculate body (MGB), which synapses directly onto auditory cortex, occurred with classical conditioning in rats [10]. These experience-dependent changes persisted for 45 days. Later, using a guinea pig model, Edeline and Weinberger extensively investigated plasticity in the dorsal (MGd), ventral (MGv), and medial (MGm) divisions of the MGB in response to associative cardiac conditioning to specific frequencies. Each area of the MGB experienced changes in receptive field properties after only a short conditioning period. Changes in the nonprimary pathway (MGd) were resilient and persisted at the one-hour post-test session [12], while changes in the primary pathway (MGv) were susceptible to decay after 1 h [13]. Both short- and long-term changes were seen in the MGm, reflecting the broad- and fine-tuned bandwidth variation of cells in this area [14]. Edeline and Weinberger concluded that the subdivisions of the MGB act in conjunction with each other and that the significance of the stimulus affects the duration of the change.

Plasticity in the cochlear nucleus has been demonstrated in a decerebrate preparation using a cat as the animal model [3,27,28]. This basic paradigm resulted in the expression of habituation and spontaneous recovery in the cells of the cochlear nucleus in response to repetitive stimulation. Alterations in neural connectivity following cochlear ablation demonstrate plasticity in even lower subcortical structures. Unilateral cochlear removal in ferrets produced changes in the number of neurons projecting to the contralateral inferior colliculus [46,47]. Ablation of the cochlear nucleus in rats resulted in new patterns of synaptic connections within the brainstem [29,30]. Illing et al. [30] further explored brainstem plasticity after cochlear ablation in rats. They observed plasticity in the superior olivary complex, ventral and dorsal cochlear nucleus, and inferior colliculus via the increased presence of GAP-43, which is abundant during synaptogenesis both in development and remodeling.

Plasticity at the level of the inferior colliculus has been observed in barn owls. Behavioral changes in sound localization following filtering or ear occlusion were accompanied by changes in auditory space maps within the inferior colliculus [21,35,45].

These animal studies showed changes occurring in receptive fields, space maps, and synaptic activity and connectivity at the first levels of sensory processing. In the only human study to our knowledge, Khalfa et al. investigated the modulation of auditory periphery by higher cortical regions in epileptic patients following resection surgery [32]. They were able to demonstrate reciprocal relationships between changes in the medial olivocochlear system and auditory cortex. Using transiently evoked otoacoustic emission recordings and equivalent attenuation calculations, they were able to assess effects of the surgery on the medial olivocochlear nucleus. Specifically, they showed evidence for corticofugal influence on the medial olivocochlear nucleus and associated changes in speech processing both in quiet and noise.

Thus, considerable evidence suggests that neuronal activity occurring in the human auditory midbrain may be dynamic. The current study was designed to investigate plasticity in the physically intact auditory system by capitalizing on the ability to quantify temporal changes using evoked potentials. A strength of evoked potentials is their use in quantifying neural synchrony and timing in the encoding of complex stimuli, such as speech.

Specific aspects of the sound structure are maintained and reflected in the neural code of the auditory brainstem [51]. The brainstem response to a speech sound consists of two components, the onset and the frequency-following response (FFR), which represent transient and sustained processes, respectively. Transient responses, with precision on the order of tenths of milliseconds, represent primarily the response to discrete events in the stimulus, such as the stimulus onset and the successive modulations caused by the vibration of the vocal folds. Sustained response components last for the duration of a periodic stimulus and reflect the overall integrity of the response with respect to the stimulus.

A speech syllable can be divided into transient and sustained portions – consonants and vowels – that share some characteristics with the brainstem response components. Consonants are rapid, transient, and generally aperiodic features of speech; they are represented by the transient components of the brainstem response and are easily disrupted by noise. Vowels are periodic, sustained signals; they are represented by the sustained features of the brainstem response, are generally much larger in amplitude than consonants and are more resistant to noise.

Stop consonants are difficult to perceive, especially for people with learning disabilities [2,6,49]. Children with language-based learning problems often exhibit deficits in auditory perception and the neural encoding of speech sounds at both cortical and brainstem levels [5,20,38,52,57,64,68], especially when background noise is introduced [1,33,63]. Commercial auditory training programs have been developed to provide remediation for auditory perception and related learning deficits [8,18,19,44,57]. The physiological consequence of this kind of training is little understood. Thus, testing children before and after undergoing such training offers an ideal opportunity to examine neural plasticity at the level of the auditory brainstem.

Normative values and test-retest reliability for the brainstem measures in this study have been established and provide a means for determining the degree to which brainstem responses may be expected to change over time [33,51]; pre- to post-training changes that exceed test–retest changes can be attributed to auditory training. Moreover, because not all children benefit in the same way from training programs, it is important to determine what pre-training neurophysiological measures are markers for successful training.

Speech-evoked brainstem activity was obtained before and after children with learning disabilities participated in a commercial auditory training regimen. Both transient and sustained components of the brainstem response to the syllable /da/ presented in quiet and in background noise were assessed. Relationships of brainstem measures to improvements in cognitive, perceptual, and academic achievement tests were also explored.

2. Materials and methods

2.1. Subjects and training regimen

Nineteen children, 8–12 years old, were included in this study. All of the subjects were native English speakers, with normal IQ (≥85 on Brief Cognitive scale or Test of Nonverbal Intelligence; range 85–135), and had normal hearing thresholds at or below 20 dB HL for octaves from 500 to 4000 Hz. The experimental group comprised nine children with learning disabilities (LD) based on diagnoses by outside professionals (child psychologists, neurologists, etc.) and their performance on study-internal measures of learning and academic achievement (see Section 2.3). Consent and assent were obtained from the parent(s) or legal guardian(s) and the children. The Institutional Review Board of Northwestern University approved all research.

Children in the experimental group participated in 35–40 independently supervised one-hour sessions of *Earobics* [9] over an 8-week period. *Earobics* is a commercial auditory training program that provides training through interactive computer games of phonological awareness, auditory processing, and language processing skills. The stimuli are presented in quiet and background noise, with both visual and auditory feedback. Children listen to sounds while playing interactive, animated computer games; they match sounds (indicating alike or different) by clicking the computer mouse on appropriate pictures or sound representations they hear. Earobics is a two-step program; Step 1 has six interactive games covering phonological awareness and processing, while five games comprise Step 2, which further develops the skills trained in Step 1 and concentrates more on language processing skills to help individuals better interpret spoken and written language [9]. Children in the experimental group underwent auditory neurophysiological and perceptual/cognitive testing prior to and within three months following completion of the training program.

The control group underwent the same battery of tests at a time interval equivalent to the trained subjects, but did not participate in the training program. This group (n = 10) consisted of both normal learning (NL; n = 5) and LD (n = 5) children who met the same inclusion criteria as those in the experimental group.

2.2. Neurophysiological testing

Auditory brainstem and cortical evoked potentials were evaluated in response to the speech syllable /da/ presented in quiet and background noise.

2.2.1. Auditory brainstem response

The brainstem response was elicited by the synthesized [34] speech stimulus /da/ (Fig. 1, top). The stimulus duration was 40 ms. Randomly alternating polarities were presented (Neuroscan, Stim, *Compumedics*) to the right ear through an insert earphone (ER-3, Etymotic Research) at 80 dB SPL with a 51 ms inter-stimulus interval. The syllable was presented in two conditions, quiet and with white Gaussian background noise (+5 dB SNR). The response was differentially recorded from Cz-to-ipsilateral earlobe, with the forehead as ground. Three thousand sweeps per polarity were collected (Neuroscan, Scan, *Compumedics*) in each noise condition. The sampling rate was 20,000 Hz and responses were online filtered from 100 to 2000 Hz. Trials with activity greater than 35 μV were online rejected. Responses to alternating polarity stimuli were added together to create a mainly neu-

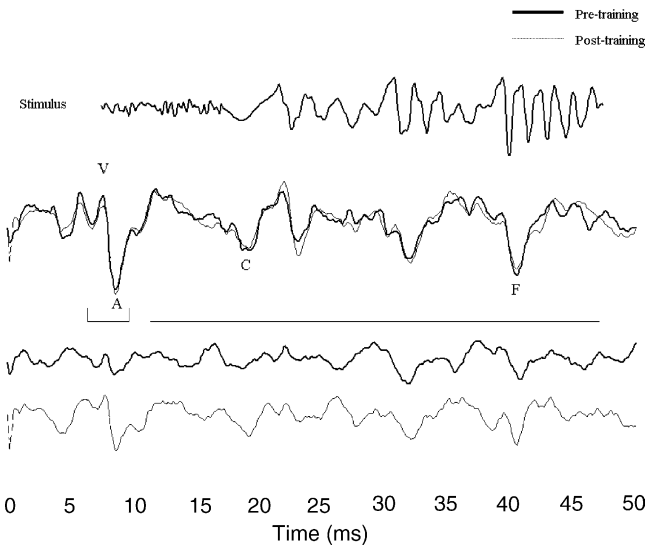

Fig. 1. Stimulus waveform and grand averages of those subjects whose quiet-to-noise inter-response correlations improved. The stimulus has been shifted to align peaks present in the stimulus with their corresponding response waveform peaks; this shift accounts for a time delay introduced by the amount of time required for the sound to traverse the ear canal to the brainstem. Peaks are labeled, the onset response is bracketed and the FFR is underlined in the quiet response. Waveforms show that the improvement of correlations can be attributed to more accurate encoding of the signal in noise, rather than a change in quiet.

ral response [23]. Throughout the testing session, the children watched a video of their choice and listened to the soundtrack at less than 40 dB SPL in the non-test ear.

2.2.1.1. Transient response. The brainstem response to /da/ consists of six major transient peaks (A–F) following the familiar I–V series. These peaks represent synchronized neural activity in response to the phonetic/acoustic characteristics of the speech syllable and represent peaks within the stimulus with remarkable precision. Peaks V, A, C, and F are the most reliable peaks in the response, exhibiting small latency variability and excellent detectability in all subjects [33]. These peaks (Fig. 1) were evaluated both in terms of timing (latency) and magnitude (amplitude). The VA complex was further analyzed by interpeak latency, area, amplitude, and slope. A wavelet-denoising technique derived from Qian Quiroga and Garcia [48] was used to aid in determining peak latencies and amplitudes of responses elicited in noise.

2.2.1.2. Sustained response. The sustained FFR component of the response (11.5–46.5 ms) (Fig. 1) was evaluated both by magnitude and timing measures. Magnitude was evaluated in two ways. RMS amplitude was calculated over the FFR epoch. The amplitude of the spectral component encompassing the fundamental frequency of the stimulus (F_0 = 103–121 Hz) was measured by fast Fourier transformation analysis. Timing also was assessed in two ways, using a cross-correlation technique. Stimulus-to-response correlations were measured, using the 10–40 ms portion of the stimulus, and the highest correlation achieved within a response lag of 6–9 ms was obtained. Quiet-to-noise inter-response correlations were also analyzed over a response range of 10–40 ms, with a noise response lag of up to 2 ms. Specific details of the methods and normative values are discussed elsewhere [5,33,51].

2.2.2. Analysis of plasticity

Plasticity in physiological measures in trained subjects was defined as changes in the neurophysiological response that exceeded those observed in the untrained control subjects. Differences between groups were measured using a repeated measures analysis of variance with test session as the within-subject factor and training group as the between-subject factor. Post-hoc tests were done to establish in which group the significant changes occurred. A criterion of $P < 0.05$ was used. For all statistical analyses involving Pearson correlations, Fisher's transformation was used to convert *r*-values to z'-scores.

2.3. Cortical response

Cortical responses to the speech stimulus /da/ presented at 80 dB SPL in quiet and noise (0 dB SNR) were recorded. The interstimulus interval was 590 ms. The sampling rate was 2000 Hz and responses were online filtered from 0.05 to 100 Hz. Cortical activity was recorded from Cz, with a nasal reference and the forehead as ground. Eyeblink was monitored with bipolar supraorbital-to-lateral canthus electrodes. P2N2 amplitudes, latencies, and quiet-to-noise inter-response correlations were measured. Similar to the technique for analyzing the inter-response correlations for the brainstem response, the cortical response to the sound presented in quiet was cross-correlated with the response recorded in background noise. The correlation was calculated over the 100–350 ms range and the highest correlation value achieved within a 50 ms lag was obtained [25]. Spearman correlations were used to identify relationships between brainstem and cortical response measures.

2.4. Perceptual and cognitive abilities testing

At both the test and retest sessions, subjects underwent a series of tests that quantified their perceptual and cognitive abilities. Subjects were evaluated on measures of auditory processing (Incomplete Words, Memory for Words, Sound Blending, Listening Comprehension [67]), mental abilities (Brief Cognitive Scale [66]), and academic achievement (Word Attack [67], Reading and Spelling [65]). Other measures of auditory perception included speech discrimination in quiet and in background noise (just-noticeable difference scores along a synthesized /da-ga/ continuum differing in F_3 onset frequency, as determined by Parameter Estimation Sequence Tracking [58]), speech identification (perception of Sentences in Noise [1]), and temporal resolution (Backward Masking). These measures have been described in detail elsewhere [1,38,68].

Spearman correlations were used to identify relationships between the brainstem response and cognitive and perceptual measures. For these analyses, if a subject showed a decrease on a perceptual/cognitive score upon retest, their "improvement" was coded as zero to diminish the impact of outliers.

3. Results

3.1. Stability of brainstem measures over time: control group

Test–retest data were collected from control subjects who did not undergo auditory training. NL and LD controls were combined into one control group because the degree of change of test–retest measures was equivalent between the NL and LD controls. Two-tailed, paired *t*-tests were conducted to establish changes that could be expected to occur over a 3–6-month time interval. These comparisons revealed that most /da/-elicited brainstem measures are stable over time. No significant differences were found in brainstem measures obtained in quiet, with the exceptions of VA interpeak amplitude and slope (both, $P < 0.02$). Onset response amplitude is known to be variable [53], so this was not a compelling change. Onset amplitudes were thus omitted from analysis of

training effects. In background noise, onset responses are often attenuated to a great extent and sometimes eliminated [51]. Therefore, these responses were not evaluated for effects of training. Peaks C and F, however, remained robust and were resistant to background noise. All FFR measures and transient response peaks C and F remained stable in quiet and background noise over the test–retest time interval.

3.2. Effects of training on brainstem measures: experimental group

Measures of onset response timing did not change in the experimental group. There was no evidence of training-associated changes in responses occurring earlier than 11 ms.

Quiet-to-noise inter-response correlations of the FFR increased significantly for the experimental group after training, but not for the control group (RMANOVA interaction, $F_{approx}(1,17) = 6.67$, $P < 0.02$; post-hoc one-tailed paired t-test, $P < 0.02$ and $P > 0.25$, respectively). Specifically, seven of the nine trained subjects showed this increase (Fig. 2). Increased quiet-to-noise inter-response correlations indicate that timing characteristics of the stimulus became encoded more precisely after training.

In order to discern whether an improvement in either the response in quiet or noise contributed more to the overall improvement in the quiet-to-noise inter-response correlations, grand average waveforms were compared (Fig. 1). Visual inspection of these waveforms suggests that responses in quiet were stable while clearer definition of noise response components emerged following training.

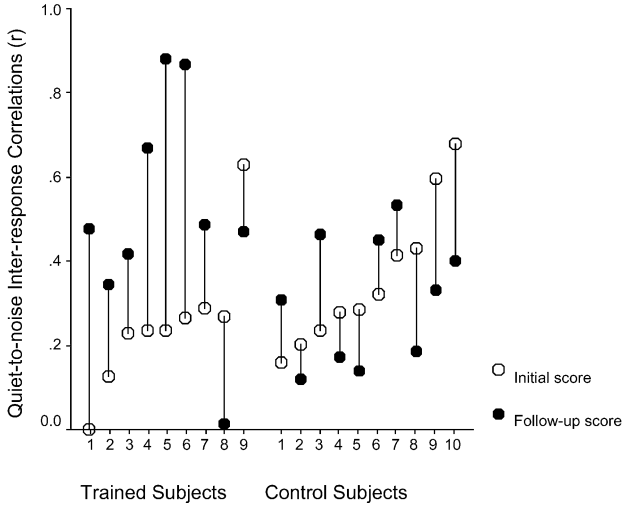

Fig. 2. Improved neural timing in noise. Quiet-to-noise inter-response correlations of trained (left) and control subjects (right). Subcortical changes in the brainstem response occurred in trained subjects, as evidenced by seven of the nine subjects with increased inter-response correlations, while control subjects did not change (z' score conversion; RMANOVA interaction, $F_{approx}(1,17) = 6.67$, $P < 0.02$; post-hoc one-tailed paired t-test, $P < 0.02$ and $P > 0.25$, respectively). Increased correlations are indicative of more similarity between quiet and noise responses, suggesting improved encoding in noise.

To quantify this observation, partial correlation analyses, controlling for values of pre-training stimulus-to-response correlations in quiet, were performed. A strong and significant relationship was found between inter-response and stimulus-to-response in noise correlations (partial correlation, 0.55, one-tailed $P < 0.01$). However, the stimulus-to-response in quiet showed no such relationship with the inter-response correlations. This confirmed the presumption that an improvement of neural timing in noise made the greater contribution to the overall increase in inter-response correlations. Following training, the overall morphology of the waveform for the response in noise more closely resembled the response in quiet, and thus the stimulus.

Additionally, trained subjects showed better wave C peak definition and a later latency in noise, unlike control subjects (RMANOVA interaction, $F_{approx}(1,17) = 7.24$, $P < 0.02$; post-hoc one-tailed paired t-test, $P < 0.01$ and $P > 0.25$, respectively). These changes may have contributed to the improved correlation between the quiet and noise responses. The training-associated change in peak C latency in noise was likely a consequence of post-training sharpening of the wave. As can be seen in the pre-training grand averaged waveform (Fig. 1), the region around peak C (approx. 19 ms) was very broad; the peak latency was not clearly identified. Furthermore, the standard deviation of peak C latency in noise decreased post-training. Thus, after training, as the peak became more pronounced, the judgment of its latency became more precise.

3.2.1. Relationships between subcortical and cortical measures

A study conducted by Hayes et al. [25] showed changes in response timing and magnitude in noise following auditory training. This was manifested by increases in cortical quiet-to-noise inter-response correlations and P2N2 amplitudes in noise. Relationships between improvements at both the brainstem and cortical levels were explored. Increases in brainstem quiet-to-noise inter-response correlations were significantly associated with cortical P2N2 amplitude increases in noise (Spearman's $\rho = 0.70$, one-tailed $P < 0.03$). Increases in stimulus-to-brainstem response in noise correlations were associated with increases in cortical amplitudes (Spearman's $\rho = 0.67$, one-tailed $P < 0.03$). Overall, improved subcortical timing was associated with improvements in the cortical response.

3.2.2. Relationships between brainstem responses and behavior

Relationships between training-related brainstem response changes and changes in perceptual and cognitive measures were examined. Additionally, pre-training brainstem response indicators of behavioral improvement were sought.

Children in the trained group demonstrated significant gains on the Incomplete Words, Auditory Processing, and

Sentences-in-Noise tests. Although brainstem changes were not directly related to improvements on those particular tests, gains in Listening Comprehension were related to changes in the brainstem response in noise. Decreases in the RMS amplitude of the FFR in noise were accompanied by improved Listening Comprehension scores (Spearman's $\rho = -0.88$, $P < 0.002$), a measure of auditory processing. No other significant relationships were found between brainstem response changes and changes on the other tests of perceptual and cognitive abilities.

3.2.3. Brainstem response markers of training success

Particular pre-training brainstem measures marked children who demonstrated significant training-associated gains in auditory processing and speech discrimination in noise. Children with later peak F latencies in noise demonstrated improvements on Incomplete Words (Spearman's $\rho = -0.90$, $P < 0.001$), while children with larger peak F amplitudes in noise showed improvements in /da-ga/ discrimination in noise (Spearman's $\rho = -0.84$, $P < 0.005$).

4. Discussion

Measures of transient onset response timing were stable over time and resistant to the effects of training; they did not change in either experimental or control subjects. Auditory training did alter sustained response timing. Brainstem response quiet-to-noise inter-response correlations, as well as FFR peak C latency in noise, differed between test sessions in children who received training, but not in control subjects. Training did not alter sustained response magnitudes.

4.1. Improved neural timing in noise

Auditory training appears to alter the brainstem response to speech sounds. Specifically, neural encoding became more resistant to the deleterious effects of background noise following training. Increases in quiet-to-noise inter-response correlations represent greater timing precision in the FFR in noise after training.

Certain assumptions can be made about the nature of plasticity within the auditory brainstem based on the latency ranges over which changes did and did not occur following auditory perceptual training. Onset responses to /da/, occurring within the first 11 ms post-stimulus onset, were relatively stable over time and were also unaffected by training. Thus, a response that arises exclusively from the primary afferent volley did not demonstrate plasticity; neural events occurring so early in the processing of auditory stimulation may be hardwired. Unlike the onset response, the FFR element of the brainstem response was found to be dynamic. Auditory training altered the neural encoding of the harmonic, periodic aspects of sound occurring 12–40 ms post-stimulus onset.

4.2. Where do the changes occur?

Isolating the precise source of neural plasticity in the auditory brainstem cannot be accomplished with far-field recordings, although the time frame of the plasticity provides considerable information regarding the likely neuroanatomical contributions. Because no changes occurred earlier than the first 12 ms post-stimulus onset, it is plausible that the inferior colliculus itself is the locus of plastic activity [37]. However, it is also possible that plasticity at sites peripheral to the inferior colliculus may be contributing to the plasticity shown in this study. Some studies have shown effects of attention on cochlear activity [17,40,41]. Galbraith et al. [16] suggests that such short latency attentional effects may affect the FFR component of the brainstem response to vowels. Therefore modulation of cochlear hair cells might influence early processing within the superior olivary complex and thus alter the activity of the inferior colliculus. Hoormann et al. [26] also corroborates the concept of early attentional modulation of the FFR.

Cortical feedback can also induce plasticity within the FFR. Intracranial recordings in human auditory cortex have observed activation as early as 12 ms in response to clicks and tone bursts. Steinschneider et al. [54] reported a similar time frame in response to a /da/ syllable. Given that the initial response in cortex occurs at such a short latency, it can be theorized that cortical feedback may regulate neural activity as early as the timeframe seen in the present study (e.g., within the first 30 ms). While the cortex may modulate activity, the locus of plasticity is not likely rostral to the inferior colliculus since the MGB and auditory cortex do not phase-lock at rates as fast as fundamental and first formant frequencies [50,60].

The corticofugal descending system is critical in manipulating signal encoding via positive feedback or lateral inhibition mechanisms [55]. Once trained or conditioned, egocentric selection [69,70] allows for the cortex to recognize the behavioral significance of an acoustic stimulus and then fine-tune its own input by altering the sound representation at lower levels. Specifically, the cortex modulates subcortical areas that encode basic stimulus features and thus improves subsequent cortical representation. Even a short-term subcortical change, lasting 1–3 h, is sufficient to influence long-term cortical changes [13,14,55,70]. Although it is still unknown precisely how corticofugal modulation is initiated, the evidence remains that subcortical regions are malleable with training and that modulation may occur in multiple domains (frequency, time, etc.).

To our knowledge training-associated neural plasticity at the level of the brainstem in humans has not been previously identified. However, extensive animal research, as reviewed above, has demonstrated regions of plasticity at subcortical levels. Classical conditioning, auditory deprivation, and cochlear ablation studies support the idea that plasticity does occur subcortically and may affect cortical processing directly. Alternatively, cortical and subcortical activity may modulate each other through corticofugal loops. The

aforementioned animal studies together with the present work demonstrate plasticity in the auditory brainstem and support the notion that early sensory processing is malleable.

4.3. Behavioral ramifications

The relationships between brainstem changes and behavioral measures supports the idea that pre-conscious alteration of the brainstem response affects auditory perception. Gains in Listening Comprehension were related to a reduction in the sustained response RMS amplitude in noise. During the prestimulus period, RMS amplitudes did not change between test sessions (paired *t*-test, $P = 0.34$), indicating that this reduction was confined to stimulus-evoked activity and not an overall reduction in physiological noise due to factors such as subject state or electrode impedance. Clearly, noisy listening environments impair perception. Subjects without extraneous noise in their brainstem response, as suggested by lower RMS amplitudes and sharper peak definition, were able to more accurately decipher what they heard, as evidenced by improved Listening Comprehension scores. A more precise brainstem response in noise may benefit the listener by providing a more accurate representation of the acoustic characteristics of the stimulus. This study also suggested that particular pre-training brainstem response measures in both quiet and noise may be related to improvements in measures of auditory processing and speech discrimination.

Clinicians and parents might be able to streamline their children's training programs based on information gained from pre-training speech-evoked brainstem response screening. This study and other related work from our laboratory [25,33] indicate that children with delayed brainstem timing are particularly likely to profit from auditory training. Thus, brainstem response screening may serve as a means to identify children for auditory training rehabilitation. Eventually, one might envision designing a training regimen tailored to a child's particular needs.

Not all children who went through auditory training demonstrated neurophysiological changes at the level of the brainstem. The amount of time between finishing training and returning for neurophysiological testing did not affect the outcome. The two subjects who did not show improved neural timing were in the middle of the group with respect to test–retest interval. Thus, the elapsed time appeared not to influence whether or not the subject exhibited timing improvements in the brainstem response. Because behavioral improvements could occur in the absence of neurophysiological changes, these changes may be sufficient, but are not entirely necessary for behavioral gains. However, a considerably larger population needs to be assessed before the "sufficient versus necessary" question can be answered definitively. It is possible that those children who showed no changes in brainstem activity had deficits that were not addressed by the training they received. Alternatively, those subjects' learning and auditory perception problems may not have stemmed from an auditory encoding deficiency at the brainstem level. Future longitudinal investigations may determine whether longer training sessions (hours per day or number of weeks) or repeated training sessions spread out over multiple 8-week periods would, in fact, alter the brainstem responses in the children who did not show physiological changes in this study. Extended research may fill in the gaps pertaining to the rigidity of the onset of the brainstem response to training. Follow-up testing would offer further information about the resilience of the neurophysiological and corresponding perceptual and behavioral effects of training.

Pre-conscious modification of sensory processing, prior to cognitive processing, may help overcome higher level deficits. Previous research [25] showed that children who went through *Earobics* training experienced changes in cortical responses to speech syllables, including accelerated maturation of the response, larger amplitudes, and improved quiet-to-noise inter-response correlations. The relationship between subcortical and cortical improvements reported here suggest that alterations in the brainstem response could have contributed to a more intact neural representation of sound at the cortical level.

4.4. Extensions of this work

This work demonstrated the existence of plasticity at the level of the human auditory brainstem and that auditory training can improve neural timing in response to sounds. There are broad-reaching implications. Previous work has shown that specific measures of the brainstem response can serve as biological markers that can identify a subset of language-impaired children with encoding deficits [6,33,64]. Consequently, the brainstem response to speech could be used in early detection of children "at risk" for these learning problems and who may benefit from auditory training. Thus, remediation can begin before children reach school age. Regardless of the age of identification and remediation, any changes in the brainstem response may be used as an objective monitor of auditory training success.

Although the children in this study underwent a general mode of auditory training, effects were transferable among sounds, since it was associated with alteration of the response to the laboratory test syllable /da/. Even so, one can imagine greater success of training programs that target specific difficulties or encoding deficits. For example, training via cue enhancement is used in other auditory training programs. The brainstem response employed here could be informative regarding effects of different forms of auditory training. Moreover, auditory training could be targeted at enhancing specific acoustic characteristics that are not encoded accurately at the brainstem. Finally, this experimental approach can be applied to other populations in which perceptual learning relevant to language and communication are of interest (e.g., second-language learning, aging, cochlear implant recipients, autistic individuals, etc.).

4.5. Conclusions

Neural encoding of sound in the human brainstem appears to be modified by auditory training. This study used measures of timing and magnitude of the brainstem response to identify possible mechanisms of brainstem plasticity. In addition, measures of brainstem plasticity were discovered to be associated with perceptual and cognitive changes. The conclusions drawn from this data set complement results drawn from cortical and subcortical animal and human studies that indicate learning-associated plasticity in the auditory pathway. Moreover, this study provides evidence that commercially available auditory training can alter the preconscious neural encoding of sound by improving neural synchrony in the human auditory brainstem.

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