Objective Biological Measures for the Assessment and Management of Auditory Processing Disorder

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Abstract: Auditory processing impairments negatively impact language learning, the ability to listen effectively in noisy environments, and the development of reading skills. Behavioral assessments of auditory processing provide valuable insight into auditory function but lack information about the biological health of the auditory pathway, and can be complicated by comorbid disorders, alertness, and motivation. The speech-evoked auditory brainstem response has recently been linked to communication skills such as speech-in-noise perception and reading ability and provides additional insight for the diagnosis and management of auditory processing disorders. This paper reviews how objective biological measures of auditory function can be used to reveal auditory system dysfunction in the absence of hearing loss.

Keywords: Auditory brainstem, auditory processing disorders, children, electrophysiology, neurophysiology, speech-in-noise perception.

INTRODUCTION

Hearing is fundamental to the development of successful language skills; deficits in hearing acuity and auditory processing can profoundly obstruct effective communication. Proper encoding of sound by the auditory system is especially important for the perception and discrimination of speech sounds, particularly consonants that can be difficult to perceive in noise [1, 2]. While hearing loss impedes the development of language and communication skills [3-9], many children with normal hearing exhibit impairments in auditory processing that likely contribute to and reflect deficits in reading and listening to speech in noise. Deficits in auditory processing skills such as tempo/rhythm perception, frequency discrimination, sounds-in-noise perception, pattern detection, and speech sound discrimination have been found for children with language learning disorders but normal hearing [10-16]. These children also show marked deficits in auditory nervous system function, both in the auditory cortex and auditory brainstem [17-29]. While the click-evoked auditory brainstem response has been used for decades in hearing assessments [30, 31], the speech-evoked brainstem response has recently been linked to speech-in-noise listening and reading skills [17-23, 32]. The speech-evoked auditory brainstem response offers a unique vantage point for assessing auditory function due to its remarkably faithful representation of the stimulus acoustics [33]. Auditory deficits contributing to impaired language and listening abilities in children are likely due to a complex interaction between sensory function and cognition. Once thought to be simply a sensory relay to the cortex, the auditory brainstem has been shown to be vastly malleable through meaningful interaction with sound [19, 34-48]. Due to the complex interaction between sensory and cognitive functions that likely occurs in impaired auditory processing, auditory brainstem measures may be particularly useful in revealing the biological correlates of communication. This paper reviews how objective biological measures of auditory function provide new insight into the diagnosis and management of auditory processing disorders (APD) and can be used to reveal auditory system dysfunction in the absence of hearing loss.

A PATIENT WITH APD

Imagine a mother bringing her nine year old son to see his doctor because he is having difficulty understanding his teacher and following directions. He seems to be able to focus his attention, but appears to not understand what is being said. Additionally, he has difficulty understanding people speaking in the presence of background noise and often “tunes out” of conversations at birthday parties and in the cafeteria at lunch. His performance in school is affected by his inability to follow spoken directions and he’s getting lost in the noise from the other students in his large classroom. Based on these symptoms, this child could have an auditory processing impairment, but how should he be evaluated?

His symptoms may be due to a number of sensory and/or cognitive deficits and so a differential diagnosis is needed. First, does the patient have peripheral hearing loss? A sensorineural or conductive hearing loss would impede his ability to understand spoken language and perceive speech in background noise. Pure tone thresholds can predict approximately 50% of the variance in speech-in-noise perception in adults [49]. Chronic otitis media and unaided sensorineural hearing loss relate to language delays and learning impairments, likely due to reduced auditory input during critical language-learning periods [3-9]. Transient hearing loss could be treatable with medication, while a genetic or induced permanent hearing loss could be aided by hearing

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1573-3963/11 $58.00+.00 © 2011 Bentham Science Publishers Ltd.

aids or cochlear implants. In either case, this child's poor listening performance is due to impaired audibility, which may be at least partly treatable. Second, does the child have typical attention behaviors? Children who have Attention-Deficit Hyperactivity Disorder (ADHD), particularly the Inattentive subtype, exhibit many of the characteristics of auditory processing disorders, including distractibility and difficulty following directions [50-52]. Nevertheless, audiologists and physicians ranked the most representative characteristics of the two disorders as being distinct, with Inattentive ADHD best characterized by inattentiveness, and auditory processing disorders being characterized by asking for things to be repeated and poor listening skills [50]. Because attention disorders are an overarching impairment, children would be impaired on both auditory and visual tasks [51]. Therefore, Inattentive ADHD may be distinguished from auditory processing disorders based on performance on visual attention tasks, which would be poor in a child with ADHD and typical in a child with impairments solely in auditory processing.

Assessment of auditory processing disorders typically includes behavioral tests that challenge the child's perceptual skills. Auditory processing skills may be measured with tests of detection, discrimination, or identification [51-54]. Stimuli can be presented to one or both ears, with the same (diotic listening) or different (dichotic listening) stimuli presented to the two ears simultaneously [51-54]. Particular skills that are important for efficient auditory processing and speech perception include temporal processing, pattern detection, and word or sentence recognition [51, 54]. Therefore, particular tests incorporate different types of tasks (detection, discrimination, identification), presentation (monaural, binaural), and skills (temporal processing, pattern detection, word or sentence recognition). Examples include dichotic digit identification, tone pattern sequencing, and temporal gap detection. Additionally, speech-in-noise perception tasks may be employed, which incorporate ecologically-valid speech stimuli and listening conditions. In all cases norms are available to compare an individual's performance to that of a group of same-aged peers and a positive diagnosis is based on abnormal performance across a number of measures.

Although auditory processing disorder batteries are meant to be comprehensive and allow for a differential diagnosis, the methods of testing are complicated by behavioral factors [52]. Poor performance on a given behavioral test may be due to a number of contributing factors other than auditory processing disorder. For example, if stimuli are verbal (i.e., speech) and the child has a reading disorder or language impairment, his/her performance might be compromised because of the verbal nature of the stimuli and not because of an auditory processing impairment. As mentioned above, attention deficit disorders may result in poor performance on psychophysical tasks overall, without an auditory-specific deficit. Performance on behavioral measures is also complicated by factors such as wakefulness, mood, and motivation that could impact performance on challenging tasks. Although some assessments may be more resistive to the effects of hearing loss, peripheral hearing loss of any kind could contribute to poor performance on behavioral assessments of auditory processing. Objective, biological measures of auditory processing sidestep some of the potential complications inherent to behavioral assessments and, most significantly, can elucidate the biological factors contributing to auditory processing. As discussed below, these objective measures of sensory function are highly related to cognitive skills such as speech-in-noise perception and auditory memory and make considerable contributions to the delineation of factors underlying auditory processing disorders.

BIOLOGICAL CORRELATES-AUDITORY BRAINSTEM RESPONSES

Recent recommendations for evaluating auditory processing include electrophysiological and electroacoustic measures of auditory function [51, 54, 55]. Evoked auditory brainstem responses are remarkably reliable and consistent across multiple assessments and are indicative of peripheral and central auditory function [30, 31, 56-59]. Click-evoked brainstem responses have been utilized as measures of peripheral hearing and central auditory function since the mid 1970s [30, 31]. Auditory brainstem responses to clicks have highly regular morphologies and response peak timing reflecting distinct neural generators. Because click responses are so highly regular, deviations in response peak timing of fractions of a millisecond are clinically meaningful. Abnormal response morphology or interpeak timing can be indicative of auditory pathway tumors or neural dysfunction such as neuropathy or demyelination due to multiple sclerosis [30]. The response to click stimuli also adapts to changes in stimulus level in characteristic ways, making these responses useful for assessing hearing thresholds in infants and those who are unable to respond to traditional audiometric testing [31]. The pattern of peak timing in response to decreasing stimulus level is indicative of the type and magnitude of hearing loss or central nervous system dysfunction [60]. For example, timing (latencies) outside normal limits for all presentation levels indicate a conductive hearing loss, while latencies outside normal limits only for lower stimulus levels indicate sensorineural hearing loss [60]. Absence of response peaks at any level may reflect neural dysfunction such as a tumor or profound sensorineural hearing loss [30]. Importantly, auditory brainstem responses are collected passively and are objective measures free of the attentional, motivational, and alertness factors that may complicate behavioral assessments of auditory function.

Speech-evoked brainstem responses faithfully represent many acoustic elements of the stimulus, including stimulus timing, fine structure (harmonics), and the fundamental frequency (pitch; see Fig. (**1**) and [33] for a review). The fundamental frequency of the stimulus and its lower harmonics are represented through neural phaselocking, with harmonics above the phaselocking limits of the brainstem, approximately 1200 Hz, likely reflected in response timing [18, 61-63]. As with click-evoked responses, deviations in response timing of fractions of milliseconds may indicate a peripheral hearing impairment. Additionally, for children with normal hearing thresholds and click-evoked responses, deviations in response timing can differentiate poor readers from good readers [17]. While the click-evoked response is mature by approximately age 3 [31, 60], the speech-evoked brainstem response does not appear to be mature until approximately age 5 [57]. Both click and speech-evoked

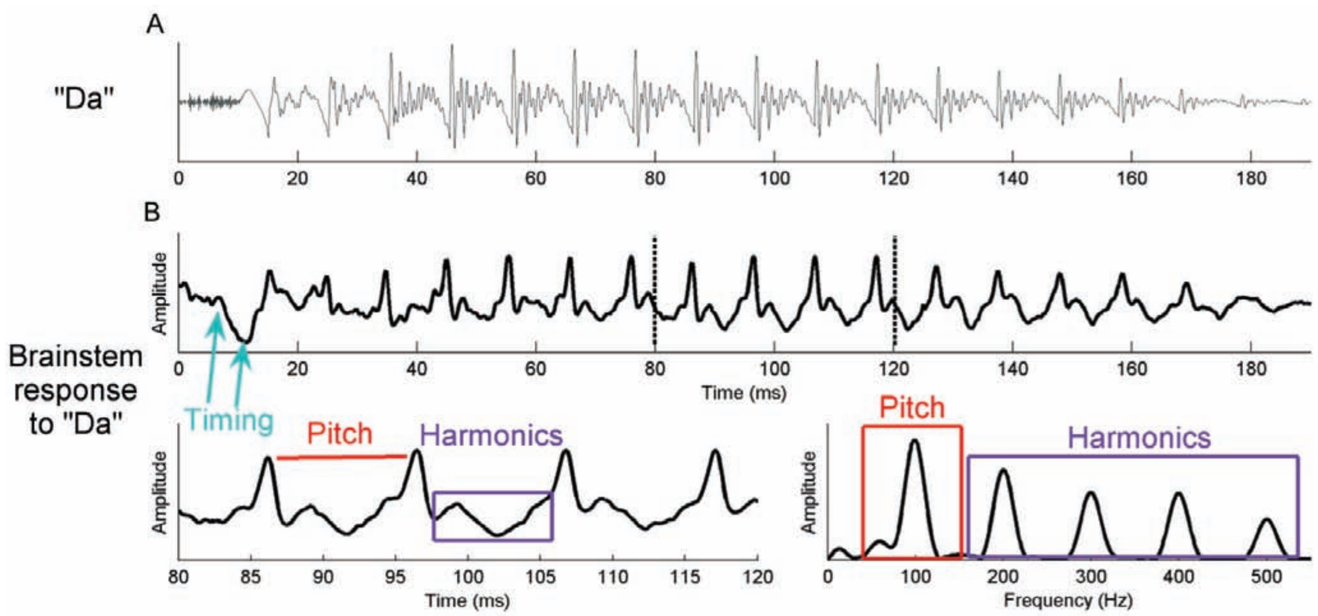

Fig. (1). Brainstem responses to speech sounds faithfully represent stimulus timing, pitch, and harmonics. **A**) The stimulus [da], shifted in time for visual purposes to reflect the neural conduction lag. **B**) The auditory brainstem response to [da] visually mimics the waveform of the stimulus in absolute timing as well as in periodicity. The portion of the response enlarged in the bottom panel is marked with black lines. Stimulus timing, pitch, and harmonics are preserved in the response, with pitch and harmonic representation best revealed in the frequency spectrum of the response (bottom right).

responses are extremely reliable and replicable across multiple test sessions [30, 31, 56-59].

In children with normal peripheral hearing (as assessed by an audiogram and click-evoked brainstem responses), the speech-evoked brainstem response can be predictive of speech-in-noise perception and reading ability. Recent analytical modeling revealed that reading and speech-in-noise perception have largely independent neural correlates, but are both related to certain neural measures [32]. While reading impairments and auditory processing disorders are often co-occurring, we will focus our discussion on the neural correlates of speech-in-noise perception as poor understanding of speech in noisy backgrounds is a hallmark characteristic of auditory processing impairments.

Representation of Vocal Pitch

Successful speech-in-noise perception relies on the ability to isolate and track a target voice in a complex auditory environment [64, 65]. Many cues enable the listener to distinguish and follow one voice from others, including spatial location, loudness, temporal continuity, vocal quality, and linguistic content of the message [64, 66]. One cue, vocal pitch, may be especially important [66]. Increasing the difference in fundamental frequency (an important element for the perception of pitch, [67]) between two competing speech streams makes the target stream more salient and distinguishable from a competitor or when in the presence of background noise [68-70]. Because vocal pitch is an important cue for isolating and following a target speech stream in background noise, we hypothesized that brainstem encoding of the fundamental frequency of speech sounds would be related to speech-in-noise perception. Children with poor speech-in-noise perception do indeed have weaker representation of the fundamental frequency than children with good speech-in-noise perception, see Fig. (**2A**) [21]. Speech-in-noise perception was assessed with the Hearing In Noise Test [71] and children were grouped based on their performance when the speech and the background noise came from the same spatial location, i.e., when pitch cues might be the most beneficial for perceiving the target speech over the background noise [21]. The same effect was found for young adults when responses were recorded to speech stimuli presented in noise, with poor speech-in-noise perceivers having weaker representation of the fundamental frequency than good speech-in-noise perceivers in increasing background noise [56]. In both studies these differences were largest for the response to the formant transition portion of the syllable [da], which represents the most acoustically complex and time-varying portion of the signal that is vulnerable to misperception in noisy listening conditions [1, 2]. Importantly, good and poor speech-in-noise perception groups were equated on IQ, audiometric threshold, and click-evoked brainstem responses [21], and speech-evoked brainstem representation of the fundamental frequency and audiometric threshold were not correlated [56]. The absence of differences in peripheral hearing indicates that speech-in-noise perception is linked to aspects of auditory function that are independent of hearing sensitivity.

Studies of speech-in-noise perception in adults further support the notion that speech-in-noise perception deficits can occur independently of peripheral hearing impairment [49, 72]. Deficits in impaired auditory working memory and attention can contribute to impairments in speech-in-noise perception in older adults with normal hearing [49, 64, 72]. If successful speech-in-noise perception relies on identifying and tracking one voice in competing background noise, then simple perception of the voice of interest is not sufficient. Instead, the linguistic message must be followed and understood over time, likely relying on auditory working memory. Adult musicians, who could be considered auditory experts, have better speech-in-noise perception and better auditory working memory than non-musicians, with both groups having normal audiometric hearing [73]. While musicians show enhanced auditory working memory and speech-in-noise perception, children with poor auditory processing appear to have weaker auditory working memory skills. A large-scale assessment of auditory processing skills in school-aged children found that inconsistent performance on the auditory processing tasks, which the authors suggest is reflective of poor auditory attention, correlated with parent reports of speech-in-noise perception [74]. As stated above, many symptoms of auditory processing disorder and attention deficit disorder are similar [50], however deficits were only found for auditory processing and not visual, highlighting that the impairments were modality specific and not a global attention deficit. Given these links, it is likely that children with poor speech-in-noise perception have impaired auditory working memory and additionally auditory brainstem dysfunction (e.g., weaker encoding of the fundamental frequency), again highlighting the interplay between cognitive and sensory functions indicative of central auditory processing disorders.

Pattern Detection

A key aspect of utilizing signal-specific cues for speech-in-noise perception is the ability to identify an acoustic element as a continuous and meaningful signal, in other words, the ability to detect patterns in the acoustic environment. We have found that neural representation of lower speech harmonics, those important for the perception of pitch, is enhanced when the syllable [da] is presented in a predictable (repetitive) sequence relative to when it is presented intermixed with seven other speech stimuli occurring randomly [19]. We suggest that the nervous system is able to benefit from the predictability of a stimulus by increasing the representation of repeating acoustic elements, which may aid in isolating and locking on to one voice in competing noise [19]. This effect is also seen in adults in response to musical notes, where the response to the whole musical phrase is improved over the course of the recording and the response

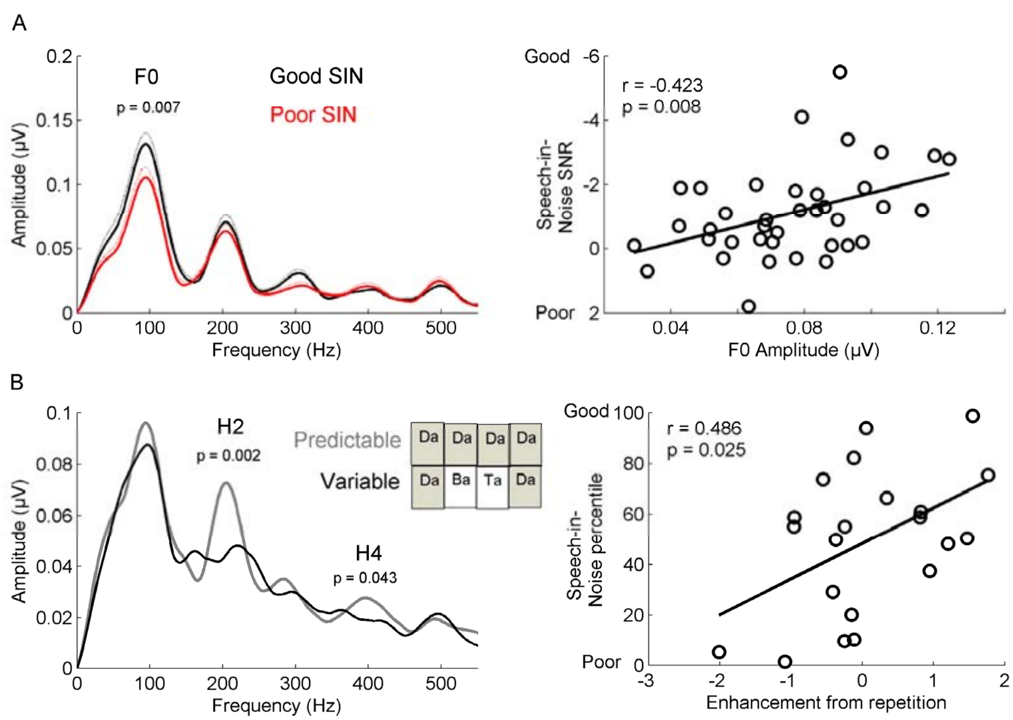

Fig. (2). Speech-in-noise perception is dependent on pitch representation and pattern detection, both aspects important for tracking one target voice over time. **A**) Good speech-in-noise (SIN) perceivers (black) have more robust encoding of the fundamental frequency of the speech sound [da] presented in quiet than poor SIN perceivers (red). Strength of fundamental frequency encoding is correlated with speech-in-noise perception across the whole group. *Note, the y-axis has been inverted to be more cohesive with the lower panel. The direction of good and poor SIN perception is marked. **B**) Brainstem representation of pitch-related harmonics is enhanced when the [da] stimulus is presented in a Predictable condition (gray) relative to a Variable condition (black). The degree of enhancement with repetition is correlated with SIN perception and absent in poor readers. The direction of good and poor SIN perception is marked.

to the second note of a repeated sequence shows even greater enhancement with repetition [75]. In children, the degree of benefit from repetition correlates with speech-in-noise performance, with better speech-in-noise perceivers showing the greatest benefit from repetition, see Fig. (**2B**) [19]. Children with poor reading ability showed no benefit from repetition [19]. Previous studies of sound perception and discrimination in children with dyslexia suggest that they are unable to lock onto and benefit from repetition of sounds to be used as standards in the listening tasks, suggesting they are unable to form "perceptual anchors" [76]. Theories of language learning suggest that young children are able to utilize the regularities and patterns of speech in their environment to determine which speech sounds are meaningful in their language [77-79]. The inability to identify patterns in the environment could affect early language learning, the creation of sound-to-meaning relationships, and lead to impaired speech-in-noise perception. In support of this theory, children with language impairments are unable to make use of patterns in their auditory environment when learning a pseudo-language [16], suggesting that pattern detection mechanisms can continue to be impaired throughout childhood.

Timing Degradation in Noise

The degree to which neural timing is degraded by background noise is also predictive of speech-in-noise perception. Young children, and those with reading impairments, are more adversely affected by increasing background noise than older children and adults [10, 11, 80-83]. The increased susceptibility of these populations to the degrading effects of background noise is reflected by subcortical neural responses; the auditory system responds less robustly to speech presented in background noise because the signal characteristics of the evoking stimulus are degraded. Auditory brainstem responses are reduced in amplitude and also delayed in time when stimuli are presented in background noise [84]. Good and poor speech-in-noise perceiving children have the same timing of response peaks when speech is presented in quiet but the response timing delay when speech is presented in background noise is much larger for the poor speech-in-noise perceivers than the good perceivers, see Fig. (**3A**) [20]. Along with pitch and spatial location cues, temporal cues are important for auditory stream segmentation [64, 66], and greater degradation of response timing in noise may lead to impaired processing of temporal cues in noise [20]. Adult musicians, who were noted above to have better speech-in-noise perception than non-musicians, additionally have more robust brainstem responses to speech presented in background noise [36]. That the neural encoding of speech is malleable with life-long musical training suggests that auditory-based training may alleviate neural encoding deficits associated with impaired speech-in-noise perception (more on this premise below).

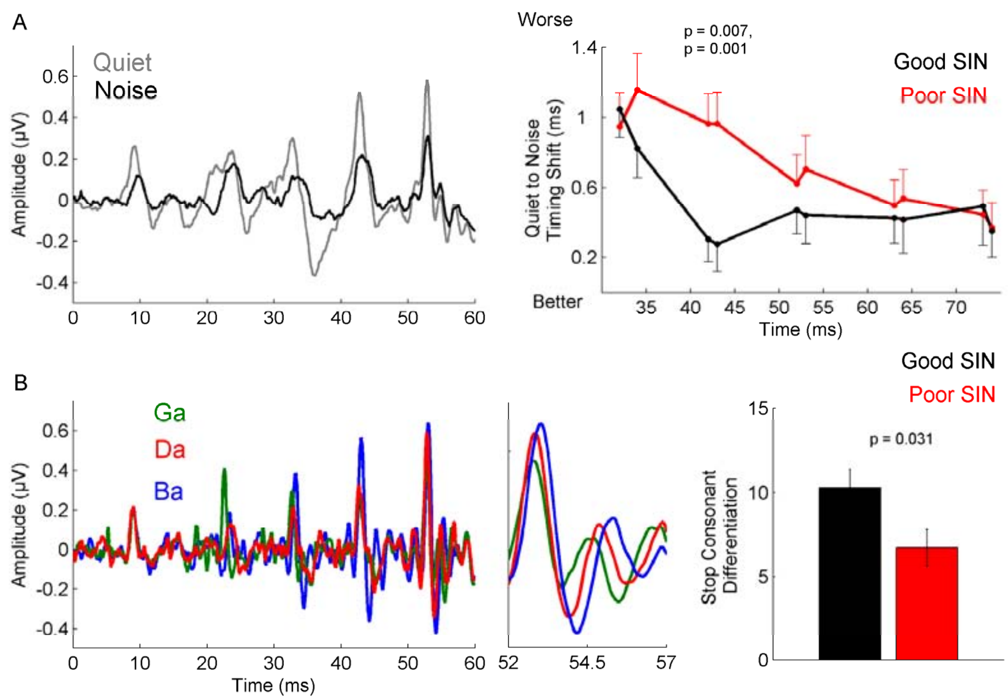

Fig. (3). Response timing reflects resistance to degradation in noise and differentiation of contrastive speech sounds, both linked to speech-in-noise skills. **A**) Responses to [da] presented in noise (black) are delayed relative to responses to [da] in quiet (gray). Poor SIN perceivers (red) have greater timing delays with the addition of noise than good SIN perceivers (black). **B**) Brainstem representations of [ga] (green), [da] (red), and [ba] (blue) syllables follow and expected timing pattern that reflects the differing formant frequencies among the stimuli. Good SIN perceivers (black) have significantly greater timing differences among the three responses, indicating better brainstem differentiation, than poor SIN perceivers (red).

Timing to Represent Harmonic Differences

Stop consonants (such as ba, da, and ga) are notoriously difficult to perceive in background noise because they are comprised of rapid frequency changes and transient elements [1, 2, 85]. The formant transition between a stop consonant and a following vowel includes frequency sweeps of many hundred Hertz (Hz) occurring over a fraction of a second [85]. The exact configuration of formants defines which consonant and vowel are being produced. The ability of the nervous system to fully represent formant-related harmonics is crucial for the correct perception of consonants and, as a result, the verbal message [86]. Although the auditory brainstem is able to represent frequency content (such as the lower harmonics discussed above) through phase-locking, this method of representation is limited to ~1200 Hz [61, 62]. Higher frequency content, such as that corresponding to most speech formants, occurs above the phaselocking limits of the brainstem and appears to be encoded through response timing [18, 63]. Responses to [ga] occur earlier than responses to [da], which in turn occur earlier than responses to [ba], reflecting the descending formant frequencies among the three stimuli [18, 63]. Importantly, the presence and magnitude of this latency pattern among responses correlates with speech-in-noise perception [18]. Good speech-in-noise perceivers have greater subcortical differentiation of these three stimuli as reflected by greater timing differences among responses to the three syllables, see Fig. (**3B**) [18]. Besides verbal content being another cue that may be used for tracking one target voice over time in background noise [64], the ability to understand the content of the message is obviously crucial for successful speech-in-noise perception and communication. Stream segmentation skills are useless if comprehension of the verbal message is impaired.

In sum, converging evidence indicates that speech-in-noise perception depends on the ability of the nervous system to isolate and track a target voice in competing background noise (using various cues such as vocal pitch and tempo), robustly represent target sounds in the presence of background noise, and faithfully represent acoustic elements important for the comprehension of the verbal message. Importantly, these nervous system functions can be measured objectively and reliably in humans.

AUDITORY PROCESSING AND READING ABILITY

Children with learning and language disorders can have impaired speech-in-noise perception relative to their typically-developing peers and perform poorly on a number of psychophysical tests of auditory perception [10-15]. Additionally, auditory processing skills and speech-in-noise perception in young children are predictive of later scholastic achievement [87-89]. One might hypothesize that the neural correlates of reading overlap with those of speech-in-noise perception and that some children with reading impairments could qualify as having auditory processing disorders based on behavioral and neural measures. That both hypotheses are supported by recent results highlights the complex relationship between auditory function and reading ability. The neural measures reflecting pattern detection, timing degradation in noise, and timing to represent harmonics discussed above are also related to reading ability [18-20], and recent analytical modeling of the neural correlates of reading and speech-in-noise perception found that measures of pattern detection significantly predicted variance in both reading and speech-in-noise skills in a group of children with a wide range of reading abilities [32]. Additionally, reading disorders and auditory processing disorders often co-occur [23, 25, 90]. Of a cohort of children with suspected auditory processing disorders, almost 50% of children had additional impairments in reading or language functions [90]. In a similar study of children with developmental dyslexia, all children performed poorly on at least one measure of auditory processing and 70% were classified as having auditory processing disorders (performance at least 2 standard deviations below the mean on two or more tests; [23]). The remaining 30% had impaired brainstem encoding of the stop consonant [da], suggesting that neural responses to speech may identify children with auditory processing impairments who have been missed by behavioral assessments [23]. This highlights the potential impact of brainstem responses to speech in the assessment and management of children with communication disorders.

UTILITY OF BIOLOGICAL MEASURES

As discussed above, behavioral measures of auditory processing and hearing thresholds are unable to provide information about the biological nature of observed impairments. Speech-evoked brainstem measures do yield biological correlates of performance on certain language and listening tasks. Importantly, they target the auditory pathway as a site of dysfunction contributing to the presenting complaint. The specific aspect of impaired speech-evoked brainstem activity, such as encoding of the fundamental frequency, harmonic encoding and/or pattern processing discussed above, yields considerable insight into the biological nature of the auditory deficit. Moreover, objective physiological measures sidestep some of the factors that can limit behavioral assessments such as attention, alertness, motivation, and comorbid language or reading impairments. Survey measures used as screening tools are subjective, and adult evaluations of a child's auditory processing skills may not truly reflect his/her auditory processing ability and risk for APD [91]. Evoked auditory brainstem responses, on the other hand, are objective and passively elicited. Speech-evoked brainstem response measures are linked to speech-in-noise perception, the child's auditory experience, and may be particularly reflective of auditory dysfunction, even in the absence of poor performance on dichotic and diotic listening tasks. Additionally, poor performance on behavioral measures may be corroborated or refuted by these neural measures, which could serve as metric for ruling in or out true auditory processing impairment as the cause of poor behavioral performance. These objective, physiological measures provide an additional viewpoint in the assessment of auditory processing disorders and have the potential to reveal underlying biological correlates of deficient auditory processing. Because the auditory brainstem has been shown to be malleable with life-long experience with sound [34-39], as well as short-term auditory training [41-43], these measures could be used to track training-related change in neural function and, in conjunction with behavioral measures, best identify which children would benefit the most from auditory training.

TRAINING-RELATED CHANGES IN AUDITORY BRAINSTEM RESPONSES

While auditory brainstem responses are generally recorded during passive listening conditions, these responses nonetheless reflect how sound has been used during a lifetime. Auditory subcortical function is experience dependent; it is malleable through short-term and long-term experience with sound [19, 34-47]. Numerous studies have shown that musicians have enhanced brainstem responses relative to non-musicians, likely due to their lifelong, multisensory interaction with music and the establishment of sound-to-meaning relationships [34-36]. Musician-related benefits are correlated with the starting age of musical training and amount of practice at the time of testing [34, 35, 37], highlighting that benefits are seen only with active interaction with meaningful sound. Similar effects are found for life-long language experience. Speakers of tonal languages have more accurate brainstem encoding of meaningful pitch contours in that language than non-tonal language speakers; however, language-related benefits are not seen for pitch contours that simply mimic the frequency change and are not linguistically meaningful [38-40]. Additionally, animal studies have revealed rapid and long-lasting brainstem neuroplasticity in response to behaviorally meaningful stimuli [45-47]. These results suggest that neuroplasticity arises from meaningful interaction with sound but not simply from repeated exposure.

Neural changes can also be seen after short-term auditory training for both adults and children with auditory or language impairments. Adults with impaired speech-in-noise perception who underwent targeted speech-in-noise training showed greater efferent brainstem activity after training, with auditory efferent activity before training predicting the degree of improvement with training [43]. Children with learning impairments who engaged in computer-based auditory training games showed more robust brainstem responses to speech presented in noise after completing the training [41]. Similar improvements have been shown for cortical responses to speech presented in noise, responses reflecting attention to one speech stream over another, and activity during reading-related tasks [29, 92-95]. Computer-based auditory training games can yield a number of benefits in language and reading skills for children with a wide variety of reading and language impairments, as well as for children who are typically-developing [96-98]. Similarly, enhanced auditory input of meaningful speech through a classroom FM system can result in improvements in speech-in-noise perception and classroom attention for children with auditory processing disorders [99]. As discussed above, life-long musical experience positively impacts auditory processing and neural function important for speech perception [34-37] and evidence suggests that musical training in children is linked to reading ability [100-102]. Active musical training may also serve as a particularly effective training paradigm for children with poor auditory function that affects communication skills [48, 103]. Thus, converging evidence indicates that auditory training can enhance auditory function behaviorally and biologically in children with auditory and learning impairments.

In all cases, training-related benefits are likely due to the ability to relate sound to meaning. Although children show improvement on language-related skills and in neural markers of directed attention, they do not necessarily improve on the training games themselves [93, 96]. These results suggest that auditory attention is a crucial element for engendering training-related improvements. With improved auditory attention, children learn to extract meaningful sound from background noise, increasing the opportunity to establish sound-to-meaning relationships. Animal studies have revealed that brainstem plasticity is mediated by descending modulation from the auditory cortex [45-47], and it is possibly through auditory attention that cortical activity influences brainstem function in humans. Therefore, children with auditory processing impairments may benefit from auditory training using computer-based games, assistive listening devices, or experience with music through improvements in auditory attention and creation of sound-to-meaning relationships. Due to its inherent stability yet malleability with auditory experience and demonstrated link to cognitive-language skills (such as speech-in-noise perception), the speech-evoked auditory brainstem response could be utilized as a metric to assess training related change in auditory function. Additionally, auditory brainstem responses before training may be predictive of training-related gain, as was demonstrated previously in adults [43].

CONCLUSIONS

Numerous studies have revealed that auditory processing skills are crucial for successful language learning and later academic achievement [3-15, 87-89]. Auditory processing can be impaired in the absence of peripheral hearing loss and in these cases central auditory dysfunction likely exists. Multiple measures of the speech-evoked auditory brainstem response are predictive of communication skills, such as speech-in-noise perception and reading ability [17-24]. Beyond providing a biological dimension for assessing the origin and nature of listening disorders, speech-evoked responses add sensitivity to standard behavioral assessments. Speech-evoked responses are objective, free of the subjectivity and inherent complications of behavioral tests, and quick to measure. Coupled with the fundamental experience-dependence of the auditory system established through decades of research on animal models [45-47, 104-106], training-related improvements in auditory function in humans suggest that children with auditory processing disorders are likely to benefit from auditory training, assistive listening devices, or musical experience [29, 41-43, 48, 92-95]. Through these meaningful experiences with sound, auditory attention is increased, sound-to-meaning relationships are developed, and children with auditory processing impairments may show improvements in auditory brainstem function due to cognitive-sensory interactions common in the auditory system. As detailed in this review, auditory brainstem function may serve as a key biological indicator of auditory processing disorders, inform the aspects of auditory processing that may be affected, suggest which patients may be most likely to benefit from auditory training, and provide a metric of improvement after remediation. The reliability of responses within an individual in conjunction with the tight links between auditory brainstem function and cognitively-based communication skills recommend this measure as an important addition to any APD testing battery.

CONFLICT OF INTEREST

The authors report no conflicts of interest, monetary or otherwise.

ACKNOWLEDGEMENTS

We would like to thank Samira Anderson for her review and critique of the manuscript. Work reviewed here was supported by the National Science Foundation (BCS-0921275) and the National Institutes of Health (DC010016).

REFERENCES

[1] Nishi K, Lewis DE, Hoover BM, Choi S, Stelmachowicz P. Children's recognition of American English consonants in noise. J Acoust Soc Am 2007; 127: 3177-88.

[2] Miller GA, Nicely PE. An analysis of perceptual confusions among some English consonants. J Acoust Soc Am 1955; 27: 338-52.

[3] Briscoe J, Bishop DVM, Norbury CF. Phonological processing, language, and literacy: A comparison of children with mild-to-moderate Sensorineural hearing loss and those with Specific Language Impairment. J Child Psychol Psychiatry 2001; 42: 329-40.

[4] Halliday LF, Bishop DVM. Frequency discrimination and literacy skills in children with mild to moderate Sensorineural hearing loss. J Speech Lang Hear Res 2005; 48: 1187-203.

[5] Bess FH, Dodd-Murphy J, Parker RA. Children with minimal Sensorineural hearing loss: Prevalence, educational performance, and functional status. Ear Hear 1998; 19: 339-54.

[6] Holm VA, Kunze LH. Effect of chronic otitis media on language and speech development. Pediatrics 1969; 43: 833-9.

[7] Freeman BA, Parkins C. The prevalence of middle ear disease among learning impaired children: Does higher prevalence indicate an association. Clin Pediatr (Phila) 1979; 18: 205-12.

[8] Feagans L, Sanyal M, Henderson F, Collier A, Appelbaum M. Relationship of middle ear disease in early childhood to later narrative and attention skills. J Pediatr Psychol 1987; 12: 581-94.

[9] Zinkus PW, Gottlieb MI. Patterns of perceptual and academic deficits related to early chronic otitis media. Pediatrics 1980; 66: 246-53.

[10] Bradlow AR, Kraus N, Hayes E. Speaking clearly for children with learning disabilities: Sentence perception in noise. J Speech Lang Hear Res 2003; 46: 80-97.

[11] Ziegler JC, Pech-Georgel C, George F, Lorenzi C. Speech-perception-in-noise deficits in dyslexia. Develop Sci 2009; 12: 732-45.

[12] Goswami U, Wang HL, Cruz A, *et al.* Language-universal sensory deficits in developmental dyslexia: English, Spanish, and Chinese. J Cogn Neurosci 2011; 23: 325-7.

[13] Tallal P, Miller SL, Jenkins WM, Merzenich MM. The role of temporal processing in developmental language-based learning disorders: Research and clinical implications. In: Blachman B, editor. Foundations of Reading Acquisition and Dyslexia: Implications for Early Intervention. Mahwah, NJ: Lawrence Erlbaum Assoc. Inc.; 1997. p. 49-66.

[14] Wright BA, Lombardino LJ, King WM, *et al.* Deficits in auditory temporal and spectral resolution in language-impaired children. Nature 1997; 387: 176-8.

[15] Halliday LF, Bishop DVM. Auditory frequency discrimination in children with dyslexia. J Res Read 2006; 29: 213-28.

[16] Evans JL, Saffran JR, Robe-Torres K. Statistical learning in children with specific language impairment. J Speech Lang Hear Res 2009; 52: 312-35.

[17] Banai K, Hornickel J, Skoe E, *et al.* Reading and subcortical auditory function. Cereb Cortex 2009; 19: 2699-707.

[18] Hornickel J, Skoe E, Nicol T, Zecker SG, Kraus N. Subcortical differentiation of stop consonants relates to reading and speech-in-noise perception. Proceedings of the National Academy of Sciences 2009; 106: 13022-7.

[19] Chandrasekaran B, Hornickel J, Skoe E, Nicol T, Kraus N. Context-dependent encoding in the human auditory brainstem relates to hearing speech in noise: Implications for developmental dyslexia. Neuron 2009; 64: 311-9.

[20] Anderson S, Skoe E, Chandrasekaran B, Kraus N. Neural timing is linked to speech perception in noise. J Neurosci 2010; 30: 4922-6.

[21] Anderson S, Skoe E, Chandrasekaran B, Zecker SG, Kraus N. Brainstem correlates of speech-in-noise perception in children. Hear Res 2010; 207: 151-7.

[22] Basu M, Krishnan A, Weber-Fox C. Brainstem correlates of temporal auditory processing in children with specific lanugage impairment. Develop Sci 2010; 13: 77-91.

[23] Billiet CR, Bellis TJ. The relationship between brainstem temporal processing and performance on tests of central auditory function in children with reading disorders. J Speech Lang Hear Res 2010.

[24] Wible B, Nicol T, Kraus N. Atypical brainstem representation of onset and formant structure of speech sounds in children with language-based learning problems. Biol Psychol 2004; 67: 299-317.

[25] Sharma M, Purdy SC, Newall P, *et al.* Electrophysiologyical and behavioral evidence of auditory processing deficits in children with reading disorder. Clin Neurophysiol 2006; 117: 1130-14.

[26] Cunningham J, Nicol T, Zecker SG, Kraus N. Neurobiologic responses to speech in noise in children with learning problems: Deficits and strategies for improvement. Clin Neurophysiol 2001; 112: 758-67.

[27] Abrams DA, Nicol T, Zecker SG, Kraus N. Auditory brainstem timing predicts cerebral dominance for speech sounds. J Neurosci 2006; 26: 11131-7.

[28] Abrams DA, Nicol T, Zecker SG, Kraus N. Abnormal cortical processing of the syllable rate of speech in poor readers. J Neurosci 2009; 29: 7686-93.

[29] Warrier CM, Johnson K, Hayes E, Nicol T, Kraus N. Learning impaired children exhibit timing deficits and training-related improvements in auditory cortical responses to speech in noise. Exp Brain Res 2004; 157: 431-41.

[30] Musiek F, Shinn JB, Jirsa RE. The auditory brainstem response in auditory nerve and brainstem dysfunction. In: Burkard RF, Eggermont JJ, Don M, editors. Auditory Evoked Potentials: Basic Principles and Clinical Application. Baltimore, MD: Lippincott Williams & Wilkins; 2007, p. 291-312.

[31] Sininger YS. The use of auditory brainstem response in screening for hearing loss and audiometric threshold prediction. In: Burkard RF, Eggermont JJ, Don M, editors. Auditory Evoked Potentials: Basic Principles and Clinical Application. Baltimore, MD: Lippincott Williams & Wilkins; 2007. p. 254-74.

[32] Hornickel J, Chandrasekaran B, Zecker SG, Kraus N. Auditory brainstem measures predict reading and speech-in-noise perception in school-aged children. Behav Brain Res 2011; 216: 597-605.

[33] Skoe E, Kraus N. Auditory brainstem response to complex sounds: A tutorial. Ear Hear 2010; 31: 302-24.

[34] Musacchia G, Sams M, Skoe E, Kraus N. Musicians have enhanced subcortical auditory and audiovisual processing of speech and music. Proc Natl Acad Sci USA 2007; 104: 15894-8.

[35] Wong PCM, Skoe E, Russo N, Dees T, Kraus N. Musical experience shapes human brainstem encoding of linguistic pitch patterns. Nat Neurosci 2007; 10: 420-2.

[36] Parbery-Clark A, Skoe E, Kraus N. Musical experience limits the degradative effects of background noise on the neural processing of sound. J Neurosci 2009; 29: 14100-7.

[37] Strait DL, Kraus N, Skoe E, Ashley R. Musical experience promotes subcortical efficiency in processing emotional vocal sounds. Annals of the New York Academy of Sciences: Neurosciences and Music III 2009; 1169: 209-13.

[38] Krishnan A, Xu Y, Gandour J, Cariani P. Encoding of pitch in the human brainstem is sensitive to language experience. Cogn Brain Res 2005; 25: 161-8.

[39] Xu Y, Krishnan A, Gandour J. Specificity of experience-dependent pitch represenation in the brainstem. Neuroreport 2006; 17: 1601-5.

[40] Krishnan A, Swaminathan J, Gandour J. Experience-dependent enhancement of linguistic pitch representation in the brainstem is not specific to a speech context. J Cogn Neurosci 2009; 21: 1092-105.

[41] Russo N, Nicol T, Zecker SG, Hayes E, Kraus N. Auditory training improves neural timing in the human brainstem. Behav Brain Res 2005; 156: 95-103.
[42] Song JH, Skoe E, Wong PCM, Kraus N. Plasticity in the adult human auditory brainstem following short-term linguistic training. J Cogn Neurosci 2008; 20:1892-902.
[43] deBoer J, Thornton ARD. Neural correlates of perceptual learning in the auditory brainstem: Efferent activity predicts and reflects improvement at a speech-in-noise discrimination task. J Neurosci 2008; 28: 4929-37.
[44] Galbraith GC, Bhuta SM, Choate AK, Kitahara JM, Mullen TAJ. Brain stem frequency-following response to dichotic vowels during attention. Neuroreport 1998; 9:1889-93.
[45] Atiani S, Elhilali M, David SV, Fritz J, Shamma S. Task difficulty and performance induce diverse adaptive patterns in gain and shape of primary auditory cortical receptive fields. Neuron 2009; 61: 467-80.
[46] Gao E, Suga N. Experience-dependent plasticity in the auditory cortex and the inferior colliculus of bats: Role of the corticofugal system. Proc Natl Acad Sci USA 2000; 97: 8081-6.
[47] Bajo V, Nodal F, Moore D, King A. The descending corticocollicular pathway mediates learning-induced auditory plasticity. Nat Neurosci 2010; 13: 253-60.
[48] Kraus N, Chandrasekaran B. Music training for the development of auditory skills. Nat Rev Neurosci 2010; 11: 599-605.
[49] Helfer KS, Wilber LA. Hearing loss, aging, and speech perception in reverberation and noise. J Speech Lang Hear Res 1990; 33: 149-55.
[50] Chermak GD, Tucker E, Seikel JA. Behavioral characteristics of auditory processing disorder and attention-deficit hyperactivity disorder: Predominantly inattentive type. J Am Acad Audiol 2002; 13: 332-8.
[51] Jerger J, Musiek F. Report of the consensus conference on the diagnosis of auditory processing disorders in school-aged children. J Am Acad Audiol 2000; 11: 467-74.
[52] Baran JA. Test battery considerations. In: Musiek F, Chermak GD, Eds. Handbook of (Central) Auditory Processing Disorder. San Diego, CA: Plural Publishing Inc.; 2007. p. 163-92.
[53] Schow RL, Seikel JA. Screening for (central) auditory processing disorder. In: Musiek F, Chermak GD, editors. Handbook of (Central) Auditory Processing Disorder. San Diego, CA: Plural Publishing Inc.; 2007. p. 137-62.
[54] American Speech-Language-Hearing Association. (Central) auditory processing disorders. The role of the audiologist. Rockville, MD, 2005.
[55] Hall JWI, Johnston KN. Electroacoustic and electrophysiologic auditory measures in the assessment of (central) auditory processing disorder. In: Musiek F, Chermak GD, editors. Handbook of (Central) Auditory Processing Disorder. San Diego, CA: Plural Publishing Inc.; 2007. p. 287-315.
[56] Song JH, Nicol T, Kraus N. Test-retest reliability of the speech-evoked auditory brainstem response. Clin Neurophysiol 2011; 122: 346-55.
[57] Johnson K, Nicol T, Kraus N. Developmental plasticity in the human auditory brainstem. J Neurosci 2008; 28: 4000-7.
[58] Lauter JL, Oyler RF. Latency stability of auditory brainstem responses in children aged 10-12 compared with younger children and adults. Br J Audiol 1992; 26: 245-53.
[59] Edwards RM, Buchwald JS, Tanguay PE, Schwafel JA. Sources of variability in auditory brain stem evoked potential measures over time. Electroencephalogr Clin Neurophysiol 1982; 53: 125-32.
[60] Hood LJ. Clinical applications of the auditory brainstem response. Clifton Park, NY: Delmar Learning; 1998.
[61] Liu L-F, Palmer AR, Wallace MN. Phase-locked responses to pure tones in the inferior colliculus. J Neurophysiol 2006; 95: 1926-35.
[62] Aiken SJ, Picton TW. Envelope and spectral frequency-following responses to vowel sounds. Hear Res 2008; 245: 35-47.
[63] Johnson K, Nicol T, Zecker SG, *et al.* Brainstem encoding of voiced consonant-vowel stop syllables. Clin Neurophysiol 2008; 119: 2623-35.
[64] Shinn-Cunningham BG, Best V. Selective attention in normal and impaired hearing. Trends Amplification 2008; 12: 283-99.
[65] Best V, Ozmeral EJ, Kopco N, Shinn-Cunningham BG. Object continuity enhances selective auditory attention. Proc Natl Acad Sci USA 2008; 105: 13174-8.
[66] Bregman AS. Auditory Scene Analysis: The Perceptual Organization of Sound. Cambridge, MA: MIT Press; 1990.
[67] Meddis R, O'Mard L. A unitary model of pitch perception. J Acoust Soc Am 1997;102:1811-20.
[68] Assmann PF. Fundamental frequency and the intelligibility of competing voices. Proceedings of the 14th International Congress of Phonetic Sciences 1999.
[69] Binns C, Culling JF. The role of fundamental frequency contours in the perception of speech against interfering speech. J Acoust Soc Am 2007; 122:1765-76.
[70] Darwin CJ, Hukin RW. Effectiveness of spatial cues, prosody, and talker characteristics in selective attention. J Acoust Soc Am 2000; 107: 970-7.
[71] Nilsson M, Soli SD, Sullivan JA. Development of the Hearing In Noise Test for the measurement of speech reception thresholds in quiet and in noise. J Acoust Soc Am 1994; 95: 1085-99.
[72] Dubno JR, Dirks DD, Morgan DE. Effects of age and mild hearing loss on speech recognition in noise. J Acoust Soc Am 1984; 76: 87-96.
[73] Parbery-Clark A, Skoe E, Lam C, Kraus N. Musician enhancement for speech in noise. Ear Hear 2009;30(6):653-61.
[74] Moore D, Ferguson M, Edmondson-Jones A, Ratib S, Riley A. Nature of auditory processing disorder in children. Pediatrics 2010; 126: e382-e390.
[75] Skoe E, Kraus N. Hearing it again and again: On-line subcortical plasticity in humans. PLoS ONE 2010; 5: e13645.
[76] Ahissar M, Lubin Y, Putter-Katz H, Banai K. Dyslexia and the failure to form a perceptual anchor. Nat Neurosci 2006; 9: 1558-64.
[77] Saffran JR. Statistical language learning: Mechanisms and constraints. Curr Directions Psychol Sci 2003; 12: 110-4.
[78] Maye J, Werker JF, Gerken L. Infant sensitivity to distributional information can affect phonetic discrimination. Cognition 2002; 82(3): B101-B11.
[79] Storkel HL. Learning new words: Phonotactic probability in language development. J Speech Lang Hear Res 2001; 44: 1321-37.
[80] Boets B, Ghesquiere P, van Wieringen A, Wouters J. Speech perception in preschoolers at family risk for dyslexia: Relations with low-level auditory processing and phonological ability. Brain Lang 2007; 101: 19-30.
[81] Brady S, Shankweiler D, Mann V. Speech perception and memory coding in relation to reading ability. J Exp Child Psychol 1983; 35: 345-67.
[82] Jamieson DG, Kranjc G, Yu K, Hodgetts WE. Speech intelligibility of young school-aged children in the presence of real-life classroom noise. J Am Acad Audiol 2004; 15: 508-17.
[83] Wilson RH, Farmer NM, Gandhi A, Shelburne E, Weaver J. Normative data for the words-in-noise test for 6- to 12-year old children. J Speech Lang Hear Res 2010; 53: 1111-21.
[84] Burkard RF, Don M. The auditory brainstem response. In: Burkard RF, Don M, Eggermont JJ, editors. Auditory Evoked Potentials: Basic Principles and Clinical Applications. Baltimore, MD: Lippincott Williams & Wilkins; 2007. p. 229-53.
[85] Delattre PC, Liberman AM, Cooper FS. Acoustic loci and transitional cues for consonants. J Acoust Soc Am 1955; 27: 769-73.
[86] Kraus N, Nicol T. Brainstem origins for cortical "what" and "where" pathways in the auditory system. Trends Neurosci 2005; 28: 176-81.
[87] Benasich AA, Tallal P. Infant discrimination of rapid auditory cues predicts later language development. Behav Brain Res 2002; 136: 31-49.
[88] Boets B, Wouters J, Van Wieringen A, De Smedt B, Ghesquiere P. Modelling relations between sensory processing, speech perception, orthographic and phonological ability, and literacy achievement. Brain Lang 2008; 106: 29-40.
[89] Corriveau KH, Goswami U, Thomson JM. Auditory processing and early literacy skills in a preschool and kindergarten population. J Learn Disabil 2010; 43: 369-82.
[90] Sharma M, Purdy SC, Kelly AS. Comorbidity of auditory processing, language, and reading disorders. J Speech Lang Hear Res 2009; 52: 706-22.
[91] Wilson WJ, Jackson A, Pender A, *et al.* The CHAPS, SIFTER and TAPS-R as predictors of (C)AP skills and (C)APD. J Speech Lang Hear Res 2011; 54: 278-91.

[92] Russo N, Hornickel J, Nicol T, Zecker SG, Kraus N. Biological changes in auditory function following training in children with autism spectrum disorders. Behav Brain Funct 2010; 6(60).

[93] Stevens C, Fanning J, Coch D, Sanders L, Neville H. Neural mechanisms of selective auditory attention are enhanced by computerized training: Electrophysiological evidence from language-impaired and typically developing children. Brain Res 2008; 1205: 55-69.

[94] Temple E, Deutsch GK, Poldrack RA, *et al.* Neural deficits in children with dsylexia ameliorated by behavioral remediation: Evidence from functional MRI. Proc Natl Acad Sci USA 2003;100: 2860-5.

[95] Gaab N, Gabrieli JDE, Deutsch GK, Tallal P, Temple E. Neural correlates of rapid auditory processing are disrupted in children with developmental dyslexia and ameliorated with training: An fMRI study. Restor Neurol Neurosci 2007; 25: 295-310.

[96] Moore D, Rosenberg JF, Coleman JS. Discrimination training of phonemic contrasts enhances phonological processing in mainstream school children. Brain Lang 2005; 94: 72-85.

[97] Tallal P, Miller SL, Bedi G, *et al.* Language comprehension in language-learning impaired children improved with acoustically modified speech. Science 1996; 271: 81-4.

[98] Merzenich MM, Jenkins WM, Johnston P, *et al.* Temporal processing deficits in language-learning impaired children ameliorated by training. Science 1996; 271: 77-81.

[99] Johnston K, John A, Kreisman N, Hall J, Crandell C. Multiple benefits of personal FM system use by children with Auditory Processing Disorder (APD). Int J Audiol 2009; 48: 371-83.

[100] Foregard M, Schlaug G, Norton A, Rosam C, Iyengar U. The relation betwen music and phonological processing in normal-reading children and children with dyslexia. Music Perception 2008; 25: 383-90.

[101] Overy K. Dyslexia and music: From timing deficits to musical intervention. Ann N Y Acad Sci 2003; 999: 497-505.

[102] Anvari SH, Trainor LJ, Woodside J, Levy BA. Relations among musical skills, phonological processing, and early reading ability in preschool children. J Exp Child Psychol 2002; 83: 111-30.

[103] Schon D, Boyer M, Moreno S, *et al.* Songs as an aid for language acquisition. Cognition 2008; 106: 975-83.

[104] Fritz J, Shamma S, Elhilali M, Klein D. Rapid task-related plasticity of spectrotemporal receptive fields in primary auditory cortex. Nat Neurosci 2003; 6: 1216-23.

[105] Fritz J, David S, Yin P, Shamma S. Behavioral gating of responses to auditory stimuli in ferret prefrontal cortex. Association for Research in Otolaryngology; February 14-19; Baltimore, MD2009.

[106] Suga N, Xiao Z, Xiaofeng M, Weiqing J. Plasticity and corticofugal modulation for hearing in adult animals. Neuron 2002; 36: 9-18.

Received: May 01, 2011 Revised: May 20, 2011 Accepted: May 20, 2011