Chapter 3
Auditory Processing Disorder: Biological Basis and Treatment Efficacy

Nina Kraus and Samira Anderson

Abstract Auditory processing disorders contribute to communication difficulties in children with language-based learning impairments and in older adults who have trouble hearing in background noise. Therefore, deficits in auditory processing are widespread among these diverse populations. For this reason, it behooves both scientific and clinical communities to consider optimum techniques for assessing and managing these deficits. The auditory brainstem response to complex sounds (cABR) provides an objective index of the biological health of the central auditory system. The cABR is also a sensitive indicator of training-induced neuroplastic changes and can therefore be used to assess treatment efficacy. Once integrated into clinical practice, use of the cABR may facilitate more widespread evaluation and treatment of auditory processing disorders.

Keywords Auditory aging • Auditory-based learning impairments auditory training • cABR • Central auditory function • Frequency following response • Objective assessment • Real-world environments • Speech in noise • Temporal processing

N. Kraus (✉)
Departments of Communication Sciences, Neurobiology and Physiology, and Otolaryngology, Northwestern University, 2240 N. Campus Dr., Evanston, IL 60208, USA
e-mail: nkraus@northwestern.edu
URL: http://www.brainvolts.northwestern.edu

S. Anderson
Department of Hearing and Speech Sciences, University of Maryland, College Park, MD 20742, USA
e-mail: sander22@umd.edu
URL: http://www.hearinbrainlab.umd.edu

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3.1 Introduction

The concept of an auditory processing disorder (APD) has been around for decades. Myklebust (1954) first defined APD as a disorder of auditory perception despite normal audiometric thresholds. In the 1970s, behavioral tests of auditory processing were developed and normative values were established based on performance of individuals with known cortical lesions. Now these behavioral tests are often used to assess auditory processing in children and adults who do not have identified anatomical abnormalities but have apparent hearing difficulties in difficult listening situations.

The most common manifestation of APD is difficulty understanding speech in noise. Deficits in auditory processing are prevalent in children with learning disabilities (Bradlow et al. 2003; Sharma et al. 2006). Children with dyslexia have poorer speech-in-noise (SIN) perception than children who are typically developing (Bradlow et al. 2003). They also have difficulty recognizing speech degraded by the removal of temporal fine structure cues, demonstrating that a speech perception deficit can occur in the presence of either external or internal noise (Ziegler et al. 2009). In addition to deficits in SIN perception, children with dyslexia have poorer performance compared to children who are typically developing on commonly used tests of auditory processing, such as the Pitch Pattern Sequence Test (Musiek 1994), the Dichotic Digits Test (Musiek 1983), and the Random Gap Detection Test (Dias et al. 2012). Given the evidence that children with learning disabilities often have APD, routine screening for APD may be beneficial in such children.

Older adults may also be affected by auditory processing deficits. Older adults have more trouble understanding speech in noisy environments than younger adults, even with audiometrically normal hearing thresholds (Gordon-Salant and Fitzgibbons 1993; Souza et al. 2007). These deficits may arise from decreased ability to process the fast temporal changes in speech (Grose et al. 2006; Gordon-Salant et al. 2007). Older adults have more difficulty identifying words that differ in temporal segmental speech cues (i.e., “dish” vs. “ditch” or “beat” vs. “wheat”) than young adults (Gordon-Salant et al. 2006, 2008), which may account for the older adult’s difficulty when trying to perceive these cues in compromised environments. Temporal processing deficits have also been revealed by electrophysiological studies. Older adults have delayed neural timing for the onset, offset, and consonant–vowel regions of the brainstem response to speech syllables compared to younger adults (Anderson et al. 2012; Clinard and Tremblay 2013) and they have decreased gap detection amplitudes in cortical responses (Lister et al. 2011; Harris et al. 2012). Current evaluation of hearing difficulties in older adults is typically limited to assessment of audiometric thresholds and speech perception in quiet despite the fact that the number one complaint of older adults is trouble hearing in noise. Therefore, assessment of auditory processing is warranted when an individual reports greater hearing difficulty than would be predicted from audiometric thresholds.

Referrals for APD evaluations from educators, psychologists, speech-language pathologists, and other professionals are increasing, and parents are demanding these services when they learn of the existence of APD on the Internet and other media sources. Yet, despite the need for APD assessment and the availability of behavioral assessments, audiologists have been reluctant to include APD assessment in their clinical practices. A gap exists between the research supporting an auditory processing basis for learning impairments and speech perception deficits and the application of this knowledge in a clinical setting.

Several factors contribute to the lack of translation into clinical practice. One issue is a disagreement about whether APD exists as a separate entity apart from deficits in cognitive functions such as attention and memory (Cacace and McFarland 1998; Moore et al. 2010). Furthermore, APD is often comorbid with other learning problems such as dyslexia or attention deficit disorder (Sharma et al. 2009), with possible effects on the validity of the test results. Clinicians disagree on the criteria for APD diagnosis. Wilson and Arnott (2012) used nine different diagnostic criteria to determine the rate of APD diagnosis in 150 school-age children who completed an APD test battery and found that the rates of diagnosis varied from 7.3 to 96.0 %. Finally, clinicians are unsure of the efficacy of the treatments purported to improve auditory processing. Although benefits of training and/or FM systems for children with APD have been reported (Sharma et al. 2012), consensus has been hampered by disagreement about what constitutes an APD diagnosis and the paucity of outcome studies. Existing studies are difficult to compare because of methodological differences (Fey et al. 2011; Wilson et al. 2013). Conclusive outcome studies may be an unrealistic expectation given the different ways that APD is defined and the difficulties encountered when conducting longitudinal studies. In summary, some individuals have inordinate difficulty hearing speech in noise or paying attention to relevant sounds and excluding irrelevant stimuli, suggesting an auditory processing disorder. Large-scale studies in clinical settings combining behavioral and biological metrics are likely to be revealing and to provide guidance to clinicians.

Given that the attention and memory requirements of behavioral assessments of APD may reduce their validity, an objective assessment is needed for diagnostic evaluation and to document treatment efficacy. Electroencephalography (EEG) is the primary tool for evaluating infant peripheral hearing ability, but its use can be extended to evaluation of central auditory function. In children with learning problems, the ability to discriminate along a continuum of syllables differing in the spectral content of the formant transition correlates with the magnitude of mismatch negativity responses (MMNs) (Kraus et al. 1996). The middle latency response (MLR) has been used to diagnose APD and assess treatment benefits (Schochat et al. 2010). The use of the MLR is limited by between-subject variability, but this can be minimized by using between-ear amplitude differences rather than absolute amplitudes to determine the presence of an APD (Weihing et al. 2012). Typically, individuals with normal auditory processing have equivalent amplitudes when either the right or left ear is stimulated, but individuals with APD show unilateral deficits.

The auditory brainstem response to complex sounds (cABR; also called the frequency following response, or FFR) is another EEG evaluation that has recently been used to evaluate auditory processing disorders in a variety of clinical impairments, including dyslexia, SIN perception deficits, APD, hearing loss, and aging. Because the cABR resembles the evoking stimulus acoustically and visually (Galbraith et al. 1995), the accuracy of encoding specific speech features, such as timing, pitch, and harmonics, is feasible to assess to an extent that is not possible when using slower, cortical potentials (MLRs) and late latency responses (MMNs). The following sections will describe the features of the cABR and its clinical applications for assessment of APD and therapeutic outcomes.

3.2 cABR: Objective Assessment of Central Auditory Function

The cABR's origins can be dated back to the frequency following response in the late 1960s and early 1970s. The term frequency following response (FFR) is used because the waveforms in the response reproduce the fundamental frequency of the stimulus (Marsh and Worden 1968). Moushegian et al. (1973) first demonstrated that the FFR can be recorded from the vertex of the human scalp. Initial experiments used simple sounds such as sine waves or tone bursts (Gardi and Merzenich 1979; Hall 1979), but in the 1980s Greenberg published the results of recording FFRs to vowels (Greenberg 1980) and to complex tones (Greenberg et al. 1987).

It was initially thought that the FFR could be used to assess infant hearing, but the FFR is more robust for low-frequency tones (Gardi et al. 1979), limiting its utility for the assessment of high-frequency thresholds. However, the last decade has seen demonstrations of the utility of the FFR for evaluating clinical disorders, including learning disabilities (Ghannoum et al. 2014; Malayeri et al. 2014), reading impairments (Banai et al. 2009; Hornickel and Kraus 2013; White-Schwoch et al. 2015), specific language impairment (Basu et al. 2010), autism (Russo et al. 2009), SIN perception deficits in children (Anderson et al. 2010a, b), APD (Billiet and Bellis 2010; Filippini et al. 2012), attention-deficit/hyperactivity disorder (Jafari et al. 2014), and age-related hearing difficulties (Anderson et al. 2013a, b; Clinard and Tremblay 2013).

The term cABR was adopted to differentiate these recordings from those made to simple and periodic stimuli (Skoe and Kraus 2010). Many of the aforementioned studies were conducted using the syllable [da], which contains an initial stop consonant burst, a consonant-vowel transition, and a steady-state vowel. Therefore, the cABR includes a response to a transient consonant in addition to the periodic, steady-state response that characterizes the traditional FFR. As mentioned earlier, the cABR's fidelity to the evoking stimulus permits evaluation of the encoding accuracy of speech components important for everyday communication—timing, pitch, and timbre (Fig. 3.1). The evaluation of these components has been useful in understanding the biological bases of the aforementioned clinical populations. For example, children with reading disabilities have delayed timing and reduced representation of the first formant harmonics in speech compared to children with

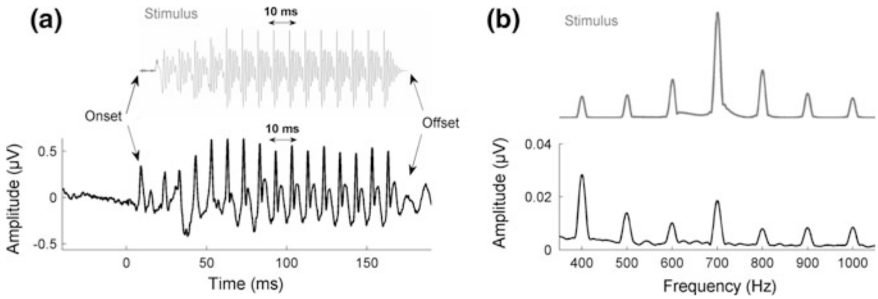

Fig. 3.1 When the stimulus waveform 170-ms [da] is temporally shifted to account for neural conduction, the stimulus timing of the onset and offset is apparent in the response waveform (average responses of 15 young adults with normal hearing). The periodicity of the stimulus waveform, with repeating peaks every 10 ms corresponding to the F_0 of 100 Hz, is also replicated in the response waveform (**a**). The harmonics of the response (average responses of 15 young adults) mirror those of the stimulus (**b**)

normal reading ability (Banai et al. 2009; Hornickel et al. 2009). Children with autism have less accurate pitch tracking than children who are typically developing (Russo et al. 2008). Finally, older adults with good SIN performance have better subcortical representation of the fundamental frequency (F_0) and less neural degradation in noise than older adults with poor SIN performance (Anderson et al. 2011). Each of these clinical communication disorders affects distinct components of the cABR, resulting in a unique neural signature for specific impairments (Kraus and Nicol 2014; Kraus and White-Schwoch 2015).

Another important feature of the cABR is its high reliability, a necessary condition for use in a clinical setting. Measures of pitch, timing, and timbre are reliable from session to session in school-age children (Hornickel et al. 2012a) and in young adults (Song et al. 2011). Further studies need to be conducted to determine cABR reliability in infants and older adults, two populations in which assessment may be unreliable due to immature development or variability associated with aging.

Finally, cABR features can be modified with experience. The cABR arises largely from the inferior colliculus (IC) in the midbrain (Chandrasekaran and Kraus 2010), a hub of intersecting connections of afferent and efferent fibers (Bajo and King 2012; Garcia-Lazaro et al. 2013). Animal models have demonstrated that connections between auditory cortex and IC are essential for auditory learning (Gao and Suga 2000; Bajo et al. 2010). Human studies have demonstrated that features of the cABR can be modified with online learning (Skoe et al. 2013b; Escera and Malmierca 2014), with as little as 1 week of training (Song et al. 2008), through classroom FM systems (Hornickel et al. 2012b) or through lifelong language experience (Krishnan et al. 2010; Krizman et al. 2012) and music training (reviewed in Kraus and White-Schwoch 2016). Therefore, given its reliability and its sensitivity to individual differences in auditory processing, the cABR may be ideal for evaluating the efficacy of APD training programs.

3.3 Integrating the cABR into Clinical Practice

A new EEG assessment has a high likelihood of being adopted into clinical practice if it can be incorporated into an existing platform used for other testing, such as hearing screening or diagnostics. The first clinical system, BioMARK, was built on an existing platform in common use in clinical sites in 2005. It was developed at Northwestern University by the Kraus Lab and was commercialized by Bio-logic Systems Corporation (Natus Medical, Mundelein, IL). King et al. (2002) first reported brainstem responses to a speech syllable in children with learning impairments, and Johnson et al. (2005) reported deficient sound encoding in children with learning or auditory processing disorders using the Bio-logic System. This particular system used a 40-ms [da], which contained an initial stop consonant burst followed by a consonant–vowel (CV) transition. The short length of the syllable makes it suitable for clinical assessment, as the total recording can be accomplished in less than 20 min. The inclusion of the CV transition permits evaluation of the most perceptually vulnerable region of the speech syllable (Miller and Nicely 1955). The system includes a template with marked peaks (onset peak: V, onset trough: A, FFR peaks: D, E, and F, and offset peak: O) to facilitate clinician peak picking (Fig. 3.2).

Since 2011, the cABR has been available as a research module from Intelligent Hearing Systems (IHS; Miami, FL). This version permits researchers or clinicians to use a variety of stimuli of different lengths. Using a full-length speech syllable is useful for comparing responses to different regions of the stimulus—the onset, transition, steady state, and offset (Fig. 3.3). Neural timing delays in clinical populations are often specific to the onset, offset, and transition regions of the stimulus (Anderson et al. 2010a, 2012).

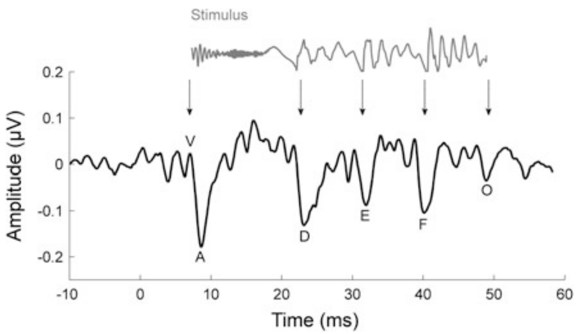

Fig. 3.2 The 40-ms [da] and its average response obtained from 25 infants aged 3–11 months using the BioMARK clinical EEG system. The onset peak and trough (*V* and *A*), FFR peaks (*D*, *E*, and *F*), and offset peak (*O*) correspond to the onset, FFR, and offset of the stimulus when it has been shifted to account for neural conduction time [Adapted from Anderson et al. (2015)]

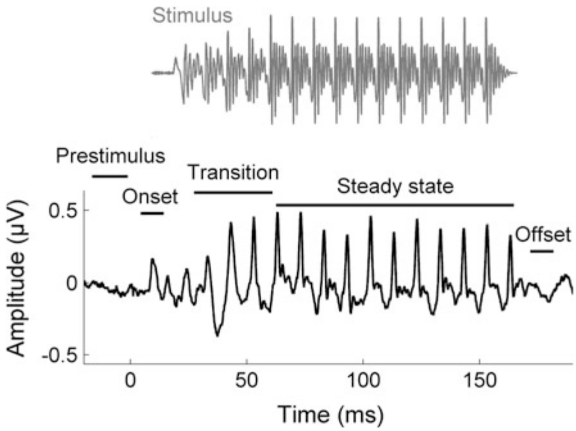

Fig. 3.3 The 170-ms stimulus [da] and the average response waveform of 15 older adults with normal hearing (aged 60–69 years). The prestimulus, onset (~8 ms), transition (20–60 ms), steady state (60–120 ms), and offset (~185 ms) are marked on the response waveform [Adapted from Anderson et al. (2012)]

Another benefit of the full-length syllable is the ability to compare phase differences between responses to two different stimuli. For example, an individual's responses to the syllables [ga] and [ba] should be in phase with each other in the steady-state vowel region, which is acoustically identical between the syllables. However, the responses to the consonant–vowel transitions should be out of phase, as differences between the stimuli in the formant transition are reflected in the phase of the response (Skoe et al. 2011). A cross-phase analysis allows the clinician/researcher to evaluate the extent of brainstem consonant differentiation in an individual (Fig. 3.4).

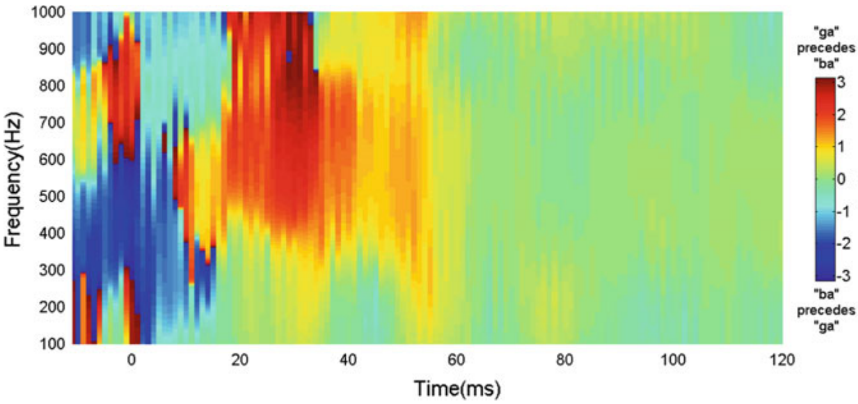

Fig. 3.4 Cross-phaseogram obtained from an individual 10-month-old infant. In the transition region (~20–60 ms), the phase of the response to [ga] leads [ba], indicated by the *red* color, in the formant transition region (400–720 Hz), as expected given tonotopicity of the auditory system. In the steady-state region (60–120 ms), the responses of the two syllables are in phase, as indicated in *green*

Clinical use of the cABR can expand the diagnostic capabilities of an evoked potential instrument. The current clinical protocol focuses on the ear; the cABR would expand testing to include auditory processing to the midbrain, reflecting influences of the corticofugal pathway, and would provide an objective assessment of auditory processing and treatment efficacy. Sections 3.4–3.7 describe how the cABR has been used to increase understanding of auditory processing impairments in children and in older adults and how it has been used to document treatment efficacy of training programs in real-world settings.

3.4 Evaluation of APD and Auditory-Based Learning Impairments

Some children with learning impairments, either dyslexia or specific language impairment (SLI), have deficits in auditory skills compared to typically developing children. For example, children with learning impairments may have difficulty perceiving rapidly presented auditory stimuli (Tallal 1980; Wright et al. 1997). Children with dyslexia may also have impaired perception of syllable onsets because of the inability to lock onto amplitude envelope modulations of speech (Goswami et al. 2002). Furthermore, there are no appreciable differences on auditory processing tests between groups of children with APD and with SLI (Miller and Wagstaff 2011). Therefore, objective and more granular evaluations of auditory processing skills in children with APD or SLI are warranted.

Similarities also exist between children with APD and children with auditory neuropathy spectrum disorder (ANSD), a disorder characterized by normal outer hair cell function with disrupted auditory nerve activity (Zeng et al. 2005). Individuals with ANSD have fluctuating hearing levels and may even have normal audiometric thresholds (Kraus et al. 1984, 2000). However, they exhibit poor temporal processing with elevated gap detection and temporal masking thresholds, and they have difficulty detecting signals in noise (Zeng et al. 2005). However, unlike individuals with ANSD, for whom the click-evoked ABR is absent, children with APD typically have normal click ABR latencies. The APD deficit is more subtle than that of ANSD and may be revealed only with the use of a complex stimulus (Filippini and Schochat 2009; Hornickel and Kraus 2013).

A pattern of cABR findings has emerged in children with reading impairments: they have delayed neural responses and reduced representation of higher speech harmonics (Banai et al. 2009; Malayeri et al. 2014) (Fig. 3.5). These findings may arise from a decrease in the synchrony of neural firing, which can lead to delayed response peaks and greater intertrial variability (Don et al. 1976; Schaette et al. 2005). Increased intertrial variability was found in a rat model of dyslexia (Centanni et al. 2014) and in poor readers compared to good readers (Hornickel and Kraus 2013). A similar neural difficulty is found in the FFRs of children with SLI.

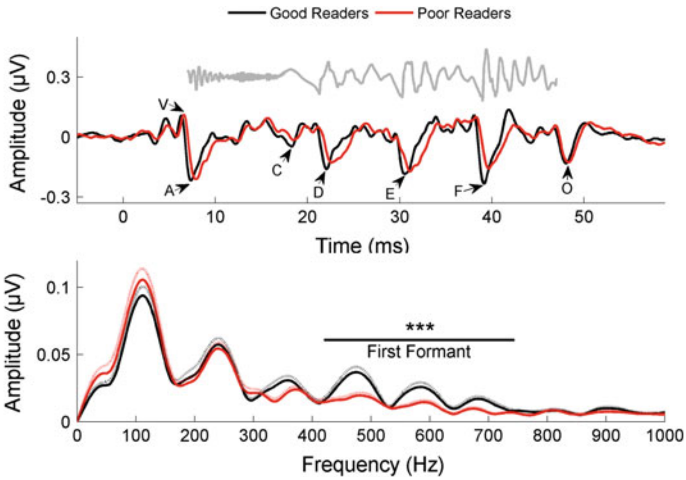

Fig. 3.5 Comparison of cABRs to a 40-ms [da] in children, ages 7–15, who were divided into groups of good ($N = 35$) and poor ($N = 28$) readers. *Top* Poor readers (*red*) have delayed latencies compared to good readers (*black*) for all seven peaks in the cABR. *Bottom* Poor readers have reduced representation of the first formant compared to good readers. *Dotted line* 1 S.E. ***$p < 0.002$ [adapted from Banai et al. (2009), *Cerebral Cortex*, 19(11), 2699–2707]

Compared to children with normal language abilities, children with SLI have degraded frequency tracking to tonal sweeps, especially at higher presentation rates, suggesting a disruption in sustained neural phase locking of the FFR generators in the brainstem (Basu et al. 2010). The inability to accurately represent the acoustic elements of speech that are critical for phonemic discrimination may impair the internal mapping of sound necessary to develop language or reading.

Delayed neural timing is also found in normal-hearing children with relatively poor speech-in-noise performance but only when comparing responses obtained in a background-noise condition to those obtained in quiet. The effects of noise on brainstem responses include delayed latencies and reduced amplitudes (Burkard and Sims 2002). Anderson et al. (2010a) found that 8- to 12-year-old children with poor SIN perception have greater noise-induced peak latency delays than age- and hearing-matched children with good SIN perception when comparing responses to a speech syllable obtained in quiet and in six-talker babble. This noise-induced delay was also seen in children who were divided into groups of good and poor readers (Fig. 3.6). Sperling et al. (2005) hypothesized that a noise-exclusion deficit prevents the formation of perceptual categories across sensory domains, contributing to reading difficulties. The finding of noise-induced delays in children with deficits in both SIN perception and reading suggests a common neural mechanism underlying these impairments.

However, children with reading versus SIN perception deficits appear to have distinct as well as the aforementioned overlapping neural signatures. Distinctions

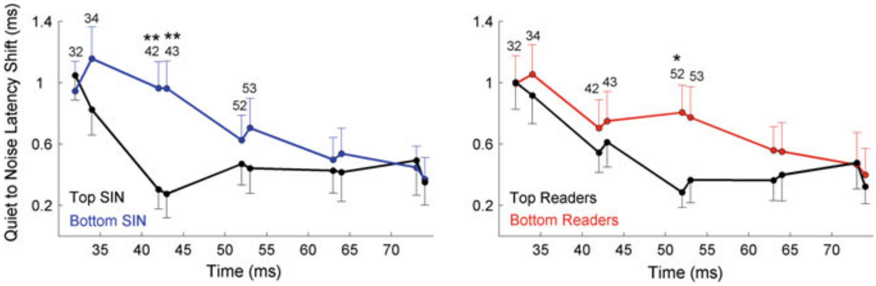

Fig. 3.6 Noise-induced latency shifts are greater for children with poor SIN perception (*blue*) than for those with good SIN perception (*black*), left, and are greater for children with poor reading (*red*) than for those with good reading (*black*), right. These latency delays were noted only for the consonant–vowel transition region of the syllable. Error bars = 1 S.E. $*p < 0.05$, $**p < 0.01$ [Adapted from Anderson et al. (2010a)]

are evident in the spectral content of their responses. Unlike children with reading problems, children with poor SIN perception have reduced amplitude of the F_0 rather than the higher harmonics (Anderson et al. 2010b). The F_0 and lower harmonics contribute to pitch perception (Meddis and O'Mard 1997), and pitch, along with spatial, timing, and harmonic cues, aids in speaker identification and auditory object formation (Oxenham 2008; Shinn-Cunningham and Best 2008). Locking onto a speaker's particular voice aids in stream segregation and is necessary to understand speech in a background of multiple talkers (Bregman 1990). Therefore, weak representation of the F_0 may impair the listener's ability to focus on a speaker's voice.

Few studies have used the cABR to investigate neural speech processing in children who have been diagnosed specifically with an APD independent of a reading or language impairment. Rocha-Muniz et al. (2012) compared cABR responses to a 40-ms [da] in three groups of children aged 6–12 years who were typically developing, diagnosed with an auditory processing disorder, or diagnosed with a SLI. They found that both the APD and SLI groups of children had abnormal cABR results compared to the normally developing group, but the abnormalities differed. Both groups with disorders had delayed peak timing compared to the typically developing group, but the timing delays in the SLI group were more pervasive than in the APD group. In addition, the SLI group had reduced amplitudes for the high-frequency region of the stimulus (721–1,154 Hz) compared to either the APD or typically developing group. These results are slightly different from those of the Banai et al. (2009) study, which found reduced amplitudes for both the mid (410–755 Hz) and the higher harmonics (755–1,130 Hz) in the group with reading impairments compared to the group with normal reading ability, but no information was provided regarding reading ability in the groups in the Rocha-Muniz et al. (2012) study.

Behavioral testing of APD is typically restricted to children older than the age of six because the language demands and testing requirements of memory and attention exceed the abilities of younger children. The cross-phaseogram analysis, as mentioned in Sect. 3.2, evaluates subcortical differentiation of speech sounds. Impaired ability to accurately represent speech sounds is an example of an auditory processing disorder and may result in reading and language impairments. In a study of 3- to 5-year-old preschoolers, responses were recorded to the syllables [ba] and [ga] and cross-phaseograms were obtained (White-Schwoch and Kraus 2013). These children were also administered a phonological processing test (Clinical Evaluation of Language Fundamentals–Preschool-2, CELF-2P, Pearson, San Antonio, TX) and were divided into groups of low and high phonological processing skills. The children who had higher phonological processing showed greater phase differences in their responses between the [ba] and [ga] syllables than the children with lower phonological processing (Fig. 3.7). A follow-up study demonstrated that subcortical encoding of consonants in noise in preschool children predicts scores on tests of phonological processing a year later (White-Schwoch et al. 2015). Because reliable FFRs to a speech syllable have been obtained in

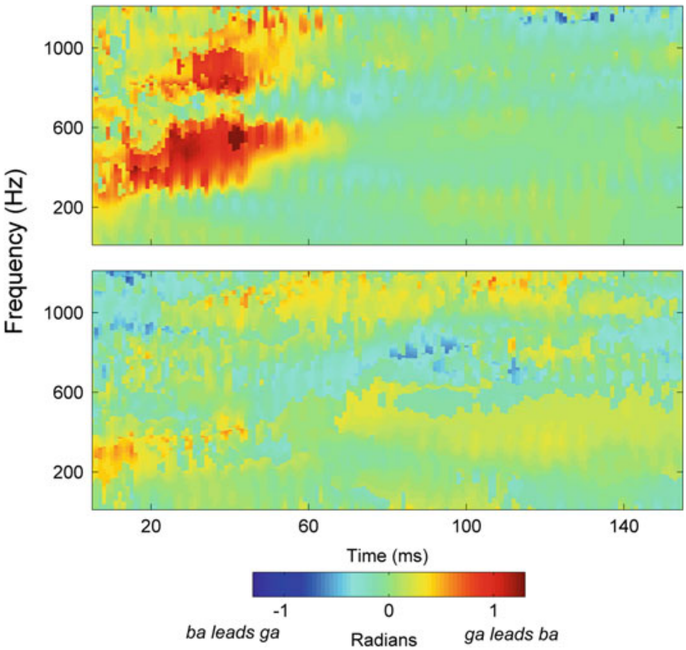

Fig. 3.7 Preschool children with better phonological awareness scores (*top*) have greater subcortical differentiation of stop consonants, as measured by larger phase differences, than age-matched children with poorer phonological awareness scores (*bottom*). The *red* region in the *top panel* shows the expected phase lead of [ga] before [ba] in the transition region, while there are no phase differences in the *bottom panel* illustrating data from children with less developed phonological (prereading) skills [Adapted from White-Schwoch and Kraus (2013)]

infants (Jeng et al. 2010; Anderson et al. 2015), perhaps these kinds of measures can be used to target at-risk infants and children who would benefit from intervention for language-based learning impairments.

3.5 Treatment of APD and Auditory-Based Learning Impairments

Other barriers to the inclusion of auditory processing evaluations in audiologic practices are the limited insurance payments for services and the belief by some clinicians that there are no effective treatment strategies for APD. The evidence of training benefits using electrophysiologic assessments is limited, but the click-evoked middle-latency response and the tone burst-evoked P300 may detect positive training outcomes in children with APD (Wilson et al. 2013). Because the cABR is reliable and meaningful in individuals and reveals myriad aspects of auditory processing, it can provide an effective assessment of the efficacy and nature of training benefits for auditory processing.

Two common interventions for APD are improving access to the signal through the use of an assistive listening device and providing auditory-based training to strengthen neural sound processing. FM systems are most often used in classrooms with children with hearing loss, but recommendations for its use with children with APD are increasing. Classroom noise often exceeds recommended levels (ANSI 2002; Knecht et al. 2002), putting the child with APD at a disadvantage compared to his or her peers. An FM system improves the child's access to the teacher's voice, effectively increasing the signal-to-noise ratio (SNR), and can be used to offset the deleterious effects of a noisy environment. The cABR was used to evaluate neural auditory processing and phonological skills in children with poor reading skills following 1 year of FM use (Hornickel et al. 2012b). Three groups of 8- to 12-year-old children were compared: an experimental group of children with reading impairments who used an FM system in the classroom, a control group of children with reading impairments who did not use an FM system, and another control group of children who were typically developing. Each group underwent a battery of tests before the beginning and after the end of the school year. The experimental group wore the FM system during school hours throughout the academic year. Two key findings emerged. In brainstem responses to a 170-ms [da], response consistency improved (intertrial variability decreased) in children who wore the FM systems, but there were no changes in response consistency in the other groups. Furthermore, the group who used the FM system was the only group that improved on phonological awareness (CTOPP) and basic reading (Woodcock–Johnson III Test of Achievement Basic Reading Cluster Score, HMH Riverside Publishing, Rolling Meadows, IL). Importantly, pretraining response consistency predicted the extent of improvement on phonological processing, suggesting that the cABR can be used to predict individual benefit from FM use (Fig. 3.8).

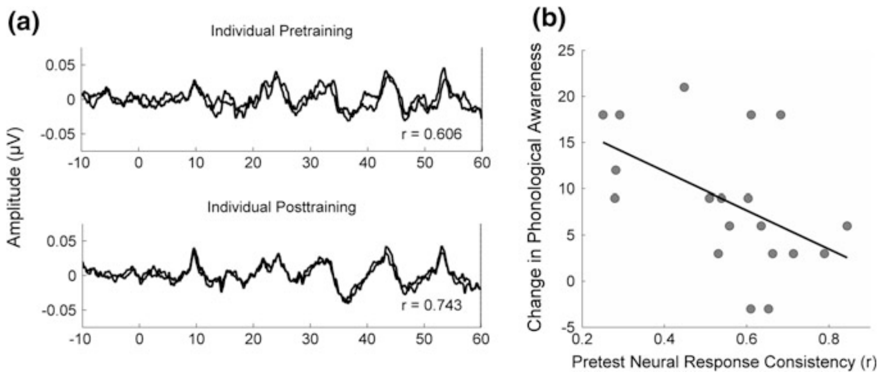

Fig. 3.8 cABR averages taken at two different times in the recording session (*gray* and *black*, respectively) in an individual child's response at pre- and posttraining sessions. The *r*-value is a measure of the degree of correlation (response consistency) between the two waveforms at each session. At the posttraining session, the waveforms are more closely aligned and have a higher *r*-value (**a**). The pretraining measure of neural response consistency predicts the change in phonological awareness after FM use during one academic year. Lower pretraining response consistency scores are associated with greater improvement in phonological awareness (**b**). [Adapted from Hornickel et al. (2012b)]

The cABR has also been used to document benefits from computer-based auditory training programs. Children with learning disabilities (8–12 years) underwent 35–40 h of Earobics training (Houghton Mifflin Harcourt Learning Technology, Boston, MA) over the course of 8 weeks (Russo et al. 2005). Earobics provides interactive training to improve phonological awareness, auditory processing, and language processing. The children's responses to a 40-ms [da] were elicited in quiet and in white Gaussian background noise (+5 SNR) before and after training. The responses in quiet and noise were cross-correlated to yield a measure of response degradation in noise—lower correlation values indicate greater noise degradation. Higher quiet-to-noise correlation values were seen after training, whereas no changes were seen in a control group. This training was accompanied by improvements in perception of sentences in noise, suggesting that more precise neural encoding of speech in noise is a factor in perceptual performance.

Training benefits were also documented with the cABR in children with SLI or APD. Responses to a 40-ms [da] were recorded in quiet and in white noise (+5 SNR) in four groups of children: typically developing ($N = 7$; no training), APD ($N = 9$, training), SLI ($N = 6$, training), and SLI ($N = 7$, no training). These children were also tested on a battery of behavioral APD tests, including a speech-in-noise test (details not provided), the Dichotic Digits (Musiek et al. 1991) or Staggered Spondaic Words Test (Keith et al. 1987), and the Pitch Pattern Sequence Test (Musiek et al. 1980). The training groups received 50 min of auditory training per week for eight weeks. The training consisted of practice on dichotic listening, pattern sequencing, and listening to speech in competing noise.

All four groups were tested before the initial visit and then 12 weeks later. Both the SLI and APD training groups had earlier brainstem latencies for the onset and initial peaks of the FFR elicited in noise but not in quiet, and no changes were seen in the control groups. Although the SLI and APD groups had significantly delayed latencies compared to the typically developing group before training, these differences disappeared after training. In addition, only the training groups had better behavioral performance on the Dichotic Digits or Staggered Spondaic Words Test and the Pitch Pattern Sequence Test at the second visit. No changes were seen on the speech-in-noise test in any of the groups. This study demonstrates the feasibility of using the cABR for evaluating treatment efficacy. However, the lack of an APD control group, random assignment, and small sample sizes limit interpretation of the results. More rigorous studies are needed to demonstrate efficacy of APD treatment.

3.6 Aging Effects on Auditory Processing: Spotlight on Hearing in Noise

Older adults, even those with audiometrically normal hearing, report trouble hearing in background noise, echoing one of the primary elements of APDs. This difficulty may arise, in part, from deficits in auditory temporal processing. Older adults are less able than younger adults to follow the fast-changing temporal cues that allow a listener to distinguish between words that differ on a single temporal dimension, such as voice onset time or formant transition duration (Gordon-Salant et al. 2006, 2008). Furthermore, older adults have more difficulty recognizing time-compressed speech (Gordon-Salant et al. 2007) and discriminating on the basis of temporal order compared to younger adults (Fogerty et al. 2010). Studies using speech materials may be affected by language or cognitive factors, but these deficits have also been found in studies using nonspeech materials. Older adults have larger gap detection thresholds (Schneider and Hamstra 1999; Phillips et al. 2000), larger duration discrimination thresholds (Fitzgibbons and Gordon-Salant 1995; Kumar 2011), and reduced temporal order discrimination compared to younger adults (Fitzgibbons et al. 2006; Shrivastav et al. 2008). Based on a review of 65 articles on central auditory aging, a task force concluded that the difficulties experienced by older adults may arise from a combination of factors including neurodegeneration along the auditory pathway and cognitive declines (Humes et al. 2012). The cABR is affected by both neurodegeneration and top-down cognitive influences (Kraus and White-Schwoch 2015) and is therefore a sensitive metric of auditory aging and can reveal a neural basis for central auditory processing deficits in older adults.

The use of the cABR permits evaluation of central auditory abilities in older adults without the confounds of linguistic or cognitive factors that may affect behavioral results. One primary finding across studies that supports a deficit in central processing is delayed neural timing (cABR peak latencies) in response to the consonant–vowel transition of speech syllables (Vander Werff and Burns 2011; Anderson et al. 2012). This delay is similar to that seen in children with SLI, poor reading, and APD. These studies have been conducted in individuals with "clinically normal hearing." Because the definition of "normal hearing" may include thresholds ranging from −10 to 25 dB HL, it would be useful to determine if a relationship between latency and pure-tone threshold exists within this normal range, especially in older adults. Other characteristics in common with children with language-based learning deficits include decreased trial-to-trial response consistency and diminished representation of the higher harmonics in older adults compared to younger adults (Anderson et al. 2012). Furthermore, similar factors characterize children and older adults who are good or poor SIN perceivers. The neural signature underlying successful ability to hear in noise, robust representation of the F_0 and higher quiet-to-noise correlations, is present in both children and older adults (Fig. 3.9; Anderson et al. 2011).

To better understand the factors supporting speech understanding in older adults, structural equation modeling was used to determine the contributions of peripheral hearing status (audiogram, otoacoustic emissions), life experience (music, socioeconomic status, physical exercise), cognitive function (attention, memory), and subcortical sound processing (F_0 and first formant representation and quiet-to-noise correlations) to SIN perception (based on the QuickSIN and the HINT) in 120

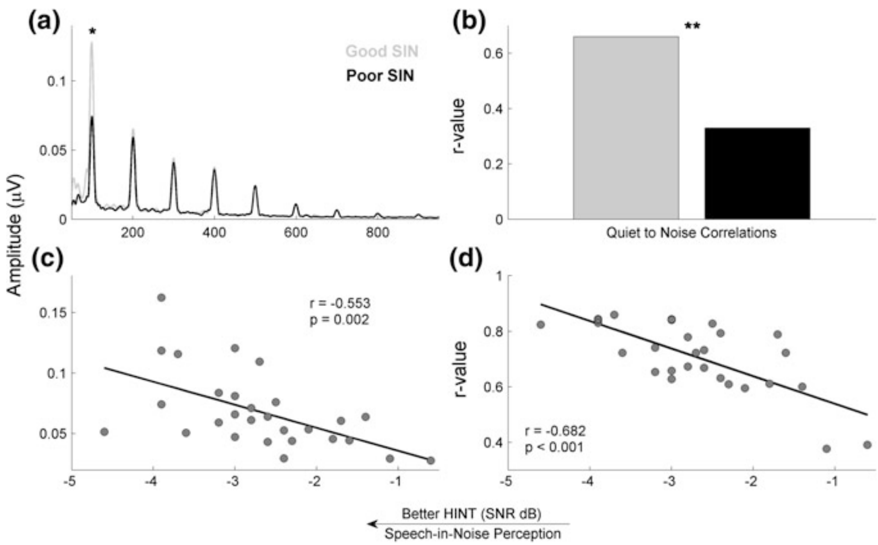

Fig. 3.9 Older adults with good SIN perception have greater strength of the F_0 than age- and hearing-matched older adults with poor SIN perception. All participants had clinically normal audiometric thresholds (**a**). Older adults with good SIN perception have higher quiet-to-noise correlation values than older adults with poor SIN perception (**b**). Better SIN perception is associated with higher F_0 amplitudes (**c**) and higher quiet-to-noise correlations. (**d**) $*p < 0.05$, $**p < 0.01$ (**c**, **d**). [Adapted from Anderson et al. (2011)]

middle- to older-aged adults, 55–79 years, with hearing levels ranging from normal to moderate sensorineural hearing loss (Anderson et al. 2013c). Both cognitive and subcortical processing contributed significantly to SIN perception, while neither life experiences nor peripheral hearing loss made significant contributions. However, it is expected that the contribution of peripheral hearing loss would be a significant factor in a data set that included more individuals with hearing loss. Furthermore, life experiences that are characterized by enrichment or deprivation may also affect neural speech encoding. For example, music training and language exposure can strengthen subcortical speech encoding (Wong et al. 2007; Parbery-Clark et al. 2012), whereas an impoverished upbringing may lead to decreased trial-to-trial response consistency and reduced representation of the first formant harmonics (Skoe et al. 2013a).

Although the cABRs in children with language-based learning impairments and older adults are influenced by peripheral and cognitive factors, there are likely different etiologies. In older adults, the deficits noted in the cABR may arise from peripheral neurodegeneration, cognitive declines, and changes in the balance of neurotransmitters. Animal models have demonstrated peripheral neurodegeneration after noise exposure in the absence of hair cell death. The degeneration can manifest as a delayed loss of auditory nerve fibers after recovery from noise exposure (Kujawa and Liberman 2006) or as an acute loss of auditory nerve terminals (Kujawa and Liberman 2009), although it remains undetermined if these noise-exposed animals have behavioral deficits processing sounds in challenging environments. Similarly, aging mice that have not had noise exposure experience cochlear synaptic loss and a decrease in auditory nerve fibers before there is detectable change in hearing thresholds or numbers of hair cells (Sergeyenko et al. 2013). This cochlear neuropathy is likely to affect the precision of sound encoding, particularly in the auditory brainstem where precise synchrony is required to produce a response (Bharadwaj et al. 2014). Therefore, the temporal processing deficits noted in the cABR in previous studies may arise, in part, from cochlear neurodegeneration. Additional studies in mice, assessing the cABR following exposures defined by Kujawa and Liberman (2009) as synaptopathic, would be useful in establishing the extent to which cABR changes are induced after noise exposure (cf. Shaheen et al. 2015). The cABR may also be affected by the local changes in the auditory brainstem and midbrain and top-down changes from auditory cortex. There is widespread speculation that decreased ABR amplitude after synaptopathic damage will specifically result in SIN deficits. Age-related changes in the balance of excitatory and inhibitory neurotransmitters occur in cochlear nucleus (Schatteman et al. 2008; Wang et al. 2009), inferior colliculus (Walton et al. 2002; Caspary et al. 2008), and auditory cortex (Hughes et al. 2010; Caspary et al. 2013). It is most likely, as stated in the Humes et al. (2012) consensus report, that temporal processing is affected by the interacting effects of an impoverished auditory signal and declines in day-to-day top-down modulation of responses.

Auditory processing deficits in children are likely to result from a failure to make effective sound-to-meaning connections that are necessary building blocks for learning language (Hornickel and Kraus 2013). This failure may result from a genetic predisposition or from environmental factors, such as impoverished experiences, noise exposure, or ototoxic drugs, which result in a reduction in the quality of sound processing in the auditory brainstem and cortex. Decreased sensory input associated with hearing loss may also lead to degradation of auditory stimulus representation that interferes with the establishment of sound-to-meaning pathways (Balen et al. 2009). It should be noted that APD is a heterogeneous impairment that may arise from one or more sources of impairment or delayed development including auditory nerve, brainstem, auditory cortex, prefrontal cortex, corpus callosum, or other areas (Medwetsky 2011). The cABR may be influenced by impairments in these areas, but the neural signatures may depend on the specific nature of the impairment. For example, difficulty hearing in noise is associated with reduced representation of the F_0 whereas a reading impairment is associated with reduced representation of higher harmonics.

3.7 Treatment of Auditory Processing and Speech-in-Noise Perception Deficits in Older Adults

Auditory-based training induces neuroplasticity in adults that is reflected in changes in cABR and cortical evoked responses. Just 8 days of word-identification training on the basis of differing pitch contours leads to improved subcortical pitch tracking in young-adult nontonal language speakers (Song et al. 2008). This neuroplasticity is associated with real-world listening benefits. Young adults who used the commercially available Listening and Communication Enhancement program (LACE™, Neurotone, Inc., Redwood City, CA) had more robust subcortical speech representation in noise, and they also had improved scores on SIN tests (HINT and QSIN) (Song et al. 2012). Benefits of training are also seen in auditory cortex using the mismatch negativity response, with training on one stimulus generalizing to a novel stimulus (Tremblay et al. 1997).

Although training can modulate neural and behavioral responses in young adults and children, can similar benefits be achieved in older adults? Evidence from animal models is promising. Older rats that undergo frequency discrimination training have improved synchrony in auditory cortex and better perception; in fact, after training, the dot raster plots of older rats look similar to those of young rats (de Villers-Sidani et al. 2010). Therefore, one might expect similar results in older humans.

The use of computer-based auditory training, such as LACE, has become popular for a number of reasons. It permits adaptive fine manipulation of speech features and cognitive demands, allowing the user to proceed at an individual pace. The use of engaging software can increase compliance with the training (Bavelier et al. 2012) and can improve cognitive function in older adults (Anguera et al. 2013). Finally, the training can be performed at home, making it cost effective and efficient. Despite this potential, few studies have provided high-quality evidence for the efficacy of computer-based auditory training, especially in individuals with hearing loss (Henshaw and Ferguson 2013). Recently, however, a randomized controlled study was conducted to determine the benefits of an auditory-based cognitive computer-training program in older adults with hearing levels ranging from normal to moderate sensorineural hearing loss (Anderson et al. 2013d). Older adults, aged 55–70 years, were randomly assigned to one of two groups. Those who were assigned to the experimental group received 40 h of home-based training over the course of eight weeks. The training consisted of six modules that adaptively increased levels of perceptual difficulty and memory load. Participants identified stimuli that differed in direction of pitch change or in the consonant–vowel transition duration. The stimuli were presented at a faster rate or were adaptively compressed as performance improved. Those who were assigned to the active control group also received 40 h of home-based training over the course of 8 weeks. They watched educational programs on their computers on topics ranging from art to history to science and answered questions about the content of the program. The participants were blind to the training group. Participants in the experimental group had faster subcortical peak latencies in response to a speech stimulus and reduced interpeak variability; these effects were most pronounced in noise (two-talker babble; +10 SNR) and in the response region corresponding to the consonant–vowel transition. The peak latencies in the active control group members did not change (Fig. 3.10). These neural changes were accompanied by improvements in SIN performance, short-term memory, and processing speed. Follow-up testing was performed 6 months after the completion of training. Faster timing and reduced interpeak variability were still present at 6 months, but of the behavioral variables, only processing speed benefits persisted, not the improvements in SIN performance or short-term memory (Anderson et al. 2014). Work is needed to determine the schedule of booster sessions necessary for maintaining performance. In addition, the training must be inherently reinforcing to the user to encourage continued participation in the program.

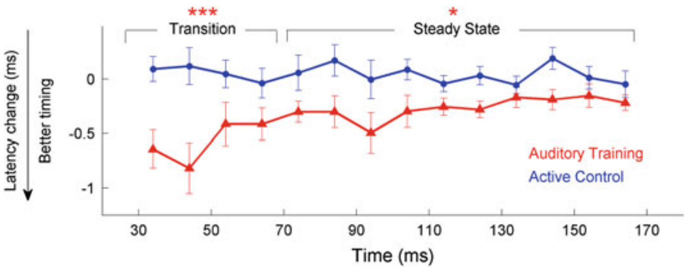

Fig. 3.10 After auditory training, older adults had earlier cABR latencies in response to speech presented in multitalker babble noise, especially in the consonant–vowel formant transition region. No latency changes were noted in the active control group. Error bars = 1 S.E. *$p < 0.05$, ***$p < 0.001$ [Adapted from Anderson et al. (2013d)]

The training studies carried out in children and older adults demonstrate the usefulness of the cABR for documenting changes in auditory processing, and that in children, aspects of the cABR can predict behavioral benefit from training (Hornickel et al. 2012a; White-Schwoch et al. 2015). More work is required to determine the predictors of training benefit in older adults. The cABR may also be useful in predicting success with other forms of intervention, particularly from the use of hearing aids. Cortical evoked responses are being used to determine benefit from hearing aids or cochlear implants in children with deafness, including those with ANSD (Roland et al. 2012; Cardon and Sharma 2013). The cABR may be similarly useful in predicting benefit in children or adults with sensorineural hearing loss that is not related to ANSD.

3.8 Challenges: Evaluating Training Efficacy in Real-World Environments

The aforementioned studies, although conducted in the home with computer-based programs or in the classroom with personal FM systems, were closely monitored and supervised by research personnel. To encourage widespread treatment for APD, it is important to document efficacy in more typical environments where rigorous control over treatment conditions may not be possible and to assess the impact of auditory training in community-based programs that have not been created by the experimenter. This has recently been achieved in two different studies that were carried out in at-risk children from lower socioeconomic backgrounds. Both of these studies used music as a medium for inducing neuroplasticity. Long-term participation in music training improves auditory expertise—SIN performance and auditory cognitive skills in children (Gerry et al. 2012; Strait et al. 2013) and older adults (Parbery-Clark et al. 2011). This enhanced behavioral performance is accompanied by improvements in the neural encoding of speech in noise (reviewed in Kraus and White-Schwoch 2016). Even a few years of music training in childhood and adolescence can partially offset age-related delays in neural timing in older adulthood (White-Schwoch et al. 2013; see also Skoe and Kraus 2012). Therefore, music may be an effective training strategy for inducing neuroplasticity and enhanced auditory function.

One study was conducted in the Chicago public schools (Tierney et al. 2013, 2015). High-school students chose between physical training (Junior Reserve Officers' Training Corps; ROTC) and music classes (choir or band); both options met three times per week. The students were evaluated with the cABR before their freshman year before the initiation of training and at the conclusion of each academic year. After 2 years, improvement was noted in subcortical timing in response to a speech syllable presented in a multitalker background in the music training but not in the ROTC group. This improvement was objectively evaluated in two ways:

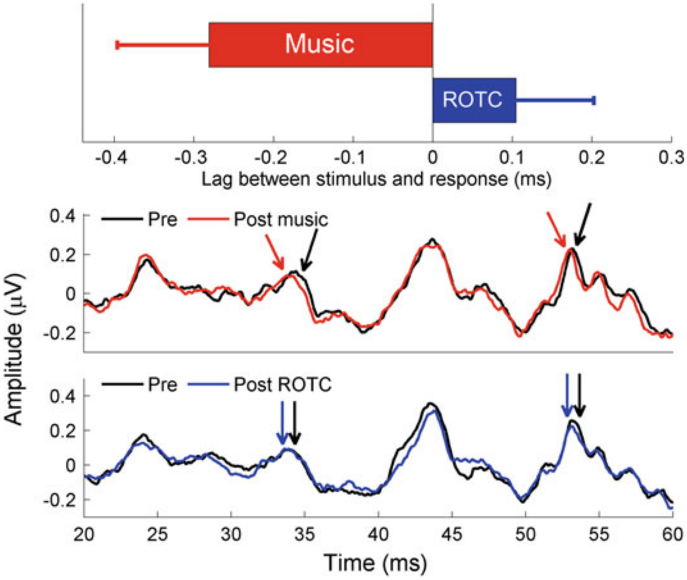

Fig. 3.11 *Top* The responses of adolescents to the syllable [da] presented in multitalker babble (+10 SNR) are shifted earlier in time after 2 years of music training, with decreased lag between stimulus and response. No changes were seen in the ROTC group. Decreased latencies are also seen in the post-waveform relative to the pre-waveform in the music group (*middle*) but not in the ROTC group (*bottom*). Error bars = 1 S.E [Adapted from Tierney et al. (2013)]

(1) identifying the response shift (stimulus-to-response lag) required to maximize the correlation between the stimulus and response, providing an objective measure of neural transmission delay at each test session, and (2) computing phase shifts between responses collected before and after training. Results indicated a decrease in stimulus-to-response lag and a negative phase shift indicated faster responses following 2 years of music training that did not occur in the physical training group (Fig. 3.11). These results demonstrate that even a modest amount of music training can improve the neural encoding of sound in adolescents (Tierney et al. 2015).

The second study (Kraus et al. 2014) was a randomized control design carried out in conjunction with Harmony Project (Los Angeles, CA), an award-winning community program that provides free music education to children in the gang-reduction zones of Los Angeles (http://www.harmony-project.org/, 2013). Children from the Harmony Project waiting list (ages 6–9 years) were randomly assigned to either defer their participation in music lessons for one year (termed Group 1) or start music lessons immediately (Group 2). The music lessons began with 2 h of musicianship classes weekly for approximately 6 months and then moved to group instruction for ≥ 4 hours per week on strings, woodwinds, or brass winds. cABRs were recorded to the syllables [ga] and [ba] before training, after 1 year, and after 2 years (Kraus et al. 2014). Results demonstrated increased

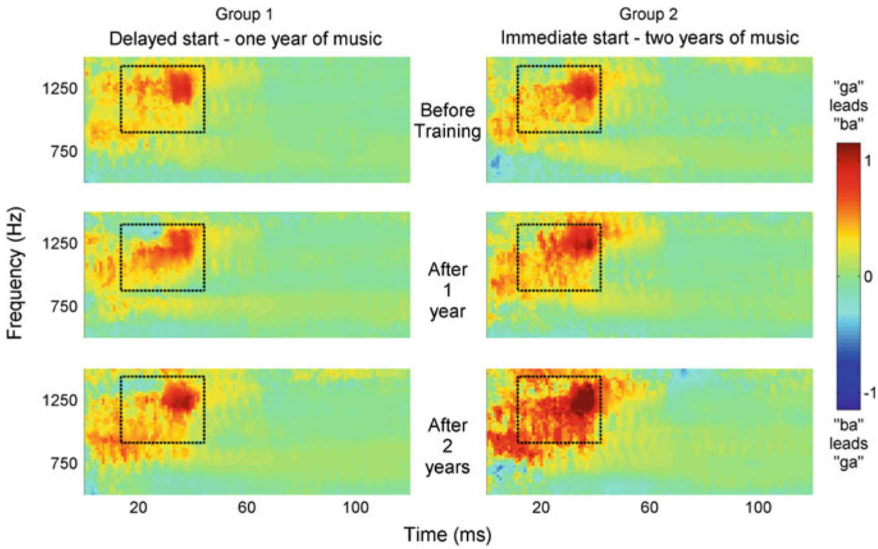

Fig. 3.12 Cross-phaseograms demonstrated an increase in subcortical differentiation between the syllables [ba] and [ga] after 2 years but not after 1 year of music training in school-age children. This increase was noted in the region corresponding to the second formant (0.9–1.5 kHz) at 15–45 ms post-stimulus onset [Adapted from Kraus et al. (2014)]

subcortical differentiation of the two syllables on the phaseogram after 2 years of music training in Group 2 (Fig. 3.12). The phase differences after 1 year were not significant in either group. It is likely that the number of hours of lessons after 1 year did not reach the threshold for producing a neurophysiological change, as the frequency of music lessons increased from 2 to 4 h per week after the first 6 months and was then more focused on a single instrument. One important aspect of this study is that the testing took place outside the lab setting in a classroom environment. Using the Intelligent Hearing Systems (IHS, Miami, FL) platform, the cABR was obtained in classrooms that were not electrically shielded, demonstrating the possibility of obtaining clean data in non-lab settings. One final point is that it takes time for music lessons to induce neuroplasticity, but these investments early in life are worthwhile because they have the potential for lifelong payoffs, as noted in White-Schwoch et al. (2013), who found that the benefits of music training in elementary and high school (earlier neural timing) persisted into older adulthood.

These two neuroeducational lines of work are important for a number of reasons. Most of the music studies cited in this chapter referred to individuals who had an extensive history of training leading to a professional music career. But these children received the amount of training that would be feasible to provide in the public schools, demonstrating the power of music education and the need to continue to maintain music in the public school curriculum. Furthermore, both groups of children came from environments of lower socioeconomic status with fewer opportunities to engage in enriching experiences. Music training, an enriching activity with many possible social and recreational benefits, can at least partially ameliorate the deficits imposed by growing up in an impoverished environment. Finally, the studies demonstrate the feasibility of using the cABR to assess neurophysiological changes in real-world environments and in existing training programs, not just those that are experimentally created.

3.9 Future Directions

The biological nature of APD is poorly understood, in part due to the heterogeneous etiologies that may contribute to APD. Ideally, future studies of APD will include methodologies that clarify the sensory-cognitive interactions that are at play in this disorder. In addition to behavioral and cABR assessments, cortical evoked responses, functional magnetic resonance imaging, and magnetoencephalography will all contribute to a better understanding of the diverse nature of this disorder. cABR is likely to be especially viable in the clinic because of its documented reliability in individual subjects and its precision of reflective processing in the central nervous system. A better understanding of other potential causes of neurodegeneration of central auditory structures, such as history of exposure to noise, ototoxic agents, and traumatic brain injury, may also contribute to a better understanding of APD. The Kraus Lab continues to develop technology to bring the cABR into widespread clinical use as a measure of auditory processing.

The biological evidence for training efficacy is indisputable, but several questions remain unanswered. Future studies should determine optimal strategies for producing changes in different populations and how these strategies can be tailored to individual needs. The community-based studies described in Sect. 3.8 did not find improvements before two years of training. This fact is important for setting appropriate expectations. For example, a large study failed to find generalization effects after 6 weeks of online training, concluding that “brain training” does not improve general cognitive function (Owen et al. 2010), but perhaps the effects would have been realized after a longer training period. Determining factors that lead to changes in individuals will help to elucidate the biological mechanisms underlying these improvements. Large population studies are necessary to determine efficacy and to provide support for third-party payment. The cABR can be used to answer these questions.

Research on cABR/FFR is developing quickly across multiple domains (Kraus et al. In press). More work is needed to inform the efficacy of using the cABR in the assessment and management of APD in clinical settings. The projects in Los Angeles and in Chicago were successful, in part, as a result of relationships formed with community leaders who are committed to helping children achieve their potential despite the disadvantages that accompany an impoverished upbringing. Similar relationships need to be forged with clinicians and teachers serving children or adults with APD to bring assessment and treatment into real-world clinics and other learning environments. The Kraus Lab neuroeducation work is an example of using community-based operations as laboratories in which to obtain scientific knowledge.

3.10 Summary

Although APD as an independent entity was identified several decades ago, the audiological community has not taken full responsibility for the assessment and management of this disorder. This reluctance is partly due to limitations in the current test battery, limited reimbursement, and a need for documentation of treatment efficacy. The cABR has proven to be sensitive to temporal processing deficits associated with auditory-based language impairments, including dyslexia, specific language impairment, and deficits in SIN perception across the life span. Because the cABR is a direct measure of auditory processing, an atypical cABR provides biological evidence of an APD. A few studies have specifically investigated cABR in children with an APD diagnosis, but more work is needed to develop criteria for classification of the cABR as typical or atypical. Furthermore, the cABR reflects neuroplastic changes in the midbrain, a hub of auditory learning, and can be used to assess efficacy of treatment. Therefore, the cABR has the potential to become an important component of the APD diagnostic and management test battery. Once integrated into clinical practice, use of the cABR may facilitate more widespread evaluation and treatment of APD.

Compliance with Ethics Requirements

Nina Kraus is chief scientific officer of *Synaural*, a company working to create a user-friendly measure of auditory processing.

Samira Anderson declares that she has no conflicts of interest.

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