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# Achieving Clear Communication Employing Sound Solutions – 2008

## Proceedings of the First International Virtual Conference on FM

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## Chapter 1

# Listening, literacy and the neural transcription of sound

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# Listening, literacy and the neural transcription of sound

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Impaired encoding of sound along the auditory pathway has been associated with various clinical conditions. Most relevant here are difficulties listening in noisy environments which are characteristic of the elderly, the hearing impaired and individuals with auditory processing disorder (APD), and difficulties in phonological processing characteristic of individuals with developmental language and reading disabilities. This review focuses on the latter group of children, which is estimated to comprise 10-15% of school age children (Vellutino et al., 2004). In addition to difficulties in reading, characteristic of 80% of all children diagnosed with learning problems (Snow et al., 1998), these children suffer from a phonological processing deficit, broadly defined as difficulties in the conscious manipulation of speech sounds. They have difficulties determining whether words rhyme, how words can be divided into their constituent syllables or phonemes and repeating non-words. While it is now agreed that poor phonological processing developmentally precedes reading difficulties, the biological basis of the phonological processing deficit itself remains poorly understood (Ramus, 2006).

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Current theories of dyslexia attribute the phonological deficit to inefficient use of, or access to, phonological representations when short-term memory is taxed (Ahissar et al., 2006; Ramus et al., 2008) perhaps resulting from a general deficit in dynamic tuning to the characteristics of incoming stimuli (Ahissar, 2007), rather than to deficient phonological representations which would result from deficient encoding of phonological features. We describe here a series of investigations revealing that in a subgroup of children with poor reading and poor phonological processing, encoding of speech at sub-cortical levels of the auditory system is impaired. We propose that this impairment in encoding the acoustic-phonetic elements of speech sounds may translate to the formation of abnormal sub-lexical (input) phonological representations and thus contribute to the development of language and reading disabilities. Also possible is that developmental language impairment impedes experience-dependent tuning of auditory function. We argue that optimal subcortical transcription is shaped by interactions between cortical and subcortical auditory mechanisms through the corticofugal pathway during development as reviewed in this article.

Here, we focus on the encoding of speech-sounds at the upper brainstem/midbrain (the speech-ABR) in humans. We start by describing the fidelity of encoding within an individual, and how encoding is affected by expertise. We then turn our attention to studies describing how this high fidelity is compromised in children with language based learning problems and how encoding at the level of the auditory brainstem is related to auditory processing at the cortex. Because current electrophysiological techniques provide reliable means to test sub-cortical, but not cortical encoding of sound at the individual listener level, we propose that these properties of sub-cortical auditory processing carry special relevance to the study and understanding of APD. Namely, these properties allow us to define an individual as having an APD if specific elements of their response are significantly disrupted. We can then ask whether individuals manifesting a certain physiological pattern also share similar perceptual, literacy-related and cognitive profiles, and whether current definitions of APD, language disorders or learning problems can account for the observed profiles, or whether these physiological deficits and accompanying profiles "cut across" diagnoses.

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## Fidelity of subcortical encoding of sound: Characteristics of normal sub-cortical encoding of speech sounds

Synchronized neural activity in response to sounds can be measured non-invasively in humans by means of auditory evoked potentials. Simple (brief non-speech) stimuli evoke an orderly pattern of responses from the auditory nuclei in low brainstem (waves I – III) and rostal (waves V-Vn, the FFR) brainstem nuclei, clinically known as the click-evoked ABR (Boston et al., 1985; Møller, 1999; Møller et al., 1985; Sohmer et al., 1977; Worden et al., 1968). Slight deviations from the timing of the normal pattern are associated with hearing loss and other pathologies (Hall, 1992; Hood, 1998). Synchronized neural activity can also be measured in response to more complex sounds like synthetic vowels or consonant-vowel syllables. Here we review work on auditory evoked responses originating at rostal brainstem/midbrain nuclei that reflect the temporal and spectral characteristics of complex stimuli with remarkable precision (Galbraith et al., 1995; Banai et al., 2007; Krishnan, 2002; Russo et al. 2004; Johnson et al., 2008a; Chandrasekaran and Kraus, 2010, Hornickel et al., 2009). Please see Skoe and Kraus (2010) for a review of brainstem responses to complex sounds.

Speech is a signal whose temporal and spectral properties change continuously. Studies in animal models indicate that many of its complex properties (formant structure, pitch, voicing, etc.) can be encoded through the firing patterns of auditory neurons (Delgutte et al., 1984a; Delgutte et al., 1984b; Sachs et al., 1979; Young et al., 1979). In humans, two main classes of evoked responses (reflecting activity of large neural populations) are likely candidates to reflect these complex properties: the late waves of the auditory brainstem response (ABR), which are essentially onset responses and the frequency following response (FFR) which reflects phase locked activity of neural populations in the rostal brainstem (Batra et al., 1986; Hoormann et al., 1992; Smith et al., 1975; Worden et al., 1968), tracking the fundamental frequency and its harmonics (Galbraith et al., 1995; Hall, 1979). Please see Chandrasekaran and Kraus (2010a) for a review of brainstem origins of these responses. Our approach to study the parallels between the acoustic properties of the speech signal and the brain evoked response is based upon the source/filter model of speech production (Fant, 1970; and see Kraus et al., 2005 for a detailed review of the application of the source/filter model to speech-evoked brainstem responses) and is demonstrated in Figure 1. In this view, the acoustic properties of the signal can be classified into one of two broad classes of responses: the source class and the filter class. The source class contains all parameters used to describe the properties of the sound source (the vocal folds in the case of speech, the strings in case of string instruments). The sound wave produced by the source is modified by the filter – i.e., the shape of the vocal tract and the articulators in the case of speech or the shape of the musical instrument, and this modification produces the final acoustic structure. In the case of speech, the vocal folds produce a harmonic sound at a period determined by the rate of vibration. The filter then atte—nuates certain harmonics and enhances other harmonics to produce the formant structure of speech sounds.

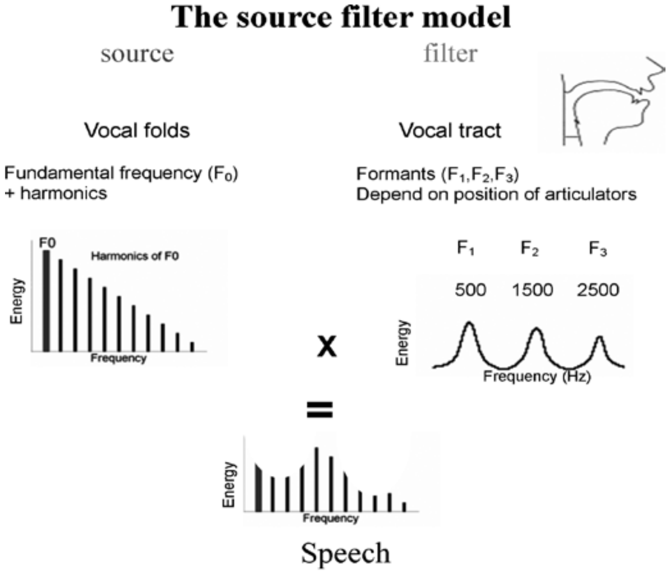


Figure 1.

In analyzing the physiological response, we hypothesize that the onset and offset transient peaks of the speech-ABR reflect mainly filter information, whereas the FFR reflects both source and filter properties of steady-state vowel-like stimuli (Kraus et al., 2005), because the neural response shows phase-locking to the fundamental frequency of the stimulus (a source property) as well as to higher frequency formants (a filter characteristic). An examination of the evoked response to synthetic, steady-state vowels reveals a series of peaks, repeating at a rate corresponding to the fundamental frequency (F0) of the vowel – a source property. Furthermore, the spectral content of the response appears to reflect the first two formants of the vowel (Krishnan, 2002). Thus, frequency domain analyses of FFRs obtained to the synthetic vowels /u/, /⊃/ and /a/ show that spectral peaks corresponding to the first and second formants, are increased in comparison to spectral peaks corresponding to the harmonics falling between F1 and F2 (Krishnan, 2002), thus reflecting filter properties as well.

We have been studying the brainstem response to the consonant-vowel syllable /da/ (Russo et al., 2004; Skoe and Kraus, 2010). The brainstem response to /da/ (da-ABR) has both an onset portion occurring 6.7 (sd = 0.25) ms after the stimulus onset and an FFR portion corresponding to the properties of the periodic and steady-state portion of the vowel /a/, as shown in Figure 2. Together, the onset and the FFR components of the da-ABR roughly reflect the acoustic parameters of the syllable /da/. The onset is a filter class response and likely represents the initiation of the consonant, as it appears to be absent when a vowel is used on its own.

The speech stimulus /da/ we have been using, and the response it evokes from a representative child are shown in Figure 2. It can be seen that the physiological response to /da/, first described in the general population by Russo et al. (2004), includes an orderly series of peaks and troughs (peaks I through O). The initial peaks (I to A) are similar to those evoked by brief click stimuli. Waves I and III probably originate in the low brainstem, whereas peaks V and A originate in the rostal brainstem (the lateral lemniscus or inferior colliculus). Supporting the similarity between waves V and A in response to speech and clicks, Song et al. (2006) have reported significant correlations between the corresponding peak latencies in response to the two types of stimuli. Peak C possibly

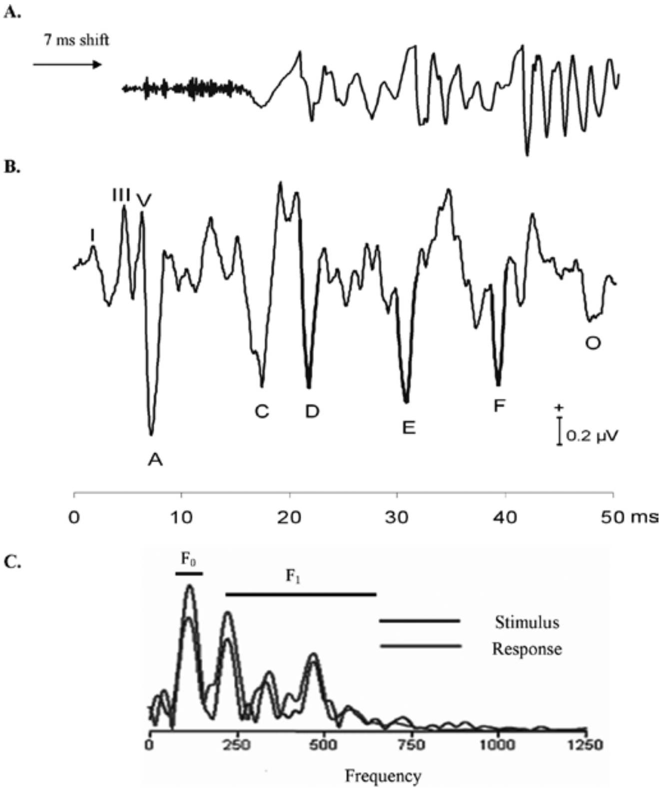


**Figure 2. Sub-cortical encoding of the syllable /da/.**

A. The time/amplitude wave form of the speech syllable /da/.

B. The time/amplitude waveform of the brainstem response from a typical child. Labels I – F denote the characteristic peaks of the response. Waves I,III originate at the low brainstem, waves V and A represent the onset of the response at the rostral brainstem. Waves D, E and F are locked to the fundamental frequency of the /da/ stimulus.

C. The spectra of the stimulus and the response from a typically developing child. Averaged over the entire stimulus and the last 40 ms of the response. Spectral peaks in the response correspond to F0 (103-125 Hz), and some of the higher harmonics comprising F1 (220-720 Hz). The stimulus has been filtered to mimic the phase-locking properties of the brainstem.

reflects the onset of voicing, whereas the later peaks (D,E and F), comprising the FFR, occur at a rate equivalent to the fundamental frequency (F0) of the sound source and correspond the vowel portion of the stimulus. Finally, peak O is likely an offset response, reflecting the end (stopping) of the sound. Figure 2C shows the spectra of the stimulus and the response, demonstrating how the major spectral peaks in the stimulus that fall within the phase-locking capabilities of the brainstem (F0 and F1) are represented in the response.

The feature of the speech-ABR that makes it useful in a wide array of studies and clinical applications is the high replicability of the response both across and within individuals. Thus, not only are the major morphological features of the response stable over time within an individual (Russo et al., 2005), the major peaks are also highly replicable between individuals (Russo et al., 2004; Akhoun et al., 2008), making deviations from the normal range easily identifiable and informative (Banai et al., 2007).

Supporting the separation between filter class and source class responses, significant correlations exist between latencies of the onset peaks V and A, which are considered filter class peaks. On the other hand, the latencies of the onset peaks are not correlated with the latencies of the FFR peaks representing F0 – a source class response (Russo et al., 2004). Because waves V and A of the speech-ABR appear to be similar to waves V and Vn of the click-evoked-ABR it may be claimed that both reflect similar types of processing. Yet, it should be noted that while in the general population the latencies of wave V to click and speech are significantly correlated, this correlation breaks down in a sub-group of individuals with learning problems whose speech-ABRs are abnormal (Song et al., 2006, see below). Furthermore, different maturational patterns characterize click- and speech- evoked responses. Whereas the brainstem response to clicks is mature by 2 years of age (e.g., Salamy, 1984), the speech-evoked response only reaches adult like timing and morphology by the age of 5 (Johnson et al., 2008b). Taken together, these two lines of evidence support the idea that brainstem structures respond differently to speech- and click-sounds.

## Malleability of subcortical encoding of sound

The remarkable fidelity of sub-cortical encoding of speech, as measured using auditory evoked potentials, could suggest that encoding in these stations is based on automatic detection of the acoustic features of sound with no regard to higher-level factors that are known to play a crucial role in perception such as expertise, attention or context. Recent studies suggest that this is not the case, and that sub-cortical encoding is affected by expertise, input from other sensory modalities and attention. Whether these influences are mediated in a top-down fashion, as predicted by the Reverse Hierarchy Theory (Hochstein et al., 2002) through the efferent, corticofugal system linking the auditory brainstem and cortex (Winer, 2006), through local mechanisms of adaptation to the acoustic properties of the input (Dean et al., 2005) or through an interaction of afferent and efferent mechanisms is unknown.

### Expertise and sub-cortical encoding of speech

Brainstem responses to speech reflect differences in linguistic experience. The phase locking of neural activity to the pitch contour (that is the changes in F0 over time also known as pitch tracking) of Mandarin words (in which pitch provides an important cue to meaning) is stronger in native Mandarin compared to native English speakers, suggesting that the brainstems of Mandarin speakers encode Mandarin words more precisely than do the brains of English speakers (Krishnan et al., 2005). These findings suggest that pitch encoding mechanisms in the human brainstem are sensitive to language experience, however, they can not resolve whether this plasticity is more consistent with corticofugal modulation of the sub-cortical structures by language experience or with statistical learning based on the input statistics of Mandarin speech sounds.

Indeed, several recent studies on the effects of experience on sub-cortical encod-

ing support both conclusions. On the one hand, Xu, Krishnan and Gandour (2006) have shown that the sub-cortical encoding advantage of Mandarin speakers disappears following slight manipulations to the acoustic properties of the Mandarin tokens, while still preserving their meaning and allowing Mandarin speakers to perceive them as good quality Mandarin sounds.
This is more consistent with a statistical learning argument than with corticofugal modulation, because it suggests that the brains of Mandarin speakers are fine tuned only to the exact contours they hear in everyday speech. In this case, knowledge of Mandarin was not sufficient to confer a brainstem encoding advantage.
On the other hand, Wong et al. (2007) have shown that musical experience results in more robust encoding of linguistic pitch-patterns in the brainstem. Because the musicians in this study were native English speakers, with no prior exposure to Mandarin, it is unlikely that their more robust encoding of Mandarin sounds was the result of learning the statistical distribution of Mandarin sounds, but of a more general influence of music training on multi-purpose pitch encoding mechanisms (though it could still be some other local general pitch extracting mechanism that is driven by music training but not by speaking Mandarin).
The findings from the Wong et al. (2007) study suggest common sub-cortical mechanisms for pitch processing in linguistic and non-linguistic contexts. These findings are consistent with behavioral findings showing that Mandarin speakers use pitch information differently from native English speakers even in a non-linguistic context when they are required to identify (but not discriminate) pitch contours (Bent et al., 2006). Providing further support to the proposition that subcortical processing of pitch in music and language has common origins, Musacchia et al., (2007) demonstrated that musicians also show more robust brainstem encoding of the English syllable /da/, in particular when the auditory syllable was presented together with a visual counterpart in a lip-reading condition (see Figure 3 for more details of this study).

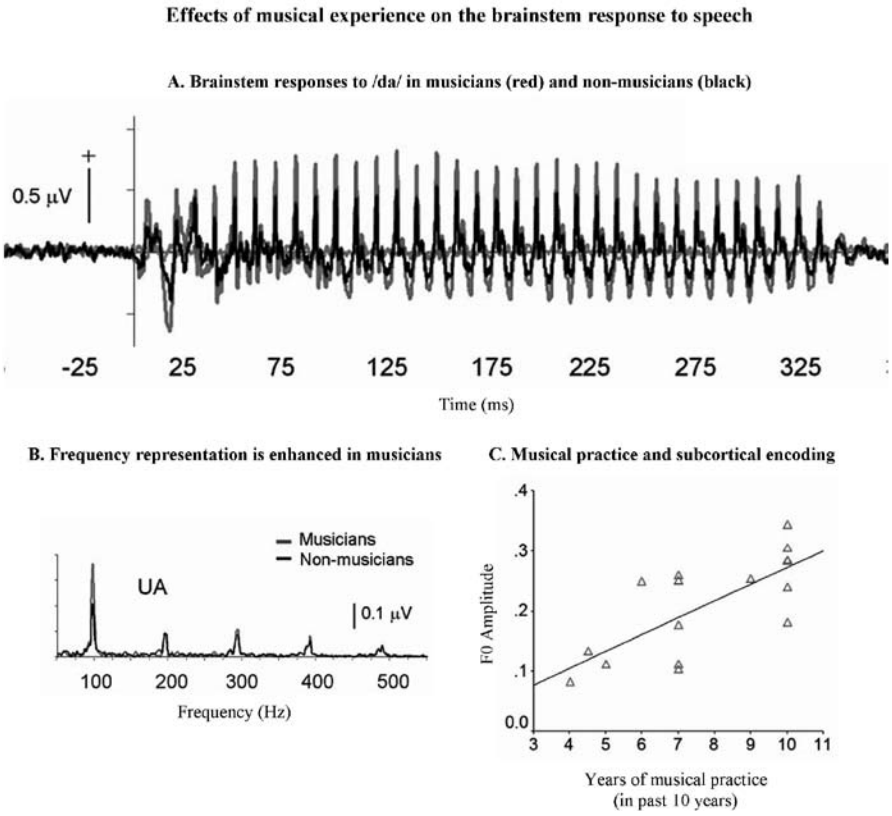
Taken together, the Wong et al. (2007) and the Musacchia et al. (2007) studies suggest that the consequences of experience extend across domains and levels of processing in the auditory pathway (see Kraus et al., 2009; Chandrasekaran and Kraus, 2010b for further discussion of this point). Moreover, despite the well-known cortical segregation of speech and music function (Zatorre et al., 2002), a common sub-cortical network for speech and music is implied. Furthermore, recent studies show that processing of multiple features within this subcortical network is enhanced in musicians (Strait et al., 2009, Lee et al., 2009, Parbery-Clark, Skoe and Kraus, 2010), thus supporting their better perceptual skills in noise (Parbery-Clark et al., 2009). Please see Chandrasekaran & Kraus (2010a) for a review of music and its relationship to noise-exclusion and learning.

## Visual influences on sub-cortical encoding of speech

The addition of visual input to the auditory speech stimulus, changes the way the brainstem encodes acoustic information as early as 11 ms after the onset of the acoustic stimulus (Musacchia et al., 2006). When a visual stimulus - a face uttering a syllable or a musical instrument being played – is presented along with the acoustic stimulus (a syllable or a musical note, respectively), the brainstem response to the speech syllable is modified by the presence of the visual stimulus, and this form of auditory-visual interaction is significantly enhanced in musicians compared to non-musicians (Musacchia et al., 2007). These findings suggest sub-cortical involvement in multi-sensory integration in addition to multi-modal cortical regions typically thought to engage in this function (Musacchia, Strait and Kraus, 2008).

## Effects of attention on sub-cortical encoding

Like visual input, attending to sound influences brainstem encoding of speech and non-speech sounds, in addition to, and earlier than the more widely documented cortical effects. Two types of attentional effects on the human FFR have been suggested.
A spatial-attention (ear-related) effect and a modality effect.
A spatial attention effect was observed in a dichotic listening



Effects of musical experience on the brainstem response to speech

A. Brainstem responses to /da/ in musicians (red) and non-musicians (black)

B. Frequency representation is enhanced in musicians

C. Musical practice and subcortical encoding

**Figure 3. Musical expertise and speech encoding at the brainstem.**

**A.** Brainstem responses to the speech syllable /da/. Musicians (red) encode the sound more robustly compared to non-musicians (black).

**B.** Frequency representation is enhanced in musicians. In musicians, the magnitude of the representation of the fundamental frequency (F0) in the brainstem is larger compared to non-musicians.

**C.** Among musicians, the magnitude of F0 representation is positively related to the amount of recent musical practice. Based on Musacchia et al., (2007).

paradigm; when two different syllables were presented simultaneously, one to each ear, and listeners were required to switch their attention between the two ears, the encoding of the fundamental frequency of the attended syllable was selectively enhanced (Galbraith et al., 1998). A small but significant effect on the FFR latency (with no effect on amplitude) was also reported with a different attentional paradigm in which listeners were required to respond to targets that occurred in the same ear as a cue ("attended") or in the contralateral ear ("unattended") (Hoormann et al., 2004). FFR amplitudes were also found to increase when attention was directed to the auditory modality (listeners were asked to count auditory targets) compared to when attention was directed to the visual modality (listeners were asked to count visual targets while ignoring the sounds) (Galbraith et al., 2003). These findings suggest the existence of crude attentional mechanisms at the level of the auditory brainstem. These mechanisms could serve to enhance auditory encoding by directing processing resources to the appropriate modality, or within the auditory modality to the appropriate ear. It is still not clear if more refined attentional processing, related to specific auditory features, occurs at the brainstem.

Taken together, the findings that language and musical experience, as well as inputs from the visual modality and attention affect auditory encoding of sound at sub-cortical levels of the auditory pathway suggest that these areas are more plastic and dynamic than was typically assumed by sensory neuroscientists, and that at least some of these influences are mediated by top-down mechanisms. Please see Tzounopolous and Kraus (2009) for review of experience-dependent brainstem activity.

## Sub-cortical encoding of speech in noise can be improved with training

Further evidence for the dynamic nature of sub-cortical auditory encoding comes from the effects of training on the speech-

ABR. Russo et al. (2005) have shown that in a group of children with LD undergoing commercial auditory training, the resilience of the brain stem to the degrading effects of background noise improved following training. Because the training was not specific to the syllable used to elicit the brainstem response, or to perception in noise, it is not likely that training affected local low-level mechanisms at the brainstem. This outcome therefore raises the possibility that the influences of training on the brainstem were mediated in a top-down fashion.

In addition to enhancing the brainstem response in noise, short-term training may improve pitch encoding in the brainstem in a way similar to that of long-term musical experience. Thus, when native English speakers were trained to use lexical pitch patterns to identify Mandarin words, tracking of some Mandarin pitch patterns in their brainstems became more precise (Song et al., 2008b).

## Vulnerability of sub-cortical encoding of sound

Our focus has been on children with language-based learning problems (LD). Previous work concentrated on cortical processing in this clinical group and suggested that various forms of auditory cortical processing are abnormal in a substantial sub-group of this population (e.g., Baldeweg et al., 1999; Bishop et al., 2004; Hari et al., 2001; Heim et al., 2000; Helenius et al., 2002; Kraus et al., 1996; Kujala et al., 2000; Lachmann et al., 2005; Moisescu-Yiflach et al., 2005; Nagarajan et al., 1999; Wible et al., 2002, Banai et al., 2009). Furthermore, in this population the sensitivity of the subcortical response to the context of surrounding stimuli (Chandrasekaran et al., 2009) and to the acoustic-phonetic differences between different stop consonants (Hornickel et al., 2009) are reduced compared to the general population. Our studies reveal that in addition to cortical processing deficits, brainstem responses to speech are abnormal in about a third of children diagnosed with language-based learning problems (Banai et al., 2005). Compared to typically developing children, in this subgroup of the LD population waves A, C, and F were found to be delayed (King et al., 2002), the onset response at the upper brainstem (waves V, A) is prolonged and less synchronized (see Figure 4), and the spectral representation of F1 (but not F0) is reduced (Wible et al., 2004). On the other hand, the brainstem responses to click in this group are normal (Song et al., 2006) suggesting that the timing deficit in response to speech sounds does not reflect a universal deficit. A similar dissociation was reported in a group of children with Specific Language Impairment (SLI) in which brainstem responses to pure tones were of normal latency, but responses to backward masked ones were delayed (Marler et al., 2005).

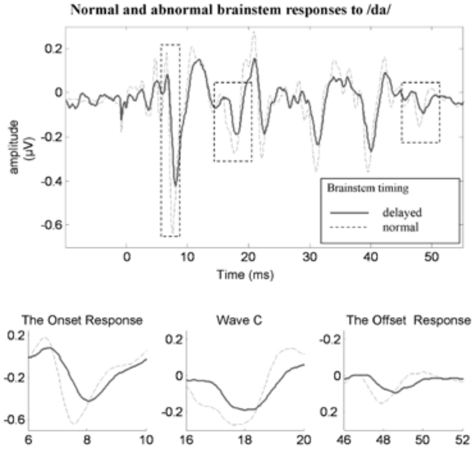


**Figure 4. Abnormal speech ABR. Top.**
Grand averages of the time domain response in children with learning problems and abnormal responses (in solid red lines) vs. typically developing children (blue dashed line). Dashed boxes mark the regions of the response that significantly differ between individuals with normal and abnormal responses.
**Bottom.** Focus on the onset (left), the transition period (middle) and the offset (right) portions of the response.

For a more complete discussion of our approach to determining whether speech-ABR is abnormal, as well as for normative data see Banai et al., 2007. It is of interest however to note here that the proportion and degree of speech-ABR deficits in all of our previous studies was unrelated to the specific diagnosis (APD, dyslexia, SLI, ADHD or LD) suggesting that perhaps similar underlying physiological bases can cut across existing diagnostic categories. It should also be noted that while these findings suggest an association between learning problems and abnormal processing at the level of the brainstem, they can not be taken to indicate causality. Nonetheless, the reliability of the response within an individual makes the speech-ABR a useful marker of auditory function in the assessment of listening and learning disorders, and has led to the translation of the research to a clinically available tool –BioMAP (Biological Marker of Auditory Processing, Bio-logic Systems Corp, a Natus Company).

## The relationships between cortical and sub-cortical auditory processing

Because abnormal cortical processing of both non-speech (Baldeweg et al., 1999; Corbera et al., 2006; Stoodley et al., 2006) and speech (Kraus et al., 1996; Schulte-Korne et al., 1998) sounds has been implicated in many cases of LD, whereas responses to acoustic clicks from structures up to the rostal brainstem were typically found to be normal in LDs (Grontved et al., 1988; Jerger et al., 1987; Lauter et al., 1993; Mason et al., 1984; McAnally et al., 1997; Purdy et al., 2002), the extent of auditory pathway deficit characterized using responses evoked by the same stimulus in the sub-group of LDs with abnormal speech-ABRs is of interest. We have examined auditory pathway encoding to the speech syllable /da/ across multiple levels of the auditory pathway.

At the lowest levels of the pathway, timing of peaks I and III in LDs with abnormal later peaks appears normal (Song et al., 2008a), placing the rostal brainstem as the lowest possible source of deficit. On the other hand, when speech-ABR is abnormal, several aspects of auditory cortical processing appear abnormal as well. First, a strong correlation between brainstem timing and the resilience of the cortical response to the presence of background noise was found (Wible et al., 2005). As shown in Figure 5A, noise had more detrimental effects on the cortical responses of individuals with delayed brainstem timing, compared to those with earlier timing, and this was true in both typically developing children and those with language based learning problems. Second, abnormal brainstem timing is associated with reduced cortical discrimination of fine acoustic differences (MMNs, Banai et al., 2005). As shown in Figure 5B, as a group, individuals with abnormal speech-ABRs failed to show an MMN at all, suggesting that delayed timing in the brainstem and cortical discrimination are related. Third, the degree of brainstem deficit is associated with the degree of laterality of cortical processing of speech sounds

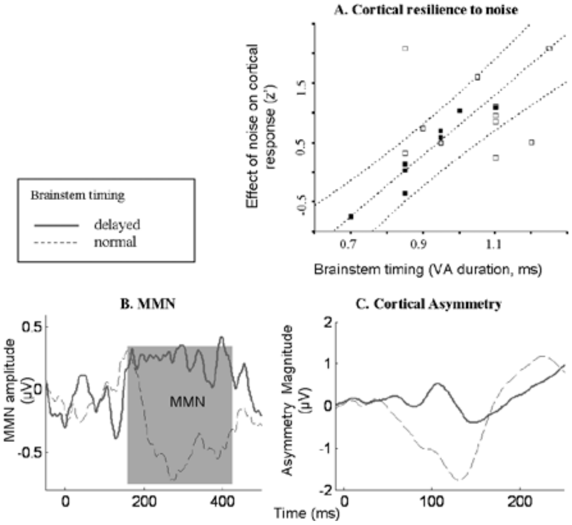


**Figure 5. Cortical processing as a function of brainstem timing.**

A. The relationship between brainstem timing (VA duration) and the cortical susceptibility to noise. Filled symbols denote typically developing children; empty symbols denote children with LD showing a similar trend across both groups. z' was computed by subtracting cortical response correlations in noise from those in quiet. The larger z', the more pronounced effect noise had on response reliability. Based on Wible et al. (2004).

B. Normally (and among individuals with early brainstem timing denoted in blue, dashed line) the cortical detection of rare acoustic evens among frequent ones is indexed by a negative deflection starting about 150 ms after stimulus onset (Mismatch negativity, MMN). This negative deflection is not present when brainstem timing is delayed (red solid line). Based on Banai et al., (2005).

C. Normally, cortical processing of speech sounds is stronger in the left hemisphere of the brain, as denoted by the left asymmetry of the cortical response of individuals with early brainstem timing (dashed line). This pattern is disrupted when brainstem timing is delayed (solid line). Based on Abrams et al. (2006).

(Abrams et al., 2006). As shown in Figure 5C, the normal pattern of leftward cortical asymmetry in response to speech sound is disrupted when brainstem timing is delayed.

Taken together these studies suggest strong relationships between auditory processing at the brainstem and the cortex. Because the brainstem and the cortex are linked by both ascending and descending pathways (see Winer, 2006 for review), these studies cannot resolve the direction of causality, namely whether a subtle timing deficit at the brainstem adversely affects cortical processing or whether abnormal cortical processing exercises abnormal feedback on the brainstem, manifested by the pattern of timing deficits observed in individuals with abnormal speech-ABR. Recent studies in animal models are consistent with the top-down direction though however (Ma et al., 2001; Palmer et al., 2006; Popelar et al., 2003). One possible route through which the descending pathway could exert its influence is by influencing selective attention which in turn aids in gating of sensory information to the cortex. If processing in the cortex is not robust enough, it may not be able to properly "tune" the sub-cortical structures to relevant acoustic features.

## Functional correlates of sub-cortical encoding of sound

How sub-cortical encoding of sound contributes to perception, language and other cognitive functions is still not clear, but studies point to relationships between brainstem encoding of speech sounds and some perceptual and literacy related measures (Banai et al., 2009, Chandrasekaran et al., 2009, Hornickel et al., 2009). It has been observed that more than 80 % of individuals with abnormal brainstem timing are poor readers (Banai et al., 2005, see Figure 6). This figure is higher than the proportion of poor readers typically observed in the highly heterogeneous group of individuals with LD that comprised the majority of our studies.

Regarding speech-perception, the picture is more complicated and tentative. Based on a review of unpublished data (Banai et al., 2007), it appears that many individuals with LD and abnormal speech-ABR can have normal speech discrimination thresholds when tested behaviorally. It therefore seems that abnormal brainstem timing does not necessarily result in impaired perception of single syllables in laboratory conditions. This observation is surprising and unintuitive if one assumes that a physiological deficit at the brainstem, with cortical correlates should have an influence on perception. However, it suggests that the link between brainstem encoding and higher-level literacy related skills is not a direct outcome of abnormal speech perception at the syllable level. Indeed, Moore et al. (2005) found that speech-sound training improved literacy-related skills but not psychophysical discrimination of speech syllables. On the other hand, in the cases where impaired perception of syllables was observed, it appears that training improves perception for individuals with abnormal brainstem timing but not for those with normal timing (King et al., 2002). In on-going work, we are studying the perception of sentences presented in challenging listening conditions in individuals with abnormal speech-ABRs to further investigate the relationship between abnormal brainstem encoding and speech perception.

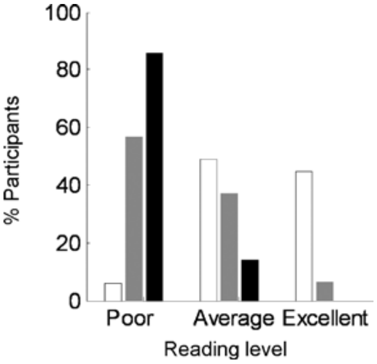


**Figure 6. Brainstem processing and literacy.**
Histogram showing the distribution of reading abilities among typically developing 8-12 year old children (unfilled bars), children with learning disabilities and normal speech-evoked ABRs (grey bars) and children with learning problems and abnormal speech-evoked ABRs (black bars). The majority of children with abnormal ABRs are poor readers. Based on Banai et al. (2005).

Poor temporal resolution, determined by elevated thresholds for the detection of backward masked tones, is characteristic of many individuals with language and learning problems (e.g., Wright et al., 1997). While it is typically assumed that cortical processing is critical for backward masking, two studies suggest that subcortical areas of the auditory pathway may also be implicated in abnormal backward masking thresholds. In the first study, Marler and Champlin (2005) have found that the auditory brainstem responses of individuals with SLI were normal when elicited with pure tones, but abnormal when the same tones were backward masked with noise. In the second study, Johnson et al. (2007) looked specifically in children with LD and poor temporal resolution (defined by performance on a backward masking task), in comparison to children with LD and normal temporal resolution. They found that as a group, children with poor temporal resolution exhibited abnormal encoding of speech at the brainstem and furthermore, that the encoding deficit was specific to the onset and offset portion of the brainstem response, with the representation of the F0 being normal, thus linking abnormal temporal resolution with speech encoding.

Evidence for the involvement of the inferior colliculus (IC, the putative neural generator of waves V and A of the speech-ABR and of the FFR) in auditory processing under challenging listening conditions, as well as in sound localization come from the few available case studies of individuals who suffered a localized lesion to the IC unilaterally or bilaterally. While a bilateral lesion involving IC seems to result in auditory agnosia (Johkura et al., 1998) or central deafness (Musiek et al., 2004), unilateral lesions may result in more subtle deficits in sound localization (Champoux et al., 2007; Litovsky et al., 2002), and in recognition of duration patterns and speech in the presence of a competing signal (Champoux et al., 2007) when the ear contralateral to the lesion is stimulated.

## Implications for APD and reading and language disabilities

### ABRs are reliable in individuals

The ABR can be recorded reliably in individuals, making it a prominent tool in the clinic (Hood, 1998). Speech-ABR is no exception (Russo et al., 2004). The relationships among speech-ABR, literacy and temporal resolution discussed above indicate that speech-ABRs may aid in the assessment and assessment of APD and learning disabilities. Furthermore, because abnormal speech-ABRs are not characteristic of a specific type of learning disorder, but rather are found among 30 % of LD individuals, irrespective of their specific diagnosis, and because APD and LD often co-occur (King et al., 2003; Sharma et al., 2006) it is also likely that they characterize at-least a sub-group of the individuals currently being diagnosed with APD. It could be that these individuals have a different type of disorder than those with behavioral manifestations of APD but normal speech-ABRs. Further research is required to establish the relationships between the behavioral symptoms of APD and brainstem encoding of speech.

### ABRs may be used to define subtypes of learning disabilities based on an objective measure

The diagnosis of learning, reading and language disabilities is based on a combination of standard behavioral and cognitive tests tapping different aspects of reading, language phonological processing and underlying cognitive factors like short term and working memory and speech processing. While efficient in identifying the cognitive underpinnings of the learning disorder, this practice may not be sensitive to differences in the underlying biology of the disorder between different children present with similar patterns of behavioral problems. We propose that the use of an objective measure, like the speech-ABR, to supplement the diagnosis can provide such information, and, as we discuss below, this information may have important implications for the choice of intervention for a given child. In particular, speech-ABR could be used to determine whether an individual child has a central auditory disorder concomitant with their learning problem.

## ABRs may be used to predict the effects of auditory training

Auditory training is often used in remediation of both learning problems and APD, but outcomes are variable and clinicians currently don't have a way of deciding if a child is a good candidate for auditory training or not. The resilience of the speech-ABR to noise can improve with training (Russo et al., 2005). Furthermore, children with abnormal brainstem timing to speech have been shown to be more likely than those with normal brainstem timing to improve their speech perception and the resilience of their cortical responses in noise following commercial auditory training (Hayes et al., 2003; King et al., 2002). These findings suggest that in addition to objectively assessing training outcomes, clinical measurements of speech-ABRs can be used to aid in deciding on a course of therapy.

Furthermore, individuals may have difficulties in other high-level language skills associated with left hemisphere function.

## APD research and diagnosis could benefit from the use of objective measures

Current diagnosis of APD is based on a battery of auditory tests, but it is often not clear how these tests relate to underlying physiological processes that may be impaired in APD. Furthermore, it is likely that APD is not a uniform phenomenon and that individuals that are impaired on some aspects of auditory function are unimpaired on others. Sub-cortical encoding can be used to define subgroups that are homogenous on a particular biological indicator (e.g. onset timing, phase locking, noise susceptibility). Then it can be determined whether individuals within these subgroups share a similar perceptual profile. Entirely feasible is that assessment of brainstem function will reveal children with auditory pathway deficits that are otherwise missed by conventional APD measures.

In addition to the speech-ABR discussed in detail in this review, another sub-cortical measure that has been used in research and that is sensitive to the presence of clinically diagnosed APD is the binaural interaction component (BIC) (Delb et al., 2003; Gopal et al., 1999). The BIC is a putative index of binaural processing. It is therefore possible to hypothesize that the BIC and the speech-ABRs may reveal two distinct subtypes of APD, with distinct perceptual profiles. Alternatively, they may both be impaired in the same population.

## The nature of CAPD

An influential current definition of APD (ASHA, 2005) suggests that the neural deficits in the central nervous system that give rise to APD may be reflected by difficulties in one or more of a long list of auditory skills including sound localization and lateralization, auditory discrimination, auditory pattern recognition, multiple aspects of temporal processing, processing of competing acoustic signals and processing of degraded acoustic signals. It also requires that these auditory deficits are not due to primarily high-order factors such as attention or memory. This heterogeneity of symptoms suggests the potential existence of distinct sub-types of APD. Attempts to define sub-profiles of APD were made by Bellis and Ferre (1999) who suggested, based on case studies and clinical observations several subtypes of APD, based on the putative underlying neurophysiology of each subtype.

1. A left hemisphere subtype characterized by deficits in auditory decoding, including deficits on auditory closure tasks, poor temporal resolution and poor performance on dichotic speech tasks (bilateral or right ear). Furthermore, individuals may have difficulties in other high-level language skills associated with left hemisphere function.
2. A right hemisphere subtype characterized by prosodic deficits including a left ear deficit on dichotic speech tasks, poor temporal patterning and poor frequency, intensity and duration

discrimination. In addition, individuals may have difficulties in other high-level skills associated with the right hemisphere such as prosody perception, sight word reading and poor pragmatic skills.

3. An integration deficit subtype characterized by deficits in tasks that indicate inefficient hemispheric transfer. Deficits include poor temporal patterning and left-ear deficit on dichotic speech tasks. Higher-level deficits may include speech in noise and localization deficits and poor performance with multimodal cues.

This model illustrates two problems inherent in the ASHA definition of APD (ASHA, 2005). First it suggests that a unimodal deficit confined to the auditory system alone is unlikely. Second, because individuals in each of the subgroups may have higher-level deficits, the idea that the auditory deficits cannot be a consequence of high-order deficits seems unlikely.

It is entirely feasible that children with speech-sound transcription deficits may comprise another group.

### It is not reasonable to expect an auditory-only disorder

The central role of the auditory modality in led let to the suggestion that modality specificity should be incorporated into the definition and differential diagnosis of APD (Cacace et al., 2005). For several reasons outlined here, we would like to claim that it is unlikely that APD is a modality specific condition. First, there is little evidence to link the general listening difficulties experienced by individuals with APD in challenging listening conditions with a specific, single underlying auditory physiological deficit. In fact, the evidence from localized IC lesions discussed above are not consistent with the APD phenotype because they result in more specific deficits than those typically present in individuals diagnosed with APD. As discussed in this article, a specific (and subtle) timing deficit at the brainstem may be related to a general form of learning disability rather than to a specific perceptual deficit. Furthermore, the brainstem deficit is strongly linked with cortical processing abnormalities (Abrams et al., 2006; Banai et al., 2005; Wible et al., 2005). Second, multi-sensory processing is carried out in structures such as IC and the auditory cortex, probably influencing the sub-cortical auditory processes reviewed in this article. In addition, these processes are influenced by higher-level factors such as attention and memory. These influences are not likely to be modality specific either. Indeed, in individuals with conditions overlapping APD such as developmental dyslexia, auditory perceptual deficits often co-occur with visual (Amitay et al., 2002; Ramus et al., 2003) and haptic deficits (Laasonen et al., 2001). Furthermore, recent studies in animal models and in humans (e.g., Alain, 2007; Brechmann et al., 2007; Moore et al., 2007; Näätänen et al., 2001; Nelken, 2004; Scheich et al., 2007) document both high-level influence on auditory function, and the presence of multiple “cognitive” processes in the auditory cortex itself, making the idea that even performance on simple auditory tasks can be dissociated from “cognitive processes” impossible. For example, auditory processing deficits may be more dependent on cognitive factors such as working memory than on auditory encoding per-se (Banai et al., 2006). It is likely that similar processes operate in individuals with CAPD, though to our knowledge, such a study has not been published.

## Summary

Sub-cortical auditory processes are more dynamic than typically thought. As discussed in this article, they interact with other modalities and factors such as attention, visual influence and experience. The role of sub-cortical auditory processes in perception and cognition is far from understood, but available data suggest that they relate to cognitive processes involved in language and music, rather than to specific aspects of fine-grained auditory perception. Taken together, the evidence challenge some of the assumptions embedded in current conceptualization of APD.

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