On the Relationship between Speech- and Nonspeech-Evoked Auditory Brainstem Responses

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Introduction

Despite decades of intensive research, the biological underpinnings of language-based learning disabilities, affecting approximately 10% of school-aged children [Torgesen, 1991], are not well understood. As a consequence, objective and early diagnosis of learning disabilities, which is desirable from a therapeutic and educational standpoint, remains a complicated matter.

The auditory brainstem response (ABR) is generated by synchronous firing of structures along the ascending auditory pathway when a sound is heard. In this study, we explored the relationship between brainstem encoding of click and speech signals in normal-learning children and in those with language-based learning problems. To that end, ABR was recorded from both types of stimuli. We found that the normal pattern of correlation between click- and speech-evoked ABRs was disrupted when speech-evoked ABRs were delayed. Thus, delayed responses to speech were not indicative of clinically abnormal responses to clicks. We conclude that these two responses reflect largely separate neural processes and that only processes involved in encoding complex signals such as speech are impaired in children with learning problems.
findings have been taken to indicate that the structural
Stein, 1997; Purdy et al., 2002; Tait et al., 1983]. These
Wood, 1993; Mason and Mellor, 1984; McAnally and
al., 1988a, b; Jerger et al., 1987; Jirsa, 2001; Lauter and
children diagnosed with learning disability [Grøntved et

cally documented normal click-evoked ABR responses in

tical the onset response and the frequency-following
response (FFR) [Johnson et al., 2005; Kraus and Nicol,
2005]. Onset responses are transient, similar to click-
evoked ABR, with peak durations lasting tenths of mil-

Second, the relationship between the onset responses to click
and speech stimuli is the primary focus of this study.

The relationship between the click-evoked and speech-
evoked ABRs is not clear. Previous studies have typi-
cally documented normal click-evoked ABR responses in
children diagnosed with learning disability [Gronveld et
al., 1988a, b; Jerger et al., 1987; Jirsa, 2001; Lauter and
Wood, 1993; Mason and Mellor, 1984; McAnally and
Stein, 1997; Purdy et al., 2002; Tait et al., 1983]. These
findings have been taken to indicate that the structural
integrity of the ascending auditory pathway in children
with a learning disability is intact. However, when mea-
surred by psychophysical tasks, approximately 30% of all
individuals with a learning disability suffer from poor
auditory processing [Ahissar et al., 2000; Amitay et al.,
2002; Banai and Ahissar, 2004; Menell et al., 1999; Ra-

more recent studies, however, suggest a subcortical
origin for learning disabilities. In these studies, a subset
of children with learning disabilities show abnormal neu-
ral encoding of a speech syllable at the level of the brain-
stem (speech-evoked ABRs) [Cunningham et al., 2001;
King et al., 2002; Wible et al., 2004, 2005; Johnson et al.,
2005]. In particular, abnormal onset responses of the
speech-evoked ABRs characterize approximately 30% of
the learning-impaired children [Banai et al., 2005]. Al-
though the timing of the click-evoked response is within
normal limits, the onset of the speech-evoked ABR ap-
ppears to be delayed and less robustly synchronized in
these children, leaving the nature of the relationships be-
tween these two measures unclear.

The current study investigates the relationship be-
tween click- and speech-evoked ABR as recorded in chil-
dren both regarded as typically developing and those clini-
cally diagnosed with a learning problem. Since both the
response to a click stimulus and the onset ABR to speech
occur in a similar time frame, and are thought to originate
from similar locations, a relationship between the two
may reflect a similar type of neural processing. In other
words, the finding that both nonspeech and speech audi-
tory stimuli (i.e. click and /da/) elicit analogous brainstem
responses within the first 10 ms from the onset of the
stimulus would suggest that these sounds activate a simi-
lar set of neural operations as they ascend along the audi-
tory brainstem pathway. Thus, we asked, are these two
measures related to each other, and if so, is an abnormal
speech-evoked ABR indicative of a clinically abnormal
click-evoked ABR? Based on previous studies, it was ex-
pected that the click-evoked ABRs of the majority of chil-
dren with learning problems would be clinically normal,
irrespective of their speech-evoked ABR, although it was
possible that their responses would be delayed but still
within clinical norms. Furthermore, it was expected that
among children with delayed speech-evoked ABRs, the
normal pattern of correlation between the speech- and
click-evoked measures would be altered, reflecting the
different processing (normal vs. impaired) of the two
types of stimuli. To this end, the relationship between
click- and speech-evoked ABR in normally developing
children and those with learning disabilities was system-
atically examined to determine if having a delayed ABR
to speech was predictive of neurophysiologic timing dif-
fferences to click stimuli.

Methods

Participants
Two hundred and thirty-four native English-speaking children
(8–12 years old) participated in this study. All participants had
normal hearing thresholds at or below 20 dB HL for octaves from
500 to 4000 Hz and IQ scores ≥ 85 as measured with the Brief
Cognitive Scale [Woodcock and Johnson, 1989] or the Test of Non-
verbal Intelligence [Brown et al., 1997]. Consent and assent were
obtained from the parents (or legal guardians) and the children
involved in the study. The Institutional Review Board of Northwe-
astern University approved all research.
Two groups participated in this study. One group comprised 119 children diagnosed with a learning problem (LP) by outside professionals (clinical psychologists, school psychologists, neurologists, etc.) and verified by their performance on study-internal standardized measures of learning and academic achievement described below. The second group comprised 115 normal-learning (NL) children who were never diagnosed with a learning problem.

**Study-Internal Measures**
A psychoeducational test battery given to all participants included subtests taken from Woodcock-Johnson Revised [Woodcock and Johnson, 1989]. These subtests were Auditory Processing (Incomplete Words and Sound Blending), Listening Comprehension, Memory for Words, Cross-out, and Word Attack. Additionally, reading and spelling skills were assessed by using subtests from Wide Range Achievement Test-3 [Wilkinson, 1993] and phonological skills were assessed by using subtests taken from the Comprehensive Test of Phonological Processing [Wagner et al., 1999]. These subtests were Elision, Phoneme Reversal, and Segmenting Nonwords.

**Stimulus and Recording Parameters**
ABRs were elicited by an acoustic click and a speech syllable, /da/, and both brainstem responses were collected in the same manner and during the same recording session. Responses were recorded from Ag-AgCl electrodes, with contact impedance of <5 kΩ, positioned centrally on the scalp, at Cz, behind the right ear lobe (reference) and on the forehead (ground). Stimuli were presented into the right ear at 80.3 dB SPL through insert earphones (ER-3, Etymotic Research, Elk Grove Village, Ill., USA). The sampling rate was 20000 Hz and responses were online bandpass filtered from 100 to 2000 Hz, 6 dB/octave. Trials with eye-blinks or other motion artifacts greater than 35 μV were rejected. During testing, the children watched a videotape with the sound level set at less than 40 dB SPL in free field so they could hear it in the non-test ear.

For the click-evoked response, the stimuli were 100 μs clicks presented at a rate of 31.1 Hz. A click is a brief square wave with broad spectral content (fig. 1). Three blocks of 1000 sweeps each were collected both in quiet and ipsilateral white Gaussian noise (+5 dB SNR) conditions. Waveforms were averaged online in Neuroscan (Compumedics, El Paso, Tex., USA). The recording window was 20 ms starting 5 ms prior to stimulus onset.

For the speech-evoked (da) response, stimuli were presented at a rate of 31.1 Hz. A click is a brief square wave with broad spectral content (fig. 1). Three blocks of 1000 sweeps each were collected both in quiet and ipsilateral white Gaussian noise (+5 dB SNR) conditions. Waveforms were averaged online in Neuroscan (Compumedics, El Paso, Tex., USA). The recording window was 20 ms starting 5 ms prior to stimulus onset.

For the speech-evoked (da) response, stimuli were presented at a rate of 11.1 Hz. The 40 ms /da/ stimulus was a five-formant synthesized stimulus [Klatt, 1980] and contained an initial 10 ms burst with frequencies centered around the beginning frequencies of formants 3–5 in the range of 2580 to 4500 Hz (fig. 1). Three blocks of 1000 sweeps each were collected in quiet. Responses of alternating polarity were added together to isolate the neural response by minimizing stimulus artifact and cochlear microphonic [Gorga et al., 1982].
Data Analysis

Experienced observers manually marked wave V and its negative trough (wave A) latencies of click-evoked responses, recorded both in quiet and noise, blind to participants’ identity and diagnostic category. The voltage difference between these two peaks was used as response amplitude. The response measures of NL and LP groups were compared. Repeated measures analysis of variance (RMANOVA) was used for statistical analysis of latency and amplitude measurements.

For the speech-evoked ABR, response measures that were considered for evaluation were wave V latency, wave A latency, VA interpeak duration, and VA interpeak slope. Experienced observers manually marked wave V and A latencies from responses recorded in quiet.

Normal and Delayed ABR Defined

As previously mentioned in the Introduction, for clinical application, values that exceed 2 standard deviations of the normal population are considered abnormal [Hall, 1992], thus this criterion was adopted for this study. Since the average click-evoked wave V latency of the normal group in our study was 5.87 ± 0.30 ms, abnormal values were defined as those exceeding 6.47 ms. The participants’ onset ABR to /da/ was considered abnormal if at least two of the aforementioned measures were beyond 1.5 SD of the normative values or at least 1 measure was beyond 2.0 SD of the normative values [Banai et al., 2005].

Results

Click-Evoked ABR

Latency and amplitude values of the click-evoked ABRs for NL and LPs are displayed in table 1 and averaged click-evoked ABRs recorded in quiet for each participant group are shown in figure 2. A 2-factor RMANOVA with group (NL vs. LP) as the between subjects factor and condition (quiet vs. noise) as the within subjects factor performed separately for latency and amplitude values revealed that these values did not significantly differ between NLs and LPs in either quiet or noise (for latency values: $F_{\text{group}} = 0.002, p = 0.964$; $F_{\text{condition}} = 210, p = 0.000$; $F_{\text{interaction}} = 1.857, p = 0.174$; for amplitude values: $F_{\text{group}} = 2.44, p = 0.12$; $F_{\text{condition}} = 166, p = 0.000$; $F_{\text{interaction}} = 0.232, p = 0.631$). Thus, background noise introduced a delay in latency and a reduction in amplitude; however, the influence of noise was similar in both groups.

When the correlations between click measures in quiet and noise in both groups were examined, the NLs and LPs showed comparable effects of background noise. Within both NL and LP groups, each showed similarly strong and moderate correlations between quiet and noise conditions in latency and amplitude, respectively, as shown in table 2.

Speech-Evoked ABR

Further analysis of ABR data involved assessment of speech-evoked responses in our participants. Upon evaluation of the onset-ABR measures to /da/, 183 children (97 NL, 86 LP) exhibited a normal response to the /da/ stimulus and 51 children (18 NL, 33 LP) exhibited abnormal response (see Methods for definition) to the same stimulus (fig. 3). Among the 18 NLs with abnormal

<table>
<thead>
<tr>
<th></th>
<th>Quiet V Lat, ms</th>
<th>Quiet VA Amp, $\mu$V</th>
<th>Noise V Lat, ms</th>
<th>Noise VA Amp, $\mu$V</th>
</tr>
</thead>
<tbody>
<tr>
<td>NL (n = 115)</td>
<td>5.87 (0.30)</td>
<td>0.37 (0.37)</td>
<td>6.14 (0.29)</td>
<td>0.19 (0.28)</td>
</tr>
<tr>
<td>LP (n = 119)</td>
<td>5.85 (0.26)</td>
<td>0.31 (0.37)</td>
<td>6.13 (0.36)</td>
<td>0.20 (0.25)</td>
</tr>
</tbody>
</table>

Table 1. NL and LP subgroup means (± 1 SD) of wave V latency and amplitude click-evoked measures in quiet and noise conditions.
speech-evoked ABR, 9 children were suspected to have a possible learning problem based on parental report or study-internal measures; however, the lack of formal diagnoses during the time of our testing precluded their inclusion in the LP group.

The waveforms of the two resulting groups are shown in figure 3. As expected, the waveform of the abnormal speech group shows a characteristic delay between waves V and A and a reduced transition slope. In addition to the VA complex measures, this grouping of speech-onset responses also showed a delayed wave III latency in response to /da/ (t = 121.36, p = 0.000). The mean latencies and standard deviations of wave III of normal and abnormal speech-onset group were 4.84 ± 0.25 and 5.07 ± 0.35 ms, respectively.

*Click-Evoked vs. Speech-Evoked Onset Responses*

The relationship between click- and speech-evoked measures was also examined (fig. 4). In our entire test population, the latency of click wave V correlated moderately, but significantly, with the latencies of speech onset response V and A (r = 0.47, p < 0.0001; r = 0.44, p < 0.0001, respectively). There was a weak correlation between click wave V latency and VA slope measure for speech (r = −0.21, p = 0.001). On the other hand, click wave V latency did not correlate with VA duration measure for speech (r = 0.07, p = 0.28). These findings suggest that while there may be some shared processing reflected in the click and speech onset latency measures, there is also a separate component unique to the processing of more complex auditory signals, such as speech. This pattern of correlation was almost identical in the NL and LP groups, suggesting that as a rule, the normal pattern of relationship between the encoding of click and speech stimuli at the brainstem level is not disrupted in individuals with learning problems.
When comparing individuals with normal and abnormal speech ABRs, a significant difference in click wave V latency was observed (5.82 ± 0.25 ms vs. 6.01 ± 0.34 ms, respectively, t = 3.847; p = 0.000) raising the possibility that delays in both reflect a similar process. However, the variance in speech ABR cannot be fully accounted for by variance in click wave V latencies. An ANCOVA with click-evoked wave V latency as the covariate and speech-evoked wave V latency as the dependent variable showed that the difference in speech-evoked wave V latency remained significant even when the click-evoked wave V latency was adjusted for variability (F = 49.463, p = 0.000). This finding suggests that the difference in click-evoked wave V latency cannot fully account for the difference in speech-evoked wave V latency.

Furthermore, the click-speech correlations were driven by those subjects with a normal /da/ response. When divided between participants with normal (n = 183) and abnormal speech-evoked responses (n = 51), the correlations between the speech and click measures were significantly reduced in individuals with delayed speech-evoked ABRs compared to individuals with normal speech-evoked ABRs (table 3).

While by definition all subjects in the abnormal speech group had VA measures that would have been considered abnormal in clinical terms (i.e. delayed or reduced by 2 standard deviations), these same subjects typically had clinically normal click-evoked ABRs. Moreover, the proportion of children with normal click-evoked ABRs did not significantly differ as a function of speech-evoked ABR (normal vs. delayed z = –0.0025, n.s.) where 99.45% of the participants exhibited normal click and normal speech-evoked ABR and 96.08% exhibited normal click and abnormal speech-evoked ABR. Thus, the speech-evoked ABR provides additional, potentially clinically significant information about sound encoding at the individual level, not provided by the click-evoked measure. These findings indicate that even though some aspects of the click- and speech-evoked ABRs are correlated, each provides a separate type of information and thus, a delayed speech-evoked measure does not necessarily predict a delayed click. Both click- and speech-evoked responses should be evaluated in order to ascertain a broader knowledge of auditory processing ability.

### Discussion

Objectively identifying children at risk for learning problems at an early stage in development constitutes an important advance in their diagnosis and prospects. Children with learning problems demonstrated wave V latencies within normal limits in response to a click stimulus presented not only in quiet, but also in the presence of background noise. Reinforcing previous findings, this large-scale study demonstrated that normal-hearing children with learning problems almost always have a normal ABR to click stimuli in quiet and noisy environments. Furthermore, these findings demonstrated a comparable influence of noise in the encoding of click stimuli in both the normal-learning and learning-impaired children at the level of the brainstem. Background noise distorted wave V latency and amplitude similarly for normal-learning and learning-impaired children in that the timing of wave V latency was delayed and the amplitude of wave V was reduced. Thus, these findings suggest that abnormal processing of brief stimuli, such as a click, in either quiet or noise is unlikely to play a role in the diagnosis of learning disability.

On the other hand, the brainstem response to speech has proven to be a mechanism for understanding the neural bases of normal attention-independent auditory function [Johnson et al., 2005; Kraus and Nicol, 2005; Russo et al., 2004]. Because a speech signal provides different acoustic information than a click (i.e. speech syllables are longer and contain less high frequency information com-

<table>
<thead>
<tr>
<th>Group difference</th>
<th>V latency</th>
<th>A latency</th>
<th>VA slope</th>
<th>VA duration</th>
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<tbody>
<tr>
<td>Normal (n = 183)</td>
<td>0.51 (&lt;0.001)</td>
<td>0.49 (&lt;0.001)</td>
<td>-0.10 (n.s.)</td>
<td>0.00</td>
</tr>
<tr>
<td>Delayed (n = 51)</td>
<td>0.27 (0.051)</td>
<td>0.11 (n.s.)</td>
<td>0.04 (n.s.)</td>
<td>-0.24 (n.s.)</td>
</tr>
<tr>
<td>Group difference</td>
<td>z = 1.93</td>
<td>z = 2.62</td>
<td>z = 0.37 (n.s.)</td>
<td>z = 1.51 (n.s.)</td>
</tr>
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</table>

Group difference shows the comparison of correlation coefficients between normal and delayed speech ABR measures.
pared to clicks), it provides additional information about neural encoding at the brainstem level and it uncovers abnormal encoding in approximately 30% of children with learning problems [Banai et al., 2005; Cunningham et al., 2001; Johnson et al., 2005; King et al., 2002; Wible et al., 2004]. Furthermore, the integrity of processing of speech at the level of the brainstem is highly related to the robustness of the cortical response in noise [Wible et al., 2005] suggesting that brainstem processing of these two types of signals may be related to cortical processing in different ways.

When the normal and abnormal speech-evoked ABR waveforms were compared, in addition to the expected differences in wave V and A, we have interestingly observed a difference in wave III. A difference in wave III latency to speech suggests a disruption of an earlier component in the response occurring lower in the brainstem. Wave III is less readily identified compared to waves V and A; therefore, it is probably not clinically useful. Further analysis to examine these differences in speech-onset responses will be explored in future studies. Since children with abnormal speech-evoked ABRs tend to show delayed wave Vs in response to clicks, it may be claimed that differences in the response to speech may be accounted for by the delayed response to clicks. Our statistical analysis has shown that this is not the case since differences in speech-evoked parameters remained significant even when click latencies were controlled. Furthermore, since click latencies were within clinical norms for the large majority (96%, see Results) of children with abnormal speech responses, they cannot be used to group individual subjects as 'abnormal.' Thus, speech-evoked ABRs possibly provide additional diagnostic information at the individual level that is hard to obtain using only clicks.

The speech-evoked response in noise was not reported here as earlier work [Banai et al., 2005; Cunningham et al., 2001; Johnson et al., 2005; King et al., 2002; Russo et al. 2004; Wible et al., 2004] demonstrated that the /da/-evoked response in quiet sufficiently provides a means to objectively identify children at risk for learning problems; moreover, Russo et al. [2004] reported that the onset waves of the /da/-evoked response in noise are not reliably identifiable. The current finding of unimpaired click-evoked responses in quiet in the LP group gave a strong indication that other factors such as stimulus complexity were responsible for the abnormal LP speech-evoked ABR.

The auditory encoding differences between the click and speech stimuli may be derived from an examination of the differences in their acoustical structures. The click stimulus is a nonperiodic, relatively simple sound that is short in duration, but whose bandwidth contains a broad range of frequencies. Conversely, consonant-vowel speech syllables, such as the /da/ used in this study, begin with rapid, relatively low amplitude transient onset features that may be especially vulnerable to disruption by background noise [Brandt and Rosen, 1980]. The vowel that follows the consonant is a sustained periodic signal that is much louder than the consonant. Thus, this higher amplitude, longer portion of the stimulus may actually mask the brief consonant onset critical for eliciting the onset portion of the speech-evoked ABR. This effect may be especially pronounced in the learning-impaired population which is known to show larger perceptual effects of backwards masking compared to normal-learning children [Wright et al., 1997]. Moreover, children with abnormal speech-evoked ABR are more likely to have increased backward masking compared to those with normal encoding of speech at the brainstem [Johnson et al., 2004]. Recent findings showing increased physiological effects of backward masking in children with specific language impairment [Marler and Champlin, 2005] further suggest that deficient neural mechanisms handling backward masking may partially explain the differences between the click- (an unmasked stimulus) and speech (consonant onset masked by the steady-state vowel)-evoked responses observed here. Marler and Champlin [2005] measured ABRs in a group of children with language problems in two conditions. In the unmasked condition, in which ABRs were evoked using a tone, responses were normal; however, when the tone was immediately followed by a masker, wave V latency was significantly delayed. This interpretation should be further explored by a systematic manipulation of the temporal position of the signal and masker.

Another feasible explanation for the differences observed between the encoding of the click and speech signals involves possible differences in neural populations recruited during the encoding click and speech auditory stimuli. Our statistical analysis (both correlational findings and ANCOVA) indicated that while the latency of click- and speech-evoked responses may share at least some common neural processing, variations in the latency of the speech-evoked waves cannot be accounted for entirely by the same physiological processes underlying the processing of the click stimulus. Thus, these findings suggest that the encoding of speech sounds may recruit processes that are not present in the encoding of the click stimuli. The processing of complex features present in speech, such as the onset and formant structures of speech
sounds, may indeed require separate processes in order to encode the sound accurately; these processes may be compromised in children with delayed speech-evoked ABRs. Our findings that the pattern of correlation between click- and speech-evoked responses differed as a function of the precision of speech encoding, together with the fact that the compromised processing of a speech signal is not an indication of abnormal processing of a click stimulus, reinforce this notion.

On the other hand, the differences between encoding of the click and speech stimuli also suggest that abnormal speech-evoked ABR may likely be based on differences in synchronization of response generators in the brainstem. Thus, if a neural system is more sensitive to effects of desynchronization, this increased susceptibility will become apparent in response to the speech stimulus which is longer in duration and has a more gradual onset compared to the click. The abnormal latency in response to the /da/ stimuli in these children may, in fact, reflect this diminished synchronization of ABR wave V-A generators through greater dispersion of latencies of neural activity that is contributing to the response [Wible et al., 2004]. Further studies, probably in an animal model, are needed to determine if the differences in encoding arise from distinct neural populations that are recruited to encode the complex features of the speech stimuli or from the differential influence of different stimuli on the same neural population.

In summary, in this study we have demonstrated the relative independence of brainstem encoding of a brief, broad spectrum click and a longer duration, harmonically and temporally complex speech syllable. At an early level of the brainstem, processing of acoustic input is differentiated based on the acoustic properties of the stimulus. This distinction suggests that evaluating each of these responses may have a unique clinical role. While normal click-evoked ABRs are an indication of the integrity of the cochlea and the ascending auditory pathway, they do not provide further information about encoding of more temporally complex signals. On the other hand, because the brainstem response to speech provides objective information about how the sound structure of speech syllables is encoded by the auditory system, it can be used to diagnose auditory processing deficits despite normal processing of click stimuli. Thus, brainstem responses to both sounds provide objective and complementary information about sound encoding in the auditory system.

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