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Neural plasticity following auditory training in children with learning problems

Erin A. Hayes*, Catherine M. Warrier, Trent G. Nicol, Steven G. Zecker, Nina Kraus

Northwestern University, 2299 N. Campus Drive, Evanston, IL 60208, USA

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Abstract

Objective: This study examined the plasticity of the central auditory pathway and accompanying cognitive changes in children with learning problems.

Methods: Children diagnosed with a learning disability and/or attention deficit disorder worked with commercial auditory processing training software for 8 weeks; control groups consisted of normal-learning and learning-impaired children who did not participate in any remedial programs. Auditory brainstem function was evaluated in response to click and speech stimuli in quiet; cortical responses to speech stimuli were obtained in quiet and noise. Academic achievement and cognitive abilities were assessed with standardized measures.

Results: Compared to controls, the trained group improved on measures of auditory processing and exhibited changes in cortical responses in quiet and in noise. In quiet, cortical responses reflected an accelerated maturational pattern; in background noise, cortical responses became more resistant to degradation. Brainstem responses did not change with training.

Conclusions: Children with learning problems who practiced with auditory training software exhibited plasticity of neural encoding of speech sounds at the cortical, but not subcortical, level of the auditory pathway. This plasticity was accompanied by improvement in behavioral performance.

Significance: This study demonstrates that in learning-impaired children working with commercial auditory processing training programs affects both the perception and the cortical representation of sound.

Keywords: Neural plasticity; Auditory physiology; Auditory processing; Reading disability; Speech sound perception and speech perception in noise

1. Introduction

Reading problems, associated with learning disabilities in 7–10% of children in the primary grades (Shaywitz et al., 1990), place children at a greater risk to be underachievers or to be implicated in criminal activities when they reach adulthood (Zinkus et al., 1979; White, 1982). Many children with reading problems exhibit deficits in the perception of speech sounds (de Weirdt, 1988; Elliott et al., 1989; Watson and Miller, 1993). This has been attributed to inadequate phonological awareness skills and/or difficulties in perceiving brief sounds (including rapid spectral changes) which occur in speech (Golden and Steiner, 1969; Godfrey et al., 1981; Lieberman et al., 1985; Werker and Tees, 1987; Liberman et al., 1989; Reed, 1989; Elbro et al., 1994; Torgesen and Barker, 1995; Kraus et al., 1996; Merzenich et al., 1996; Stark and Heinz, 1996; Tallal et al., 1996; Mody et al., 1997; Schulte-Koerne et al., 1999). Of particular importance for some learning-impaired children is that these perceptual deficits can be absent in quiet, but manifested in noise typical of everyday listening situations (Elliot et al., 1979; Brady et al., 1983; Chermak et al., 1989; Cunningham et al., 2001; Bradlow et al., 2003).

Commercially available auditory training software programs, incorporating exercises to improve temporal processing and phonological awareness skills, are widely used by learning-impaired children (Merzenich et al., 1996; Tallal et al., 1996; Morrison, 1998; Diehl, 1999). The impact of these programs on neurobiological processes associated with auditory perceptual problems is unknown, and the perceptual and cognitive benefits are still being investigated. Children with reading deficits present with heterogeneous neural, perceptual and cognitive profiles. Currently, it not known what patterns of neural, perceptual and cognitive deficits make a learning-impaired child a good candidate for successful use of the programs. Given the wide variety of exercises used in these programs, it is

* Corresponding author. Tel.: +1-847-491-2465; fax: +1-847-491-2523.
E-mail address: e-hayes@northwestern.edu (E.A. Hayes).

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logical to hypothesize that use of the programs impacts different auditory processes in children with different deficits. The common use of these programs provides practical opportunities to study auditory system plasticity while contributing to the knowledge of the programs' appropriate clinical uses.

Neuronal plasticity resulting from training and perceptual learning has been shown to involve alterations in neural connections and activity at multiple levels of the auditory pathway. For example, unilateral sound deprivation in adolescent ferrets has been shown to lead to subcortical changes (Moore, 1993), whereas frequency discrimination training in monkeys has been shown to produce alterations in the auditory cortex associated with changes in discrimination ability (Recanzone et al., 1993). When humans have been trained to discriminate speech sounds, changes in preattentive auditory neurophysiologic responses have been linked to perceptual changes (Kraus et al., 1995; Tremblay et al., 1997, 1998).

Evoked potentials, reflecting the precise timing of synchronous events in the neural encoding of stimuli, provide a sensitive index of neurophysiologic alterations related to training (Merzenich and Jenkins, 1995; Ohl et al., 2001). Relationships between evoked potentials, auditory processing and speech perception have been shown for children with language impairment (Tonnquist-Uhlen, 1996), dyslexia (Bakker and Vinke, 1985; McPherson and Ackerman, 1999), dysphasia (Holopainen et al., 1997), spelling disabilities (Byring and Jarvilehto, 1985), auditory processing disorders (Jirsa and Clontz, 1990) and learning problems (Kraus et al., 1996; Cunningham et al., 2000; King et al., 2002; Wible et al., 2002).

The present study evaluated the impact of Earobics, a commercial auditory training program, on the plasticity of cortical and subcortical central auditory pathway function in children with learning impairments. Previous work has demonstrated that many children who use similar programs exhibit improvement on measures of auditory processing and language function (Merzenich, et al., 1996; Habib et al., 1999; Merzenich et al., 1999). To elucidate neural plasticity associated with perceptual and cognitive changes following training, auditory pathway neurophysiology was examined both before (initial) and after (follow-up) the training programs, and over a similar time period in children who received no training.

2. Hypotheses

Brainstem responses to speech syllables have revealed latency delays in some learning-impaired children despite normal click-evoked latencies (King et al., 2002). Subjects with delayed brainstem responses, presumably signaling a lower-level deficit, will respond differently to training than those subjects with intact brainstem processing. Brainstem responses are not expected to change following training.

Immature cortical responses to speech syllables in quiet have been associated with poorer auditory processing skills in learning-impaired children (Cunningham et al., 2000). Following training, children will exhibit a more mature morphology (reduced amplitudes and earlier latencies) in cortical speech-evoked responses in quiet, reflecting improved auditory processing abilities.

Cortical responses to speech syllables in noise are more degraded in children with learning problems than normal-learning children (Cunningham et al., 2001; Wible et al., 2002). After training, cortical responses will become more resistant to the deleterious effects of background noise.

3. Methods

3.1. Subjects

Children between the ages of 8 and 12 years were recruited for this study through local newspapers and word-of-mouth. All subjects were initially participants in an ongoing study examining differences in auditory perception and neural encoding between normal and learning-impaired children (Listening, Learning and the Brain project (LLB)). Measures in the LLB project were selected to identify children whose learning problems include an auditory perceptual deficit. All children were native speakers of English, had normal mental ability (a verbal or non-verbal IQ measure ≥ 85) and normal binaural hearing thresholds (≤ 20 dB hearing level (HL) for octaves 500–4000 Hz). Children with learning problems (LP; attention deficit disorder and/or learning disability, diagnosed by independent clinicians) who participated in the current study exhibited a discrepancy of at least one standard deviation between measures of mental ability and reading, spelling, phonological awareness or auditory processing on the psychoeducational test battery (described subsequently), while children without learning problems (NL) scored within normal limits on the test battery. After their participation in the LLB project, families of LP children who met the criteria were provided information about the training program. LP children who served as controls were children who chose not to participate in the training program or children who enrolled in the LLB project after the training program had begun.

Children with learning problems either participated in the training program (LP-trained, $n = 27$) or were part of the test/retest control group (LP-controls, $n = 15$). LP-controls received no other form of intensive remediation and were matched for age, mental ability and academic achievement with the LP-trained children. In addition to the LP-controls, 7 children without learning disabilities were part of the test/retest control group (NL-controls). At least 20 additional NL children were also tested on each protocol measure to establish study-internal norms. Demographic and cognitive characteristics of the LP-trained, LP-

control and NL-control groups are presented in Table 1. If children were taking medications for attention deficit disorder, they were instructed to continue taking their medications during training and testing. This applied to one control and 4 trained subjects. LP-trained children were evaluated within 6 months before starting and 3 months after completing training. To control for changes resulting from normal growth and development during the test/retest interval, LP- and NL-controls were tested and re-tested over a similar period. Parental consent and the child's assent were obtained for all evaluation procedures and children were paid for their participation in the study. The research protocol was approved by the institutional review board of Northwestern University. The study took place over two consecutive summers; a cortical response measure in noise was added during the second summer. Therefore, children who were tested during the first summer (LP-trained $n = 9$ and LP-controls $n = 5$) were evaluated in quiet only.

3.2. Training

Children in the LP-trained group attended 35–40 1 h training sessions during an 8 week period. The training program was conducted by an independent agency and consisted of supervised work with Earobics Step I (developmental age 4–7 years) and Step II (developmental age 7–10 years) software (Cognitive Concepts, Inc., Evanston, IL, (Morrison, 1998; Diehl, 1999)). The Earobics programs provide training on phonological awareness, auditory processing and language processing skills through interactive games. Feedback is provided through visual and auditory modalities following each trial. Specifically, the program consists of audiovisual exercises in quiet and noise that incorporate phoneme discrimination, auditory memory, auditory sequencing, auditory attention, rhyming and sound blending skills. In some exercises, the rapid transitions of speech stimuli are elongated. Step I consists of 6 games with over 300 levels while Step II has 5 games with 600 levels of play. Step II focuses on the same skills as Step I, though at more advanced levels, and further emphasizes auditory memory and phonological skills in noise. For both programs, a child must successfully complete one level of play before moving on to a more difficult level. Auditory stimuli are presented bilaterally through headphones. Children respond by clicking the computer's mouse to indicate the number of sounds or phonemes in a stimulus or by clicking on pictures and letters on the screen. Because children presented with a wide variety of phonological and auditory processing deficits, and were below age-level on at least one measure of phonological awareness or auditory processing, they all began training with Step I to ensure mastery of basic concepts and moved on to Step II after successfully completing Step I.

3.3. Behavioral and academic achievement testing

Standardized measures of processes underlying learning and academic achievement were administered as a subset of the LLB battery. These tests included Reading and Spelling (Wide Range Achievement Test-3 (WRAT), Wilkinson, 1993); Incomplete Words, Memory for Words, Sound Blending, Listening Comprehension, Cross Out, Auditory Processing and Word Attack (Woodcock–Johnson-Revised (WJ-R), Woodcock and Johnson, 1989). Auditory Processing is a composite score derived from Incomplete Words and Sound Blending. The Brief Cognitive Scale (Woodcock–Johnson (WJ), Woodcock and Johnson, 1977) was administered to obtain a measure of mental ability. If a subject failed to achieve a score ≥ 85 on the Brief Cognitive Scale, the Test of Non-verbal Intelligence-3 (TONI-3, Brown et al., 1997) was administered. The subject was required to attain a score ≥ 85 on this alternate IQ estimate. This applied to 3 LP-trained and two LP-control subjects.

Earobics incorporates games that target skills measured by Incomplete Words and Sound Blending. These two tests were used to assess generalization of learning, while

Table 1
Subject characteristics

	LP-trained ($n = 27$)	LP-controls ($n = 15$)	NL-controls ($n = 7$)
Sex			
M	19	11	3
F	8	4	4
Diagnosis			
LD	16	12	–
ADD	3	1	–
LD/ADD	8	2	–
	mean (range)	mean (range)	mean (range)
Age (years)	9.65 (8.2–11.8)	9.97 (8.0–12.0)	10.24 (8.2–12.0)
Test/retest interval (months)	4 (2–9)	5 (2–9)	6 (2–11)
Mental ability (WJ or TONI)	105 (85–131)	109 (85–135)	128 (99–135)
Reading (WRAT-3)	91 (67–112)	96 (73–111)	113 (91–124)

Diagnoses of LD and ADD were all provided by independent clinicians, selected and paid for by the subjects' families.

improvement on the other tests would involve transfer of learning.

3.4. Neurophysiology

3.4.1. Stimuli

All stimuli were created on a Klatt digital speech synthesizer (Klatt, 1980). Detailed synthesis information has been previously published (Cunningham et al., 2001; King et al., 2002). Briefly, the stop consonants /da/ and /ga/ differ acoustically in the onset frequency of the third formant: 2580 Hz for /da/ and 2180 Hz for /ga/. The /ga/ syllable consists of a 40 ms initial formant transition, followed by a 60 ms steady-state vowel while the /da/ consists of a 40 ms formant transition, with an onset burst added to the first 10 ms.

Speech stimuli used for collection of neurophysiologic data were chosen based on their ability to reveal differences between NL and LP children. The phonemes /da/ and /ga/ acoustically incorporate initial rapid spectrotemporal transitions that are difficult for LP children to discriminate (Kraus et al., 1996). In LP children, relationships between cortical responses elicited by /ga/ and behavioral measures have previously been reported (Cunningham et al., 2001). In noise, cortical responses elicited by /da/ differ between NL and LP children (Cunningham et al., 2001, Wible et al., 2002). In addition, LP children exhibit significant differences in the auditory brainstem responses (ABR) when it is evoked by /da/ but not by a click stimulus (King et al., 2002).

3.4.2. Acquisition

A PC-based stimulus delivery system (Neuroscan Gentask) controlled time of delivery, stimulus sequence, and stimulus intensity, and triggered the PC-based evoked potential averaging system (Neuroscan Acquire). All electrode impedances were <5 kOhms. Continuous white Gaussian noise was generated by a PC system (Biologic) and mixed with the speech sound stimulus in a Studiomaster mixer board to produce a signal to noise ratio (SNR) of 0 dB. Two trained observers independently marked onset, offset and peak latencies and amplitudes and a third trained observer resolved discrepancies.

The recorded potentials are known to be pre-attentive, thus eliminating the possibility of practice effects, and allowing the children to attend to something other than the stimulus during testing. Therefore, the subjects watched videotaped movies or cartoons and were instructed to ignore the test stimuli. This procedure minimized attention to the stimuli, and made it possible for the children to sit still during the 45–90 min of repetitive stimulus presentation, significantly reducing movement artifact. Children selected the video and were quizzed about it afterwards to ensure it had engaged their attention. Stimuli were presented to the right ear through ER-3 insert earphones (Etymotic Research). The non-stimulated left ear was unoccluded to allow for listening to the soundtrack of the videotape, which was kept below 40 dB sound pressure level (SPL).

3.4.3. Brainstem neurophysiology

The ABR was collected in response to a click (0.1 ms) and randomly presented alternating polarities of /da/. Alternating polarities were added together to isolate the neural response from that of the cochlear microphonic (Gorga et al., 1985). ABRs were differentially recorded from Cz-to-ipsilateral earlobe, with forehead as ground. The sampling rate was 20,000 Hz. Responses were bandpass filtered on-line from 100 to 2000 Hz. Sweeps with noise levels which exceeded ± 35 μV were rejected from the average. Three repetitions of 1000 sweeps each were collected in response to the click as well as for each polarity of /da/. The click stimuli were presented at 80 dB SPL with an inter-stimulus interval (ISI) of 32 ms; the recording window was 20 ms, including a 5 ms pre-stimulus period. The /da/ stimuli were presented at 80 dB SPL with an ISI of 51 ms; the recording window was 60 ms, including a 10 ms pre-stimulus period. The latencies of the click-evoked wave V and the negative peak following /da/ evoked wave V (wave A) were marked and compared to normative values (King et al., 2002).

3.4.4. Cortical responses in quiet-/ga/

Cortical responses were elicited by a /ga/ stimulus, presented at 75 dB SPL, with an ISI of 490 ms. The 590 ms recording window included a 90 ms pre-stimulus period. The sampling rate was 1000 Hz. Responses were bandpass filtered on-line from 0.1 to 100 Hz. Responses were recorded from midline electrodes Fz, Cz, and mastoid electrodes A1 and A2. A nasal reference was used, with the forehead as ground and a bipolar supraorbital-to-lateral canthus electrode for eyeblink monitoring. Trials with eyeblink activity exceeding ± 100 μV were omitted from the average. Two thousand to 2500 sweeps were averaged off line for an individual's response. For this stimulus and this age range, the strongest and most reliable peaks observed were P1 and N2 (Sharma et al., 1997; Cunningham et al., 2000). Therefore the response latencies and amplitudes of these peaks were measured. The most positive peak centered at 85 ms was marked P1; the most negative peak centered at 230 ms was marked N2. Under these conditions, auditory processing (WJ-R) has been shown to be related to N2 latency in both NL and LP children (Cunningham et al., 2000).

3.4.5. Cortical responses in noise-/da/

Cortical responses were collected to 1000 stimulus presentations of /da/ in quiet and in noise (0 SNR). Stimuli were presented at 80 dB SPL and an ISI of 590 ms. The 575 ms recording window included a 75 ms pre-stimulus period. The sampling rate was 20,000 Hz and responses were bandpass filtered on-line from 0.05 to 100 Hz. Responses were recorded from Cz with reference, ground and eyeblink monitoring similar to cortical responses elicited by /ga/ in quiet. Sweeps with noise levels at any recording site

exceeding +100 μV were rejected on-line. For this stimulus, which included an enhanced onset, P1, N1, P2 and N2 responses were elicited. However, the P1/N1 response was reliably identified in fewer than half of the children in this study. The P2 and N2 peaks were clearly seen for all subjects and were chosen for analysis. The P2 and N2 peaks were the most positive and negative peaks centered at 145 ms and 235 ms in quiet, and 160 ms and 255 ms in noise. In addition, each individual's response in quiet, over the latency range of 100–350 ms, was cross-correlated to his or her response in noise. The highest correlation value within a 50 ms offset between waveforms provided a measure of the degradation of neural response timing (synchrony) in noise compared with quiet. The initial and follow-up waveforms in quiet were also correlated for each individual. This correlation had to yield $r \geq 0.6$ for the data to be considered valid for the analysis of changes in noise for this study. Data from 3 LP-trained children and two LP-control children were excluded on this basis. Correlation r-values were transformed to z scores for analysis.

3.5. Statistical analysis

On each measure, data from the trained and control subjects were pooled and divided into two groups, with equal numbers of members, based on the rank score for that measure at the initial test session. These groupings are referred to as ranking groups. For all measures, a two × two × two mixed-model repeated measures analysis of variance (RMANOVA) was performed with treatment and ranking groups as between-subjects factors and test session (initial test/follow-up test) as a within-subjects factor. For cortical responses, age at initial test was included as a covariate. Also, point-to-point t tests were performed between the grand-averaged waveforms elicited by /ga/ from each test session for each treatment group (trained, LP-controls and NL-controls). Twenty consecutive points (20 ms) had to reach significance ($P < 0.05$) for waveform differences to be considered non-spurious. In addition, cognitive and academic measures collected using standardized tests (WRAT, WJ, and WJ-R) were evaluated to identify individuals who exhibited clinically meaningful change. A follow-up improvement greater than one standard error of measurement for that test was considered a clinically significant gain on an individual measure. Chi-square analyses were performed to determine if a greater number of trained subjects than controls demonstrated improvement. To correct for the large number of statistical analyses performed, $P < 0.02$ was considered significant.

4. Results

4.1. Control groups

It was anticipated that LP-controls might differ from NL-controls on their test/retest performance on cognitive, academic or physiologic measures. If this were the case, it would be important to examine the trained children's changes with respect to each control group. However, while LP-and NL-control groups' initial and follow-up values differed for some measures, the magnitude of the test/retest differences (follow-up minus initial values) was similar across all measures for both LP-and NL-controls. Therefore, the LP-and NL-controls were combined into a single control group to account for initial to follow-up test differences attributable to retesting, maturation and development.

4.2. Behavioral and academic changes

The initial and follow-up group means for the cognitive and academic measures are shown in Table 2. The mean improvement on the Sound Blending test was greater in the trained than the control group ($F = 6.83$; $P < 0.01$) and was reflected in the trained group's mean improvement for the Auditory Processing composite measure of which Sound Blending is a part ($F = 10.17$; $P < 0.003$). Improvement on Sound Blending and Auditory Processing was independent of scores at initial testing for all groups (train group × ranking group × test session: sound blending $F = 1.65$; $P = 0.205$, and auditory processing $F = 16.46$; $P = 0.585$). Furthermore, the percent of children in the trained group who demonstrated significant improvement (greater than one standard error of the measurement) for Sound Blending and Auditory Processing was greater than the percent of controls showing such gains (Chi-square; $P < 0.02$ and $P < 0.006$, respectively). There were no significant improvements for the trained or control group on any other measures of cognitive ability or academic achievement.

4.3. Neurophysiology

4.3.1. Brainstem

Subcortical auditory pathway encoding was assessed by measuring the latencies of the ABR elicited by two different stimuli. When the ABR was elicited by click stimuli, all subjects had wave V latencies within the normal range; no changes were seen at follow-up testing. However, 56% of trained subjects, 60% of LP-controls and 29% of the NL-controls had delayed brainstem latencies (wave A, the negative peak following wave V) elicited by /da/ at initial testing (mean + 1 standard deviation of normal children, Fig. 1, reported by King et al., 2002). One LP-trained subject exhibited a wave A latency that was earlier than the mean − 1 standard deviation. Neither the click nor the /da/ evoked ABR latency measure changed for any subject from initial to follow-up testing.

4.3.2. Cortical responses in quiet-/ga/

Grand averaged waveforms for the cortical responses elicited by /ga/ at Fz, Cz, A1 and A2 are shown in Fig. 2.

Table 2
Cognitive and academic achievement and perceptual measures

	LP-trained ($n = 27$)		LP-controls ($n = 15$)		NL-controls ($n = 7$)	
	Initial	Follow-up	Initial	Follow-up	Initial	Follow-up
Incomplete Words	88 (9)	103 (10)	86 (11)	93 (8)	97 (15)	111 (17)
Sound Blending[a]	92 (11)	105 (14)	94 (10)	96 (14)	104 (15)	104 (7)
Auditory Processing[a]	89 (8)	104 (12)	90 (8)	94 (11)	101 (15)	107 (10)
Memory for Words	94 (11)	103 (13)	95 (16)	102 (14)	115 (17)	121 (23)
Cross Out	101 (14)	101 (13)	106 (14)	109 (17)	116 (15)	113 (13)
Listening Comprehension	112 (21)	120 (19)	109 (24)	117 (19)	125 (20)	134 (25)
Word Attack	92 (11)	91 (12)	92 (14)	95 (11)	113 (16)	117 (20)
Spelling	87 (10)	87 (12)	92 (14)	91 (9)	111 (15)	117 (19)

The means and standard deviations of the initial and follow-up cognitive and perceptual measures are presented. At initial testing, the LP-trained and the LP-control groups did not significantly differ for any of these measures. At follow-up testing, the mean improvement was similar for the LP-and NL-controls.
[a] Measures on which trained subjects showed significant gains compared to the combined control groups (RMANOVA, $P < 0.006$).

Point-to-point t tests of grand averaged waveforms of trained subjects exhibited a significant decrease in amplitude from 222–313 ms at Fz and 240–293 ms at Cz, while no significant changes were observed in the controls. In the trained group, the changes at Fz and Cz reflect a significant post-testing shift towards a more mature response. In particular, the observed decrease in P1N2 amplitude in the trained group is characteristic of normal maturational patterns (Oades et al., 1997; Sharma et al., 1997; Cunningham et al., 2000).

A reduction in N2 latency is also a reflection of maturation (Oades et al., 1997; Sharma et al., 1997; Cunningham et al., 2000). Training-associated reductions in the N2 latency observed at Fz were attributable to an interaction between treatment group and N2 latency at initial testing. The group of trained subjects with later N2 latencies at initial testing showed a significant decrease in N2 latency at post-test compared to all control subjects as well as to trained subjects with earlier N2 latencies at initial testing (One way analysis of variance (ANOVA), $F = 10.52$; $P < 0.001$).

In trained and control subjects, at all electrodes, the amount of change observed in cortical responses in quiet was not influenced by age ($t \leq 1.02$, $P = 0.33$). No significant changes were observed in any group from initial to follow-up testing at A1 and A2 electrodes.

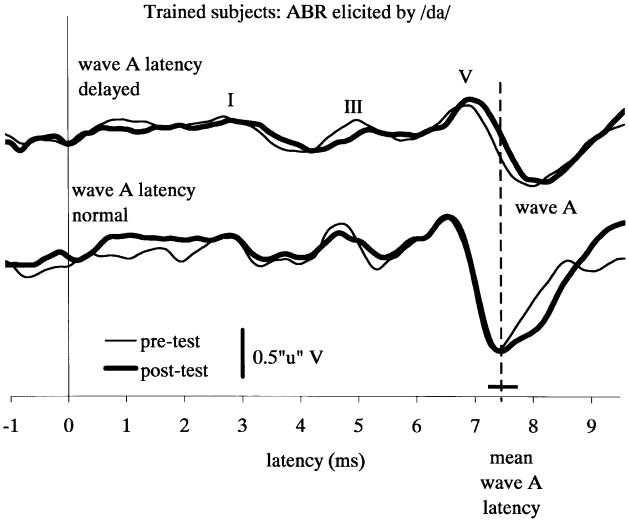

Fig. 1. ABR elicited by /da/. The mean wave A latency is marked with the dashed line, and one standard deviation by the bar that crosses through the dashed line King et al., 2002). The upper waveforms are the initial and follow-up results from a trained subject with a wave A outside normal limits, the lower waveform from a trained subject with a wave A latency within one standard deviation of a group of normal subjects (King et al., 2002). The traditional wave I, III and V peaks are marked, with wave A being the negative trough following wave V.

4.3.3. Cortical responses in noise-/da/

Compared to the quiet condition, all children exhibited reduced P2N2 amplitudes to /da/ stimuli presented in background noise (NL-controls $P < 0.002$; both LP-trained and LP-control groups $P < 0.0005$, paired samples t test). With training, the P2N2 response in quiet remained unchanged while the response in noise became more robust. As shown in Fig. 3, the trained group demonstrated a significant increase in P2N2 amplitude in noise at follow-up testing compared to control subjects. The interaction between treatment group and test session approached significance ($F = 4.12$; $P < 0.05$).

To further quantify these changes, each individual's P2N2 response in quiet was cross-correlated with their response in noise. A high correlation is expected if the waveform morphology is similar in the quiet and noise conditions. Trained subjects and control subjects showed similar quiet-to-noise correlation values (main effect of treatment group: $F = 0.10$; $P = 0.76$). However, there was an interaction between treatment group and test session such that subjects who underwent training showed a significant increase in their quiet to noise correlation while the control group did not show such a change ($F = 6.95$; $P < 0.01$). The mean increase in correlation for the trained subjects was 0.43 (SD = 0.58) while the mean correlation decreased for

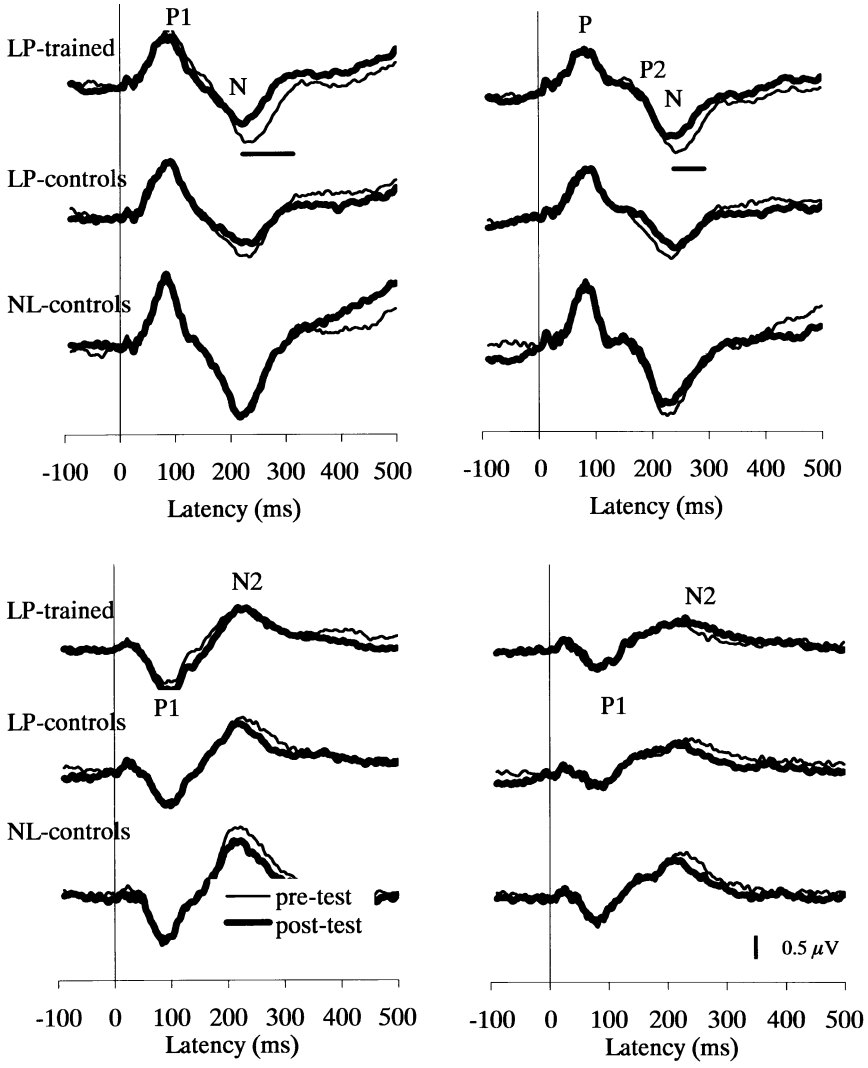

Fig. 2. Grand averaged cortical responses to /ga/. Within each panel, waveforms represent responses from LP-trained (top), LP-control (middle) and NL-control subjects. Panels represent responses recorded from Cz (upper left), Fz (upper right), A1 (lower left) and A2 (lower right). Horizontal bars indicate intervals over which point-to-point *t* tests indicated significant differences between initial and follow-up grand averaged waveforms. At the Fz recording site, LP-trained subjects exhibited a larger reduction in P1N2 amplitude than control subjects ($F = 5.79$; $P < 002$), which indicates a shift towards more mature cortical P1N2 responses (Cunningham et al., 2000). However, no significant changes were noted at the A2 and A1 recording sites (lower left and right).

both NL-controls (0.08, SD = 0.33) and LP-controls (0.35, SD = 0.78).

The trained children were divided according to their initial quiet-to-noise waveform correlations. Quiet-to-noise correlation values less than 0.74 (the mean correlation value for study-internal NL subjects) were considered 'poor' correlations while any higher values were classified as 'good' correlations. As shown in Fig. 4, trained subjects with poor quiet-to-noise correlations at initial testing showed degraded cortical responses in noise, while at follow-up testing their cortical responses in noise were enhanced, consistent with their improved quiet-to-noise correlations (Wilcoxon, $Z = 2.38$; $P < 0.02$). Trained children with good correlations at initial testing had robust cortical responses in both quiet and noise conditions. This did not change from initial to follow-up testing (Wilcoxon, $Z = 0.57$; $P = 0.60$). This demonstrates that it is the response in noise (rather than the response in quiet) that has changed after training.

4.3.4. Subcortical/cortical relationships

To assess the relationship between degraded subcortical and cortical auditory processing, each subject group was divided by ABR latency (normal vs. delayed) and evaluated for differences in cortical quiet-to-noise correlations. At initial testing, neither NL, LP-trained nor LP-control children demonstrated differences in the quiet-to-noise P2N2 correlations based on their ABR onset latency (Mann–Whitney $Z = 1.16$, $P = 0.25$; $Z = 0.89$, $P = 0.37$ and $Z = 0.87$, $P = 0.39$, respectively). Trained children with ABR /da/ wave A latencies greater than the mean +1 standard deviation of published norms (King et al., 2002)

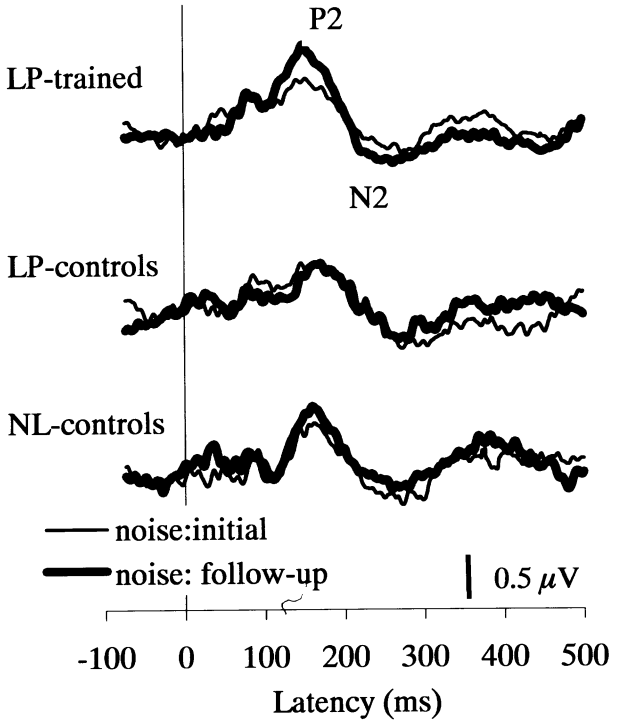

Fig. 3. Grand averaged waveforms of cortical evoked potentials P2N2 to /da/ in noise (0 dB SNR). With training (top), response amplitude increased in noise while LP-control (middle) and NL-control responses (bottom) were stable ($F = 6.56$; $P < 0.02$).

showed greater improvement in timing of cortical responses in noise than trained children with shorter latencies. This was reflected by the significant increase in quiet-to-noise P2N2 correlations at post-test in the group of children with longer ABR latencies (Wilcoxon, $Z = 2.37$; $P < 0.02$). Notably, in these children the cortical response in noise became more robust in spite of the failure of the ABR onset latency to shift to a more normal-like response. After training, no enhancement of the P2N2 amplitude in noise was observed in the group with an ABR onset latency within normal limits (Wilcoxon, $Z = 0.14$; $P = 0.89$).

4.3.5. Initial values and degree of change

On some measures, results obtained at initial testing were significantly related to the amount of change observed over the test/retest interval, regardless of treatment group or NL/LP status. Children who scored poorly at the initial test session on the cognitive tests incomplete words, memory for words, or listening comprehension made the greatest gains on these tests at follow-up testing ($F = 11.85$; $P < 0.001$; $F = 6.89$; $P < 0.01$ and $F = 9.85$; $P < 0.003$, respectively). Children with the more immature cortical responses at initial testing were the subjects who exhibited the greatest maturational changes. Finally, subjects with poor quiet to noise correlations at initial testing showed improved correlations at follow-up testing ($F = 6.05$, $P < 0.02$).

5. Discussion

This is a report of an ongoing study of the plasticity of perception and neural encoding of speech sounds in learning-impaired children. In children with learning impairments, relatively brief auditory perceptual training can alter auditory processing skills and cortical representation of speech in quiet and in noise. The trained children in this study improved on sound blending and auditory processing tasks, and showed latency and amplitude decreases in cortical potentials in quiet, along with more robust cortical responses in noise. No changes were seen in the brainstem responses.

Accelerated maturation of the P1N2 cortical responses observed after training suggests alterations in the non-primary reticulo-thalamic pathway that regulates gating of

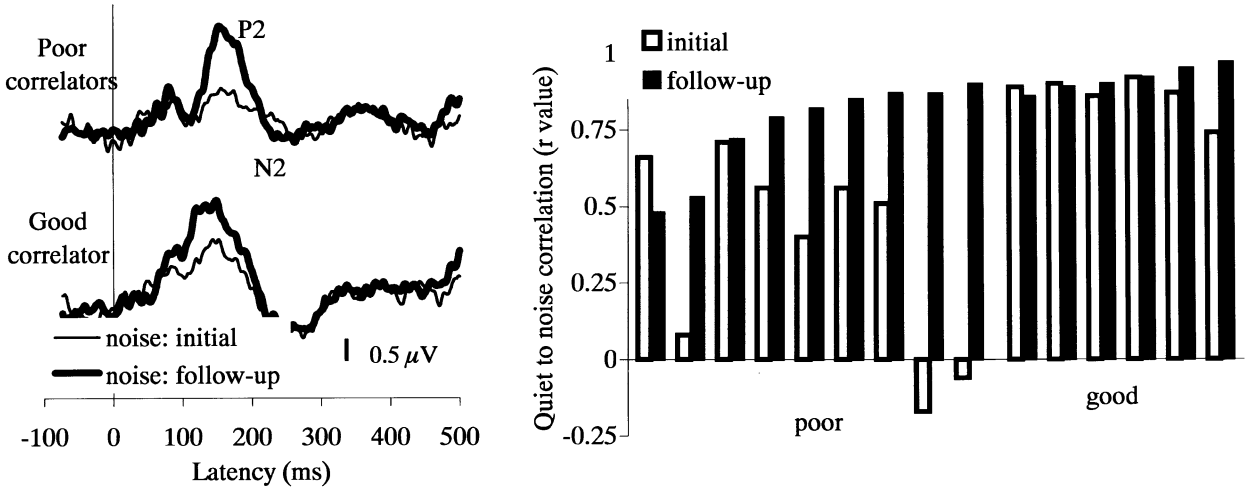

Fig. 4. LP-trained subjects with poor quiet-to-noise correlations at pre-test showed diminished cortical responses in noise. At post-test, their cortical responses in noise were enhanced (left), yielding improved quiet-to-noise correlations post-testing (right). LP-trained children with good correlations at pre-test had robust cortical responses in quiet and in noise and neither their responses (left) nor their quiet-to-noise correlations (right) changed from pre-to post-testing.

sensory information (Antonelli and Calearo, 1968; Boop et al., 1994). Accelerated maturation might also reflect changes in the sensory encoding of the acoustic attributes of the stimulus in the thalamocortical pathway (Chen and Buchwald, 1986). In children, the P1 response is usually maximal over the Fz recording site, while in adults it is maximal at Cz (Oades et al., 1997). This maturational pattern might contribute to the greater plasticity seen in the P1N2 responses at Fz compared to Cz.

It was demonstrated that although ABR responses did not change with training, alterations in the cortical responses were evident, thus highlighting the independence of plasticity at different levels of the central auditory pathway. Moreover, children with delayed brainstem responses to speech sounds exhibited the greatest improvement in the cortical representation of speech sounds in noise. This suggests that children with brainstem timing deficits are good candidates for this type of training. Although not addressed in this study, auditory neuropathy patients are another group showing brainstem timing deficits, and therefore may also benefit from auditory training (Kraus et al., 2000).

Cortical responses became more robust in noise after training. Correlation between waveforms in quiet and in noise improved, suggesting that timing deficits that contribute to difficulties in perceiving speech in noise in learning-impaired children were diminished (Bradlow et al., 2003; Wible et al., 2002). Two factors must be considered when speculating about the more robust P2N2 response in noise seen after training. Noise is known to differentially affect how the hemispheres contribute to midline recordings of cortical potentials elicited by speech sounds (Shtyrov et al., 1999). In addition, the P2 response is thought to be generated, at least in part, by bilateral activity in the supratemporal planes (Verkindt et al., 1994). This implies that the more robust representation of the P2N2 amplitude in noise after training might be attributable to a change in the relative contributions of the hemispheres to representing speech sounds in noise. Other possible sources of the more robust response in noise include the increase of synaptic strength of existing excitatory synapses, increased myelination of neuronal axons and/or the recruitment of additional neurons to existing generators (Buonomano and Merzenich, 1998; Klinke et al., 1999; Klingberg et al., 2000).

The present study demonstrated combined improvements in auditory processing and alterations in auditory pathway physiology, consistent with previous work evaluating the impact of training programs on reading impaired children and adults. In one study, two of 3 dyslexic adults showed more normal patterns of functional magnetic resonance imaging (fMRI) activity in the left pre-frontal cortex in response to rapid non-speech auditory stimuli after training with Fast ForWord. (Temple et al., 2000; Kujala et al., 2001). These two individuals also demonstrated significant improvement in language comprehension while a third subject exhibited neither physiologic nor perceptual changes. Kujala et al. (2001) used non-linguistic audio-visual training materials with reading impaired children. Compared with non-trained controls, trained children demonstrated improved and more rapid identification of printed words. In addition, the trained children displayed an enhanced mismatch negativity (MMN, a physiologic response to acoustic change) elicited by tone pairs after training. The MMN enhancement correlated with a composite measure of their reading ability. The mechanism(s) underlying a relationship between an enhanced MMN to non-speech stimuli and improvements in reading remains unclear. In a third study by Richards et al. (2000), training and assessment were phonologically based. Before training, proton echo-planar spectroscopy revealed that dyslexic boys exhibited enhanced neural activity in the left anterior quadrant, including the left frontal lobe, in response to a phonological task. The authors suggested that this might reflect more mental effort on the part of the dyslexic readers to accomplish the same phonological task as normal readers (Richards et al., 1999). One year after participating in a reading/science program developed to enhance their reading skills, subjects not only demonstrated improvement in reading, they also exhibited more normal-like patterns of neural activity in the left anterior quadrant (Richards et al., 2000).

The aspects of training contributing to perceptual and neurophysiologic changes are not clear from the previous studies, nor can they be identified from the present study. Learning impairments related to reading disabilities are caused by a variety of factors. In the current study, different activities of the program targeted different aspects of auditory perception, leading to the possibility of a wide spectrum of auditory pathway changes. It is possible that some changes take place as a natural part of maturation and learning, since some individual LP- and NL-controls showed gains on neurophysiologic and/or cognitive measures. It is also plausible that the neurophysiologic cortical plasticity seen in the LP-trained subjects could be derived from participating in supervised daily computer exercises and was independent of the auditory training aspects of the software. This explanation could also account for the neural plasticity observed in the previous studies. Ideally, a control group trained on non-auditory focused software is needed to determine which aspects of the training protocol are associated with the cognitive and neurophysiologic changes. However, practical issues have complicated assembling such a control group. Families are reluctant to commit to participation in a time-consuming project as a control. Most families of learning-impaired children are aware of the nature of the auditory training software programs and it is difficult to perform a ‘blind’ study in which families do not know whether their child is in the ‘treatment’ or ‘control’ group.

Notwithstanding the uncertainty concerning the precise aspects of training that contributed to the cognitive and neurophysiologic changes seen in the trained group, this

study sheds light on the nature and sites of plasticity of these processes in learning-impaired children. The apparent stability of the brainstem response despite training could reflect intrinsic properties and/or developmental limitations in the plasticity of subcortical pathways (e.g. changes in timing of the brainstem response may occur only in younger children). Previous work on the plasticity of auditory brainstem nuclei in animal models has shown that unilateral auditory deprivation produces the most pronounced effects on immature subcortical auditory pathways, while slower and less remarkable changes can occur in the adult system (Moore, 1993). Changes range from neuronal loss and shrinkage in the cochlear nucleus to long term alterations of projections from the cochlear nucleus to the inferior colliculus (Moore, 1994). Conditioning techniques have also been successful in modifying the receptive fields of the adult dorsal and ventral cochlear nuclei (McIntosh and Gonzalez-Lima, 1993; Woody et al., 1994). If neurophysiologic changes occurred in the brainstem that did not significantly impact processing in the inferior colliculus (believed to be the generator of the post-wave-V negativity which was studied herein (Hashimoto et al., 1981)), the changes would not have been identified in this study. The frequency following response and brainstem responses in noise could be altered by Earobics training and the changes would need to be identified with other testing procedures.

This work indicates that speech-evoked neurophysiologic measures are well suited to improve our understanding of plasticity in auditory-based learning disabilities. First, evoked responses reflect neurophysiologic timing related to speech-sound structure that cannot be seen with imaging techniques. Second, increased neural synchrony, which has been linked to perceptual learning (Merzenich et al., 1999), can be demonstrated through changes in evoked potentials. Third, auditory evoked potentials have been shown to reflect perception in normal and impaired children (Neville et al., 1993; Ponton et al., 1996; Tonnquist-Uhlen, 1996; Jordan et al., 1997; Cunningham et al., 2000, 2001). Fourth, deficits in the encoding of speech signals in quiet have been demonstrated at the auditory brainstem level and in both quiet and noise at cortical levels in learning-impaired children (Kraus et al., 1996; Schulte-Koerne et al., 1998; Cunningham et al., 2001). Consequently, there is a strong rationale for investigating the modulation of neural timing along the auditory pathway in quiet and in noise in order to assess the physiological changes associated with training in children with learning disabilities.

In this study, neural plasticity was studied in a group of learning-impaired children using a popular commercial auditory training program. Changes in cognitive and neurophysiologic measures were observed in children after a relatively brief period of training. Additional data from children trained with a variety of programs are needed to determine which neurophysiologic patterns and cognitive characteristics best predict 'success' with which auditory training programs. In addition, the underlying neurophysiologic deficits contributing to difficulties experienced by learning-impaired individuals perceiving speech in noise need to be further elucidated. Children with delayed brainstem timing in quiet exhibited more robust cortical responses in noise after training. Future work examining the brainstem and cortical responses in noise might reveal additional factors contributing to difficulties perceiving speech in noise. The use of auditory processing software-training programs to study neural and perceptual plasticity in children with learning problems should clarify the appropriate use of these programs and the extent to which neural plasticity is associated with perceptual changes.

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