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Abnormal neural encoding of repeated speech stimuli in noise in children with learning problems

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Abstract

Objectives: This study investigated whether neurophysiologic responses to repeated speech stimuli, presented in quiet and noise, differed between normal children (NL) and children with learning problems (LP).

Methods: Subjects were normal-hearing, school-age children. NL subjects scored significantly better than LP subjects on measures of reading, spelling and speech sound discrimination. Stimuli (40 ms /da/) were presented to the right ear at 80 dB SPL. Stimuli were presented in trains of four, separated within trains by 360 ms. The interval between trains was 1060 ms. Stimuli were presented in quiet and in white noise (S/N + 15). Cortical responses were recorded from an electrode placed along the midline at Cz.

Results: Correlations between the first and 4th responses were lower in noise than in quiet for LP subjects only. Response correlations in quiet were no different between groups. There were no root-mean-square (RMS) amplitude differences between groups.

Conclusions: Response correlation in noise suggested that the LP population consisted of two subgroups, one whose responses appeared relatively normal, and another whose responses were severely degraded by repetition in noise. Response correlations in noise were related to behavioral measures of auditory processing and spelling. These findings suggest that abnormal, asynchronous, auditory cortical encoding may underlie some language-based learning problems.

Keywords: Auditory evoked potentials; Auditory cortex; Learning disabilities; Speech signal encoding; Asynchrony

1. Introduction

The ability of a listener to understand real speech in a natural environment places many demands on the auditory system. Among these demands are the accurate representation of rapidly changing spectral information comprising the speech signal and the separation of this signal from background noise. While all listeners clearly demonstrate impaired perception at extremes in speaking rate and background noise, a subset of listeners experiences enhanced sensitivity to the detrimental effects of repeated stimulation and background noise. Many studies have shown that subjects diagnosed with language-based learning disabilities perform poorly when processing rapid acoustic signals (Tallal and Piercy, 1974; Farmer and Klein, 1995; Hari and Kiesila, 1996; Wright et al., 1997; Nagarajan et al., 1999; Cestnick and Jerger, 2000; Temple et al., 2000). Similarly diagnosed subjects have exceptional difficulty processing acoustic signals which are presented in the presence of noise (Jerger et al., 1987; Breedin et al., 1989; Katz, 1992; Katz et al., 1992; Welsh et al., 1996; Bellis, 1996; Chermak and Musiek, 1997; Cunningham et al., 2001). Neurobiological abnormalities accompany many of these auditory processing deficits (Nagarajan et al., 1999; Temple et al., 2000; Cunningham et al., 2001). These findings contribute to an understanding that some language-based learning disabilities are rooted, in part, in altered representations of acoustic information. Distorted encoding of acoustic speech signals could underlie weakened perception and categorization of phonemic information (Kraus et al., 1996; King et al., 2002). Such deficits could certainly contribute to difficulties in the development of reading and other language skills (Godfrey et al., 1981; Reed, 1989; McBride-Chang, 1996).

While the primary goal of the current study was to understand auditory processing in children with learning problems, there was also motivation to further understand normal neural mechanisms which underlie processing of repeated stimuli, and stimuli in noise, especially when these stresses are combined, as they are in most real listening environments. Studies of normal subjects have shown

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that cortical responses decrease in amplitude and increase in latency upon repetition of stimuli (Woods and Elmasian, 1986; Budd et al., 1998) and following the addition of noise (Whiting et al., 1998; Martin et al., 1999).

Inspired by the aforementioned findings, the present study was designed to further examine effects of stimulus repetition and background noise on the neural representation of auditory stimuli in normal and learning impaired subjects. Specifically, the intent was to expand upon previous studies, which investigated rapid or repetitive stimuli or noise in isolation, often using simple tonal stimuli. By simultaneously stressing the auditory system with stimulus repetition and background noise, and by using a complex speech stimulus, the present study incorporated conditions which simulated real listening situations more accurately than studies which incorporated some of these features in isolation. Additionally, non-linear transformations throughout the auditory system make difficult the prediction of responses to complex signal patterns based on knowledge of responses to simpler stimuli (Sachs et al., 1983; Rauschecker, 1997). Responses elicited by our paradigm thus provide further insight into the neural representation of speech under 'real world' conditions. Since learning disabilities manifest themselves outside of the laboratory in normal, everyday life, it is by mimicking real conditions that we may most accurately describe any neural abnormalities underlying such problems.

2. Methods

2.1. Subjects

Subjects were 25 English-speaking children (mean age 11.1 ± 1.8 years) with normal bilateral hearing (pure tone thresholds <20 dB HL for octaves 500–4000 Hz). These children were chosen from a pool of subjects who participated in earlier related studies conducted by this laboratory. In accordance with the approval of this research by the Northwestern University Institutional Review Board, all subjects and their legal guardians signed forms which acknowledged their informed consent. Thirteen subjects were diagnosed with a learning problem (LP) prior to inclusion in the study. These were professional diagnoses, performed independent of the current study, by clinical psychologists, school psychologists, neurologists, etc. Although mean intelligence was significantly higher for normal (NL) children (mean IQ = 122) than for LP children (mean IQ = 102), the mean for LP subjects was slightly above normal (normal IQ = 100), and all children were within or above the normal range (IQ > 85) (Woodcock and Johnson, 1977). Mean performance of LP children was significantly poorer than mean performance of NL children on standardized measures of reading and spelling (Wilkinson, 1993). LP subjects performed worse than NL subjects when discriminating stimuli along a speech sound continuum whose endpoints were the phonemes /da/ and /ga/ (Carrell et al., 1999). Both groups of children performed equally well on the same task when the speech sound continuum had endpoints of /ba/ and /wa/. These tasks required that the children indicate whether two speech sounds from along the chosen continuum were 'same' or 'different'. Stimuli were initially presented from the two endpoints of the continuum, but upon accurate discrimination, were made increasingly similar, until a stimulus pair that could be accurately discriminated 70% of the time was reached. LP subjects for this study were chosen if their /da/-/ga/ discrimination score was greater than one standard deviation beyond the mean discrimination score demonstrated by NL subjects in a previous study of a large population (Kraus et al., 1999). A similar study indicated that both NL and LP subjects were able to similarly discriminate stimuli along the /ba/-/wa/ continuum, providing evidence that there was no bias between groups in terms of understanding and performing the task; the /da/-/ga/ discrimination group differences truly reflected perceptual ability (Kraus et al., 1996). Subjects for the current study were thus chosen based on their demonstrating: (a) the ability to perform the task as reflected by normal /ba/-/wa/ discrimination, and (b) /da/-/ga/ discrimination either within (NL) or beyond (LP) the previously measured normal range. By revealing specific auditory perceptual difficulties, this second criterion made possible the selection of LP subjects whose learning problems would likely have some basis in abnormal auditory perception. A summary of group means and between-groups comparisons is shown in Table 1.

2.2. Stimuli and recording

Evoked potentials were elicited by the speech stimulus /da/. The 40 ms phoneme was generated with a Klatt (1980) digital speech synthesizer, at a sampling rate of 10 kHz (SenSyn). The stimulus was composed of 5 formants that transitioned from the consonant /d/ to the vowel /a/. The fundamental frequency (F_0) and the first 3 formants ($F_{1,2,3}$) changed linearly over the duration of the stimulus. F_0 ramped from 103 to 121.2 Hz, F_1 from 220 to

Table 1
Subject characteristics[a]

	NL ($n = 12$)	LP ($n = 13$)	P
Age (years)	11.2 (1.4)	11.0 (2.3)	NS
Speech discrimination			
Just noticeable difference			
/ba/-/wa/ (ms)	8.4 (3.4)	10.4 (3.6)	NS
/da/-/ga/ (Hz)	84 (12)	191 (74)	<0.01
Reading	118 (19)	84 (11)	<0.01
Spelling	116 (13)	83 (8)	<0.01
IQ	122 (13)	102 (12)	<0.01

[a] Values in parentheses indicate standard deviations. IQ covaried for the following comparisons: speech discrimination, reading and spelling. For reading, spelling and IQ, standard score is 100 (15).

720 Hz, F_2 from 1700 to 1240 Hz and F_3 from 2580 to 2500 Hz. F_4 and F_5 remained constant at 3600 and 4500 Hz, respectively. The initial 10 ms of the stimulus contained an onset burst in F_3, F_4 and F_5 as described by Klatt (1980). The onset burst was included, and the vowel /a/ abnormally abbreviated, because this same stimulus was to be used to elicit auditory brainstem responses (ABR) in these same subjects for a subsequent, related study. The ABR, traditionally evoked using clicks, is best elicited by stimuli with brief rise time, presented at a rapid rate. The onset burst and abbreviated vowel, allowing increased presentation rate, would both contribute to enhanced ABR recording.

Files from the Klatt synthesizer were presented by a PC-based stimulus delivery system (NeuroScan Gentask) that output the signals through a 16 bit converter. That system controlled the time of delivery, the stimulus sequence and stimulus intensity. It also triggered the PC-based evoked potentials averaging system (NeuroScan Acquire) at stimulus onset.

Stimuli were delivered monaurally to the right ear through insert earphones at 80 dB SPL. Stimuli were presented in quiet and in background noise (S/N + 15 dB). White noise was generated by a PC-based stimulus delivery system (Bio-Logic). The speech and noise signals were combined in a mixing board (Optimus) and presented to the earphone transducer (Etymotic Research ER-2). Stimuli were presented in trains consisting of four stimuli. An interstimulus interval (ISI: latency between stimulus offset and subsequent stimulus onset) of 360 ms was used to separate stimuli within trains. Pilot data indicated that this was the shortest ISI which could be used without presenting a subsequent stimulus while the response to the previous stimulus was still evolving. Such response overlap would have interfered with analyses. The intertrain interval (latency between offset of final stimulus in train and onset of initial stimulus in subsequent train) was 1060 ms.

The final averages were composed of two blocks of 500 responses, for a total of 1000 responses, per position in the stimulus train, per S/N.

Subjects were tested in a sound-treated booth and were instructed to ignore the stimuli. To promote subject stillness during recording, as well as to diminish attention to the stimuli, each subject watched a videotape of his/her choice, with soundtrack presented in free field at 40 dB SPL.

Silver–silver chloride electrodes (impedance $<5\ k\Omega$) were placed on the nose, forehead, superior and outer canthus of the left eye and along the midline at Cz. These acted as reference, ground, eyeblink monitor and active electrodes, respectively.

The recording window was 405 ms, including a 5 ms prestimulus period. Data were collected at a sampling rate of 20 000 Hz, with a gain of 5000, and were digitally bandpass filtered online from 0.05 to 100 Hz. Artifacts that measured in excess of $\pm 100\ \mu V$ were online rejected from inclusion in the averaged response.

2.3. Data analysis

Averaged responses to the first and 4th (final) stimuli in the train, presented in quiet and in noise, were analyzed. Averaged waveforms were lowpass filtered at 50 Hz. The latency range that was initially investigated was from 50 to 300 ms post-stimulus-onset. Further investigation focused on the 150–250 ms latency range. Prior to calculation of root-mean-square (RMS) amplitude, waveforms were shifted to a baseline of zero in order to remove DC drift. Within each subject, Pearson correlation *r*-values were calculated between pairs of response waveforms. To transform correlation values to an approximately normal distribution for the purposes of analysis, Pearson *r*-values were converted to *z*-scores using Fisher's transformation. Repeated measures analysis of variance (ANOVA) followed by post hoc paired and unpaired *t* tests were used for statistical analysis of correlation and amplitude measurements. To control for Type I errors during post hoc analyses, post hoc tests that resulted in *P*-values less than 0.01 were accepted as indicating significance. Additional analyses of smaller groups of subjects necessitated the use of non-parametric analyses (Mann–Whitney *U*, Wilcoxon signed-rank, Fisher's exact test, Spearman Rho).

Both RMS amplitude and correlation measurements were employed due to the difficulty in consistently identifying response waveform features across stimulus conditions (1st/4th in train; quiet/noise) and subject groups (NL/LP). Measurements of amplitudes and latencies of specific response features depend upon there being identifiable features that consistently occur in all conditions, as well as in all subjects. Stresses of stimulus repetition and background noise degraded the responses to a sufficient degree that consistent identification of peaks became a difficult task. Both RMS amplitude and correlation measures require only that the experimenter decide upon a latency range over which calculations are to be performed. These techniques facilitated the measurement of detailed features in degraded responses. An additional strength of these analytical tools is that they incorporate the vast amount of information which is present 'between the peaks' of the evoked responses, rather than focusing exclusively on a few discrete morphological features.

3. Results

3.1. Normal, unstressed response

Average responses are shown in Fig. 1. In the best cases, usually in the unstressed responses (i.e. initial stimulus in train, prior to repetition, in quiet), the normal P1/N1/P2/N2 complex could be observed. These consist of the positively deflected P1 occurring around 75 ms post-stimulus-onset, followed by the N1 negativity. These are followed by the second major positive deflection, P2, occurring around

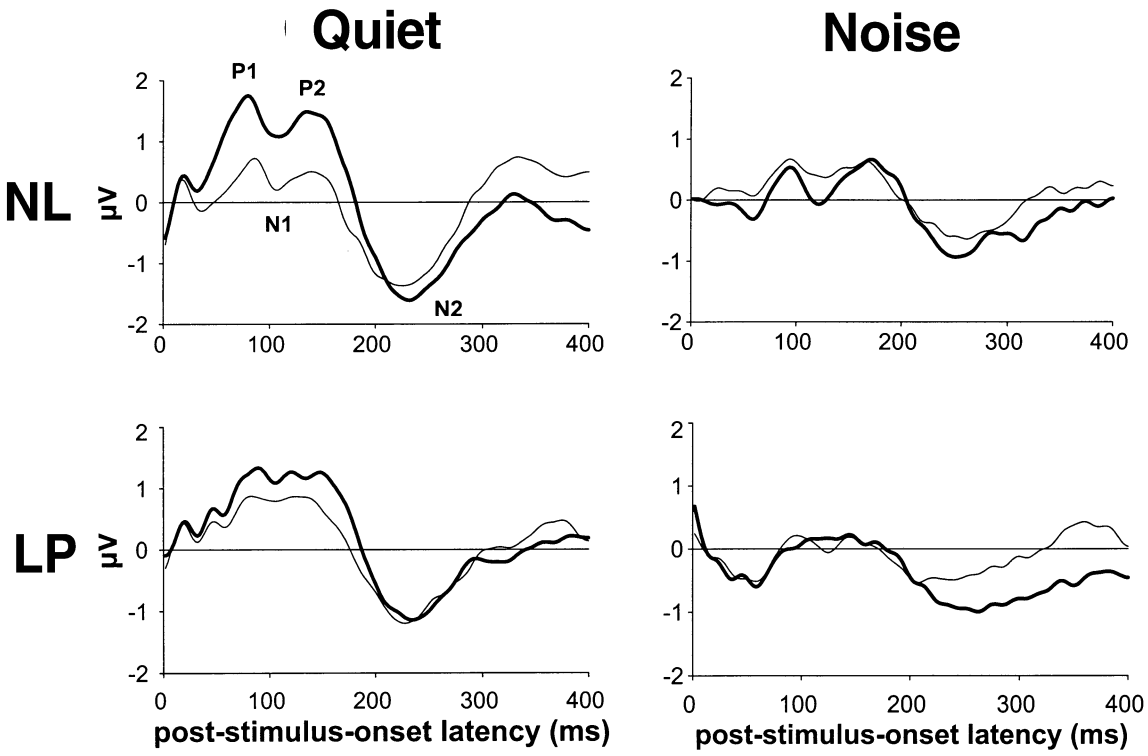

Fig. 1. This figure depicts the average responses of normal children (NL, $n = 12$) and children with learning problems (LP, $n = 13$) to the 1st (thick line) and 4th (thin line) stimuli in a train, presented in quiet and in noise. Prominent waveform features, P1/N1/P2/N2, are indicated.

150 ms, followed by the major N2 negativity. The response then gradually returns to baseline. However, response degradation due to stresses of repetition and noise, as well as individual differences between subjects, made consistent identification of these responses difficult, hence the use of more objective analytical methods (e.g. correlation, RMS).

3.2. Differences in response correlation

Combined stresses of repetition and noise affected LP subjects more than NL subjects on a measure of response correlation. The mean correlation between the 1st and 4th responses in noise was significantly lower than the mean correlation between 1st and 4th responses in quiet, in the LP subject group only (Fig. 2). The addition of noise did not significantly diminish the mean correlation between 1st and 4th responses in the NL subjects. The following pairs of responses were correlated for each subject: responses to the 1st and 4th stimuli in a train, in quiet (Q1Q4); responses to the first stimuli in quiet and in noise (Q1N1); responses to the first stimulus in quiet and the 4th stimulus in noise (Q1N4); responses to the 4th stimuli in quiet and in noise (Q4N4); responses to the first and 4th stimuli in noise (N1N4). Mean correlations were compared using a 2 (subject group) × 5 (pairs of correlated responses) ANOVA, with repeated measures of correlated-pair. There was no main effect of subject group. There was a significant main effect of correlation-pair. Post hoc paired t tests indicated Q1Q4 > Q1N1 for both subject groups. The following relationships were significant for the LP subject group only: Q1Q4 > N1N4; Q1Q4 > Q1N4.

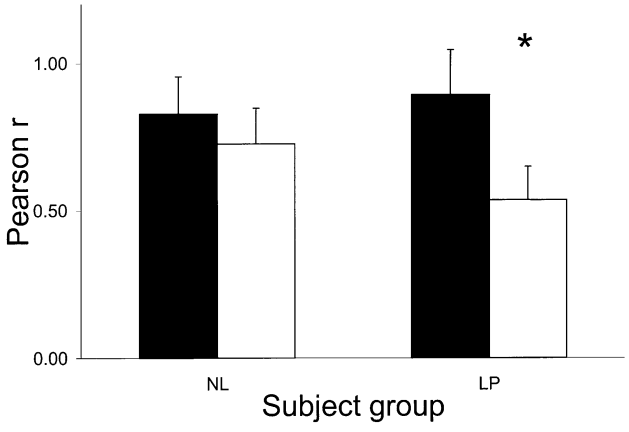

Fig. 2. Responses to the 1st and 4th stimuli in a train were correlated in order to describe the degree to which the shape of the initial response was preserved in the repeated response. Mean correlation between repeated responses was significantly worse in noise (□) than in quiet (■) in LP subjects only. There was no significant difference between mean correlations in quiet and in noise in NL subjects. In both subject groups, correlations between responses in quiet indicated that response shape and timing were fairly well preserved. The addition of noise, however, degraded the responses in LP subjects to a degree sufficient to result in significantly lower correlation. The timing and shape of the initial response was preserved by the repeated response in noise in NL subjects.

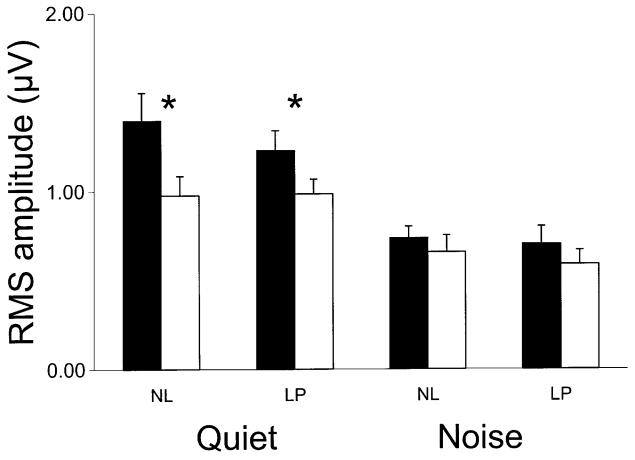

Fig. 3. Measures of RMS amplitude indicated no differences between subject groups. Patterns of RMS change within a group were similar for both groups. In quiet, the effect of stimulus repetition was to significantly decrease the amplitude of the 4th response (□) relative to the first response (■). Likewise, the addition of noise significantly diminished the response amplitude. In noise, however, the amplitude of the initial response was maintained by the repeated response.

3.3. Response correlations are especially sensitive over the 150–250 ms latency range

Patterns of response correlations in noise that were exhibited over the entire 50–300 ms response latency were also observed over the 150–250 ms range. Response waveforms illustrated the largest peaks and greatest sensitivity to combined stresses of repetition and noise over the range from 150 to 250 ms. A 2 (subject group) × 5 (pairs of correlated responses) ANOVA, with repeated measures of correlated-pair, was used to assess correlation measures over this range. There was no main effect of subject group. There was a significant main effect of correlated-pair. Post hoc paired *t* tests indicated Q1Q4 > Q1N1 and Q1Q4 > Q1N4 for both subject groups. The following relationship was significant for the LP subject group only: Q1Q4 > N1N4.

3.4. No group differences in response magnitude

Effects of stimulus repetition and/or noise on response amplitude were not different between subject groups. There were no significant between-groups differences in response RMS amplitude for any stimulus condition (Fig. 3). Patterns of change of RMS amplitude within a subject group were not different for either subject group. Effects of stimulus repetition and background noise on mean RMS amplitudes were measured using a 2 (group) × 2 (stimulus position) × 2 (S/N) ANOVA, with repeated measures of stimulus position and S/N. Significant main effects were indicated for both stimulus position and S/N. A significant interaction of these two factors was also indicated. There was no significant main effect of subject group. Within-group paired *t* tests indicated the following significant differences. The mean amplitude of the response to the 1st stimulus in a train presented in quiet was larger than the response to the 4th stimulus in quiet and was larger than the mean responses to the 1st and 4th stimuli presented in noise. The mean response to the 4th stimulus was larger in quiet than in noise. There were no significant differences between the mean amplitudes of responses to the 1st and 4th stimuli presented in noise. These patterns of within-group differences were identical for both subject groups.

3.5. Subgroups of LP subjects

Not all LP subjects were similarly affected by combined repetition and noise. A measure of response correlation in noise revealed that a subset of LP subjects appeared identical to NL subjects, while the remaining LP subjects' responses were significantly affected by combined repetition and noise. The median among LP subjects on the measure of correlation between the 1st and 4th responses in quiet and in noise, Q1Q4 and N1N4, over the 150–250 ms latency range, was used to split LP subjects into two distinct subgroups. While all subjects had similar correlations in quiet, 6 subjects had Pearson *r*-values in noise greater than 0.75, while the remaining 7 subjects had *r*-values less than 0.5. Based upon this separation, LP subjects were divided into two groups, LP_{high} ($r > 0.75$ in noise) and LP_{low} ($r < 0.5$ in noise). Correlation values for each LP child are presented in Fig. 4. Comparisons of mean response correlations in noise indicated that LP_{high} subjects were no different from NL subjects. LP_{low} subjects had a significantly lower mean correlation in noise than did NL subjects. There were no differences between the three subject groups on the measure of response correlation in quiet. Within the

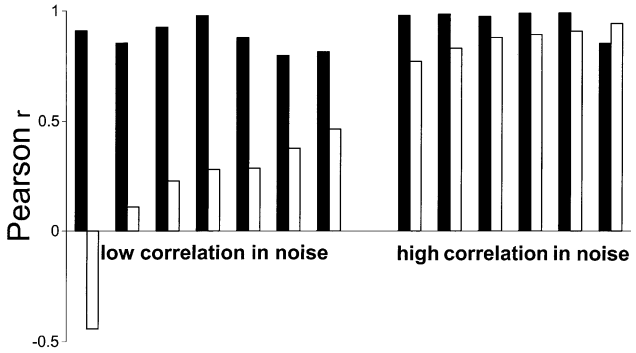

Fig. 4. One subset of LP subjects was extremely sensitive to stresses of repetition and noise, while the remaining LP subjects did not exhibit such sensitivity. Correlations between repeated responses in quiet (■) and noise (□) were calculated over the latency range 150–250 ms. Shown here are response correlations in quiet and in noise for each LP subject. All subjects exhibited comparable correlations between responses in quiet. In noise, six subjects exhibited correlations greater than 0.75, while seven subjects exhibited correlations no greater than 0.50. Comparisons with NL subjects indicated that neither subset was different from NL subjects on the measure of correlation in quiet. The LP subjects with high correlation in noise were not different from NL subjects on that measure of correlation in noise, while the subjects with low correlation in noise had significantly lower correlation in noise compared to NL subjects.

LP subjects, further analyses of intelligence, academic and perceptual measures revealed neither significant differences between the two subgroups, nor any significant correlations between these behavioral measures and the measure of response correlation in noise, over the 150–250 ms range, which was used to separate subgroups. Fisher's exact tests revealed no significant differences between correlation-based LP subgroups when subjects were also grouped according to commonly used clinical definitions of language-based learning problems (i.e. reading < 85, spelling < 85, IQ-reading > 15 and IQ-spelling > 15).

3.6. Correlation in noise is independent of amplitude

Since the mean correlation between responses was significantly lower in noise than in quiet in LP subjects only, the measure of response correlation in noise was of particular interest. This measure was subjected to further analyses in order to determine relationships between response correlation in noise and other physiological and behavioral measures.

There was concern that responses of smaller amplitude could have been more susceptible to distortion as a result of their proximity to the 'floor' of noise present in the recordings. Though two responses could have been very similarly shaped physiologically, and thus should have correlated highly, excessive effects of noise on small responses could have 'artificially' lowered response correlation. Low correlation between small responses, interpreted as degraded response synchrony, could in fact have reflected excessive effects of noise on two responses which were actually highly synchronized. This was not the case. The absolute amplitude of the first response in noise was not significantly related to response correlation in noise. Nor was the amplitude in noise of the 4th response relative to the first response (RMS N4/RMS N1) related to the correlation between responses in noise. Neither the size of the initial response in noise nor the relative change in size with repetition affected the correlation between responses. Additional modeling of responses and noise also supported this independence between response amplitude and correlation.

3.7. Correlation in noise relates to measures of behavior

There were significant relationships between measures of subjects' behavior and the correlations between physiologic responses in noise (Fig. 5). For all subjects, the correlations between 1st and 4th responses in noise were related to behavioral measures of /da/-/ga/ speech sound discrimination (partial correlation coefficient (p.c.c.) $= -0.59$), auditory processing (p.c.c. $= 0.56$) and spelling (p.c.c. $= 0.54$). IQ was controlled for during calculation of partial correlation coefficients, because mean IQ for LP subjects was significantly lower than mean IQ for NL subjects

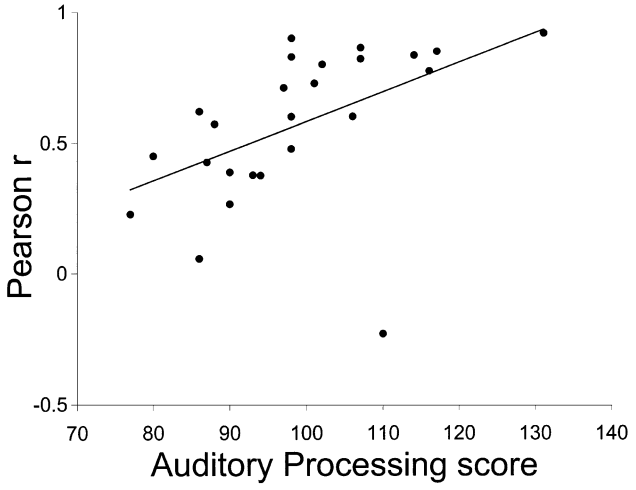

Fig. 5. A measure of the correlation between repeated responses in noise is related to performance on a battery of behavioral tasks. Shown here is the relationship between the auditory processing composite behavioral score and the correlation between responses in noise. Individual subjects (●) in whom the shape of the initial response was well preserved by the 4th response in noise (high correlation) were shown to perform well on this measure of auditory behavior (high score).

4. Discussion

This is the first study to investigate the simultaneous effects of background noise and stimulus repetition on speech-evoked cortical responses in normal and learning impaired children. This study demonstrated a deficiency in the neural representation of repeated speech stimuli in noise in children diagnosed with learning problems. Specifically, the timing and subsequent shape of the repeated responses, as reflected by the correlation between responses in noise, were distorted in the learning impaired children. By a similar measure of response correlation in noise, roughly half of the LP subjects appeared similar to normal subjects, while the remaining LP subjects exhibited responses that were highly disrupted by combined repetition and noise. A measure of response correlation in noise was related to performance on a battery of behavioral tasks involving perception and processing of multiple speech sounds.

4.1. Deficient timing, not amplitude, differentiates LP subjects

Correlation provided a means to quantify the degree to which the shape of a response was preserved by another response. In order for two responses to correlate highly, they must have similar morphologic features. These features must occur in similar positions in time. A preservation of response shape, indicated by high correlation between responses, can thus be interpreted as a preservation of response timing. Likewise, distortion of the shape of the responses, reflected by low correlation, can be interpreted as a disruption of response timing mechanisms.

The correlation between 1st and 4th responses was greater in quiet than in noise in the LP subjects; synchronous timing of the repeated responses, which was demonstrated in quiet, was significantly disrupted by the addition of noise. There was no such correlation difference for the NL subjects; synchrony that was evident in quiet was maintained in noise. Previous studies have reported that the contributions of a single neuron are minimal during processing of complex auditory stimuli; highly synchronized firing patterns from coordinated ensembles of neurons facilitate many complex cortical auditory functions (Eggermont, 1994; Nelken et al., 1994). Likewise, asynchronous cortical activity, as observed in LP subjects, could underlie auditory perceptual deficits, which could ultimately contribute to difficulties with spoken language and reading.

It was the effects of repetition and noise in combination, not isolation, which clearly differentiated between LP and NL responses. Effects of repetition alone were no different between groups; the timing and shape of the initial responses in quiet were fairly well preserved by the 4th responses in quiet, reflected by the relatively high correlations. Effects of noise alone were also no different between groups; timing of the initial responses in quiet was not maintained by the initial responses in noise, reflected by lower correlations. This finding is in agreement with studies that report that the addition of noise causes increased response latencies (Whiting et al., 1998; Martin et al., 1999). Such latency shifts would result in the observed, diminished response correlations.

The use of RMS amplitude provided a method of describing responses that was complementary to correlation measurements. While correlations describe relative changes in shape and timing, RMS amplitudes describe the average amplitude of a single response. High correlation between responses does not imply similar RMS amplitudes between responses; overall shape may be preserved, yet one response may be of a smaller or larger scale. Likewise, similar RMS amplitudes between responses do not imply high correlation; two responses may have the same average size, yet their morphologic features may be extremely different. Correlation and RMS measures in combination thus provide a comprehensive description of how responses change between conditions.

While response synchrony in noise was disrupted in LP subjects, measures of RMS amplitude told a slightly different story. In noise, though the timing and subsequent shaping of LP subjects' responses were altered by stimulus repetition, mean RMS amplitude did not change significantly with stimulus repetition. This pattern was evident in responses from NL subjects as well. While no significant changes in amplitude occurred with repetition in noise, both groups exhibited an amplitude decrease from quiet to noise, and with repetition in quiet, findings, which have been reported previously (Woods and Elmasian, 1986; Whiting et al., 1998; Martin et al., 1999). In quiet, some response mechanisms were sensitive to repeated stimulation, resulting in decreased response amplitudes upon repetition. Some neural response mechanisms that were fully enabled in quiet were disrupted in noise, resulting in smaller responses in noise. However, robust response mechanisms that continued to respond in the presence of noise were also able to repeatedly generate responses of consistent amplitude, reflected by the lack of amplitude change of responses in noise. Thus, the observed abnormal correlations between repeated responses in noise in LP subjects were not indicative of a widespread deficiency in the overall response mechanisms, but were specifically due to distortion among mechanisms that maintained response timing.

Of particular interest here is that the patterns of RMS amplitude were no different between NL and LP subjects. Previous studies reported responses that were significantly diminished or absent in learning impaired subjects in response to rapid or repeated stimuli (Nagarajan et al., 1999; Temple et al., 2000). Subjects with learning impairments have also been shown to exhibit diminished responses to stimuli in noise (Cunningham et al., 2001). In the current study, there were no amplitude differences between subject groups under any stimulus conditions. Analyses of within-group patterns of amplitude change indicated identical patterns for both groups. Some disagreement among results may be due to differences between stimuli. For example, some previous studies used tonal stimuli to demonstrate effects of stimulus repetition in learning impaired subjects (Nagarajan et al., 1999; Kujala et al., 2000), while the current study used synthesized speech. The extreme differences in complexity between speech and tonal stimuli likely contribute to differences in observed encoding (Sachs et al., 1983; Rauschecker, 1997). Complex speech stimuli have also been used to demonstrate altered encoding of rapid acoustic information in subjects with learning problems (Temple et al., 2000). These stimuli, however, did not incorporate enhanced onset features. Unenhanced speech stimuli were also used to demonstrate the effects of noise on speech sound encoding in learning impaired subjects (Cunningham et al., 2001). In the same study, responses to speech stimuli with an enhanced onset were reported to be no different between normal and learning impaired subjects. The current study employed a similarly enhanced stimulus; a burst was added to the stimulus onset. In vivo animal studies have shown that cortical auditory neurons are exceedingly sensitive to transient activity, such as stimulus onset (Phillips, 1993; Heil and Irvine, 1997). A burst of increased energy during stimulus onset provides additional information to which the auditory system is especially sensitive. Cortical sensitivity to enhanced onset energy may underlie differences among effects elicited with and without enhanced stimuli.

In addition to variations in stimuli and presentation parameters, conflicting results between studies may result from differences between subject groups. While many of the above mentioned studies also studied auditory processing in subjects with learning problems, the heterogeneity of

this population (Fletcher et al., 1992; Shaywitz et al., 1992a,b) makes it quite feasible that similarly diagnosed learning problems could arise from vastly different pathologies, resulting in variations in observed physiology. Other subtle, yet unnoticed or non-diagnosed abnormalities could contribute to subject differences between studies. Thus LP subjects from the current study may demonstrate auditory neural processing that is at odds with that demonstrated in other studies; even within the current study, there was highly variable neural processing within the LP group. Differences in subject age could also confound comparison of present results with those of other studies. The current study examined primarily pre-teen aged children. Adult subjects were studied in several of the above-mentioned studies (Nagarajan et al., 1999; Kujala et al., 2000; Temple et al., 2000). Developmental changes in the P1/N1/P2/N2 complex have been demonstrated in subjects spanning and exceeding the age group studied here (Cunningham et al., 2000). These differences, compounded by the experimental stresses under which responses were elicited, could thus contribute to interstudy variation.

Other possible sources of disagreement among amplitude results may be the analysis techniques. Previous studies reported differences in amplitudes and latencies of specifically identifiable response features. Contributions of specific features cannot be similarly isolated by RMS measurements. Combinations of increased, decreased and/or unchanged amplitudes of specific response features may not be reflected in RMS analysis that incorporates all of the features into a single measurement.

The differences between neural encoding in NL and LP children are extremely meaningful findings. Some auditory evoked neural responses, such as P300 and the mismatch negativity, conscious or preconscious responses, respectively, to a stimulus change (e.g. stimulus which is different from the previous stimuli), reflect the ability of the listener to discriminate and/or attend to sounds (Sams et al., 1985; Picton, 1992; Kraus et al., 1993). Alternatively, the P1/N1/P2/N2 potentials that are investigated here are associated with basic detection of a stimulus (Näätänen and Picton, 1987; Cunningham et al., 2000). Studies have shown that stimulus characteristics can affect morphological features of these responses. For example, N1 amplitudes were larger in amplitude and occurred later in time in response to /ba/ than in response to /da/ (Whiting et al., 1998). In the current study, differences in morphology are observed in LP subjects as a result of repetition in noise. Although the stimulus itself is unchanged, the different responses could effectively encode two distinct patterns. Different neural representations of a single stimulus could result in distinctly different percepts. Thus, a single speech stimulus could be perceived as multiple, distinct stimuli as a result of repetition in noise. Just as devastating would be if the subject perceived distorted sounds which were difficult to discriminate and recognize as speech.

4.2. A subset of LP subjects appear normal

While all LP subjects exhibited response correlations in quiet that were similar to normal subjects, roughly half of the LP subjects also had correlations in noise that were similar to normal subjects. The remaining LP subjects exhibited response correlations in noise that were significantly lower than in NL subjects. Such variability within the learning impaired population is not uncommon. While subjects with learning problems may have clinical diagnoses and/or behavioral deficits in common, the underlying physiologic mechanisms are often heterogeneous. For example, LP subjects who exhibited poor response correlations in noise are likely candidates to experience learning problems that are rooted in abnormalities among basic auditory encoding mechanisms. It is clearly demonstrated that encoding of speech signals can be severely distorted in these children, thus their language skills, learned in large part via auditory input, could suffer. Alternatively, LP subjects whose auditory physiology appeared no different from normal subjects may be affected by abnormalities of other mechanisms, such as visual processing, or by widespread deficits in more global factors, such as attention (Livingstone et al., 1991; Torgeson, 1991). These 'normal appearing' LP subjects may also have had sufficient experience to have allowed their auditory systems to develop compensatory mechanisms. Their clinical diagnoses and associated deficits may result from abnormal encoding and perception during early, critical stages of development, especially during acquisition of primary language skills. These deficits may persist, a legacy of abnormal encoding earlier in life, even though time and experience have seen the auditory system develop what appears to be more normally functioning auditory physiology.

4.3. Response asynchrony in noise relates to behavioral measures

An important finding of this study was that stimulus repetition in noise led to excessive response distortion in LP subjects. This supported theories of language-based learning disabilities that cite auditory encoding deficits as lower-level precursors of higher-level behavioral abnormalities. Lending further support to this connection between encoding and behavior is the finding that a measure of response correlation in noise was significantly related to performance on a battery of behavioral tests. Synchronous response timing, reflected by high correlation between responses in noise, corresponded to good performance on the behavioral tasks. These relationships were especially interesting given the nature of some of the behavioral tasks and their similarities to the physiologic experimental paradigm.

The composite auditory processing score is a weighted combination of scores from two subtests (Woodcock and Johnson, 1989). One of the subtests, incomplete words, requires that the child analyze a spoken word that is missing

at least one phoneme, then indicate what that word should be. For example, the child is presented the stimulus 'potay-o' and is asked to determine what word this stimulus is supposed to be. The child who responds 'potato' is awarded a correct response. The other subtest, sound blending, requires that the child synthesize a string of spoken syllables or phonemes into a word. For example, the child is presented the stimulus 'a-b-ou-t' and is asked what word the stimulus is supposed to be. The child who responds 'about' is awarded a correct response. Successful completion of both of these tasks requires coordinated involvement of many complex mechanisms. The acoustic stimulus is first transduced and encoded by the auditory system. The encoded stimulus is manipulated in the manner appropriate for the test. The manipulated stimulus is compared against the lexicon of known words. The subject selects from the lexicon the best approximation to the manipulated stimulus. The subject finally generates the appropriate motor commands in order to vocalize the selected response.

Deficient processing at any of these levels could result in poor performance on the tasks. However, let us concentrate on the very first stage of this task during which the signal is encoded by the auditory system. The stimulation paradigm for the current study was a sequence of repeated speech sounds. Neural responses to identical, repeated stimuli were distorted in noise in LP subjects. Such distorted encoding of a stimulus could underlie altered perception. In both of the behavioral tasks, subjects attended not to a single, isolated auditory event, but to a sequence of speech sounds. In order to correctly respond to a behavioral stimulus, subjects matched the entire stimulus to a recognizable word. Altered neural encoding of portions of speech stimuli, such as demonstrated in the present study, could lead to perception which is at odds with the percept intended by the speaker. Thus distortion at the initial encoding stage of the task could lead to impaired behavioral performance.

Similar connections can be drawn between speech sound discrimination performance and response correlation in noise. Both the physiologic and the speech discrimination experiments utilized similar stimuli and presentation paradigms. The discrimination task required subjects to listen to a string of phonemes, 'da-da-da-ga', and indicate the 'different' sound, 'ga'. These sequences of stimuli are quite similar to the phoneme string, 'da-da-da-da', utilized in the physiology experiments. Successful completion of the behavioral task required that the subject encode and perceive the stimuli with precision sufficient to allow discrimination of subtly different speech sounds. Distorted neural encoding of stimuli as a result of repetition could have resulted in altered perception of stimuli. Differences between the stimuli could have been minimized or eliminated entirely in distorted neural responses. Discrimination of these stimuli thus could have suffered.

The relationship between spelling ability and the correlation between responses in noise is slightly more abstract than the relationships between response correlation in noise and the auditory processing and speech discrimination tasks. A motivating factor behind the current research was the hypothesis that some 'higher level' learning problems are rooted in 'lower level' abnormalities in auditory encoding. The relationship between spelling ability and neural encoding supports this hypothesis. A child whose auditory system abnormally encodes and distorts speech signals is apt to develop poor correspondence between perceived speech sounds and the appropriate orthographic representations. This cross-modal relationship is fundamental to development of written language in children with normal hearing and vision. Thus the child whose auditory input is distorted could understandably develop difficulty in manipulating language. Single word spelling is one method of measuring the ability to manipulate language, and was indeed shown to relate to speech signal encoding.

5. Conclusions

A group of children diagnosed with language-based learning problems were shown to encode auditory information in an abnormal way. Specifically, these children exhibited distortion of the timing of cortical responses to repeated speech in noise. This measure of response distortion was related to behavioral measures that tested abilities to perceive and manipulate speech sounds. These findings further support theories that argue for abnormal sensory-encoding bases of higher-level learning disabilities.

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