

AUDITORY neuropathy affects the normal synchronous activity in the auditory nerve, without affecting the amplification function in the inner ear. Patients with auditory neuropathy often complain that they can hear sounds, but cannot understand speech. Here we report psychophysical tests indicating that these patients' poor speech recognition is due to a severe impairment in their temporal processing abilities. We also simulate this temporal processing impairment in normally hearing listeners and produce similar speech recognition deficits. This study demonstrates the importance of neural synchrony for auditory perceptions including speech recognition in humans. The results should contribute to better diagnosis and treatment of auditory neuropathy. *NeuroReport* 10:3429–3435 © 1999 Lippincott Williams & Wilkins.

**Key words:** Acoustic simulation; Auditory neuropathy; Hearing disorder; Human; Neural synchronization; Speech perception; Temporal processing

## Temporal and speech processing deficits in auditory neuropathy

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### Introduction

Synchronization of neural discharges carries important information for perception [1–3]. In the auditory system, neurons can generate action potentials synchronized to stimulus frequency up to several thousands of Hz [4] and preserve the relative timing of these action potentials passed through several synaptic stages [5]. The synchronous activities in auditory neurons may encode basic auditory percepts such as loudness and pitch [6,7] and extract complex sound features such as spectral peaks and waveform envelopes for speech recognition [8–10].

In humans, the synchronous activity of the auditory nerve and auditory brain stem pathways can be recorded from scalp electrodes as the averaged far-field potential known as the auditory brain stem response, reflecting neural population activity synchronized to the onset of acoustic stimuli [11]. In addition, the frequency-following response registers synchronized neural activity to periodical auditory stimuli and contains sufficient information for intelligible speech [12]. Despite the widely assumed importance of neural synchrony in perception, there has been no direct behavioral evidence linking disruption of neural synchronous activities and perceptual processing deficits in humans.

Here we report psychophysical and simulation results from a newly discovered hearing disorder

that may selectively affect neural synchronous activity in the auditory system. In contrast to the loss of an amplification function in the inner ear due to its susceptibility to loud sounds, ototoxic drugs and other medical factors, auditory neuropathy preserves the amplification function in the inner ear, but disrupts the normal synchronous activity in the auditory nerve [13–16]. Discharges in the auditory nerve are presumed to be desynchronous because averaged evoked potentials of the auditory nerve are absent, while otoacoustic emissions (reflecting intact cochlear amplification function) are normal. Patients with auditory neuropathy typically have speech recognition deficits out of proportion to the pure-tone hearing loss and do not benefit from amplification by conventional hearing aids. Although there was a case study [13] reporting that a patient with auditory neuropathy could not hear short-duration (tens of milliseconds) sounds, other patients had no trouble hearing these types of sounds. The apparent discrepancy between the amount of hearing loss and its disproportional speech recognition deficits in auditory neuropathy still remains unresolved. Here we report the results of psychophysical tests showing that the impaired ability to follow temporal fluctuations, rather than the detection of short-duration sounds, is likely the underlying cause for the poor speech recognition in auditory neuropathy patients. This conclusion receives further support

from a simulation of this temporal processing impairment that produces similar psychophysical and speech perception deficits in normally hearing listeners.

### Materials and Methods

We conducted two sets of empirical experiments to test the relationship between temporal and speech processing deficits in auditory neuropathy. In the first set of experiments, psychophysical data were collected in temporal integration, gap detection, and temporal modulation transfer function in auditory neuropathy subjects and three groups of control subjects. In the second set of experiments, acoustic simulations were developed based on the measured psychophysical data in auditory neuropathy subjects and were validated by obtaining similarly impaired temporal and speech processing results in normally hearing subjects.

*Subjects:* We studied eight patients with auditory neuropathy, including one with unilateral neuropathy. We also studied three controls, including the healthy ear in the unilateral neuropathy subject, one cochlear-impaired subject with a low-frequency hearing loss and six normally hearing subjects. The cochlear-impaired subject was chosen because of his unusual configuration of hearing loss. Informed consent was approved by local IRB and obtained from each individual after the nature and possible consequences of the study were explained. Normally hearing subjects included three females and three males, aged 27–35 years old; all had hearing thresholds of 20 dB HL or better for octave frequencies between 250 and 8000 Hz. Table 1 lists audiological and neurological test results of auditory neuropathy subjects and control subjects. The neuropathy subjects had a wide range of hearing loss, but averaged thresholds had a moderate 60 dB hearing loss in the low frequencies and a mild hearing loss (30–40 dB) in the high frequencies. Different from the high-frequency hearing loss seen in most cochlear-impaired subjects, the cochlear-impaired subject in this study had a low-frequency hearing loss and almost normal hearing at high frequencies. The neuropathy subjects' word recognition score ranged from 0% to 56% with an average of 18%, significantly lower than what would be expected from their pure-tone hearing loss [17]. Neuropathy subjects had normal measures of cochlear outer hair cell functions (otoacoustic emissions were present in all but AN5 and cochlear microphonics were present in all). All had absence of Waves I of auditory brainstem potentials, presumably generated by the auditory nerve, and absent acoustic middle ear reflexes

**Table 1.** Audiological and neurological test results of auditory neuropathy subjects and control subjects

Subject	Age	Gender	PTA (dB)	Speech (%)	Otoacoustic emission (dB)	Cochlear microphonic	ABR	Acoustic Reflex	Imaging	PN
AN1	50	F	32	56	TEOAE = 11.8	Present	Abnormal	Absent	DNT	Yes
AN2	53	F	15	DNT	TEOAE = 8.9	DNT	Abnormal	DNT	DNT	Yes
AN3	19	F	72	12	DPOAE = 3–15	DNT	Absent	Absent	Normal MRI	Yes
AN4	23	F	38	0	TEOAE = 5.4	Present	Absent	Absent	Normal MRI	No
AN5	17	F	62	0	Absent	Present	Absent	Absent	Normal CT	No
AN6	37	M	55	CNT	DPOAE = 4–13	DNT	Absent	Absent	Normal MRI	Yes
AN7	27	M	45	40	TEOAE = 12.3	Present	Abnormal	Absent	DNT	No
AN8	10	M	82	0	DPOAE = 3–10	Present	Abnormal	DNT	DNT	No
Average	30		50	18						
CHL	40	F	60	84	DPOAE = 5 dB at 6000 only	DNT	Present	DNT	DNT	No
N-AN8	10	M	7	100	TEOAE = 10.3	Present	Present	DNT	DNT	No

F, Female; M, Male; PTA, Pure tone average threshold at 500, 1000 and 2000 Hz; CNT, Could not test; DNT, Did not test; TEOAE, Transient-evoked otoacoustic emission; DPOAE, Distortion product otoacoustic emission; ABR, Auditory brainstem response; MRI, Magnetic resonance imaging; CT, Computer tomography; PN, Peripheral neuropathy.

to tones up to and including 100 dB HL. Brain imaging results were normal in the four neuropathy patients tested. The cochlear-impaired subject had no otoacoustic emissions except at 6000 Hz, where hearing threshold was normal, and all components of auditory brain stem potential were identified. His 84% word recognition was in keeping with the moderate pure-tone loss. The other control subject with a unilateral neuropathy (N-AN8) had normal pure-tone thresholds, otoacoustic emissions, cochlear microphonics, auditory brain stem potentials, and 100% correct word recognition for the healthy ear.

**Stimuli:** A broad-band (20–14 000 Hz) white noise was generated and controlled digitally to measure temporal integration, gap detection and temporal modulation transfer functions. The noise had a duration of 500 ms and 2.5 ms cosine-squared ramps. In the gap detection experiment, a silent interval was produced in the center of the noise. In the temporal modulation function experiment, the same 500 ms noise was used as for gap detection and was presented at a maximal comfortable sensation level on an individual basis (ranging from 29 to 52 dB SL). For the modulated signals, the presentation level was dynamically adjusted according to the modulation depth to achieve the same root-mean-square level as the unmodulated stimuli. The overall presentation level varied between subjects and was perceived to be maximally comfortable by each individual subject.

The stimulus in the neuropathy simulation experiment was produced by dividing an incoming signal into 16 third-octave bands and extracting the band-specific temporal envelope by half-wave rectification and low-pass filtering [18]. The low-pass filters were designed according to the measured temporal modulation transfer functions and covered four degrees of temporal processing impairment found in the present neuropathy patients: mild (modulation peak sensitivity  $-17$  dB and  $3$  dB, cutoff  $100$  Hz), moderate ( $-14$  dB and  $50$  Hz), severe ( $-8$  dB and  $25$  Hz), and profound ( $-2$  dB and  $15$  Hz). The low-pass filtered temporal envelopes were used to amplitude modulate the fine-structure of the original acoustic signal, resulting in a temporally smeared acoustic waveform.

**Procedure:** We used standard procedures to collect and analyze all audiological and neurological data. Pure-tone averaged (PTA) thresholds were based on thresholds at frequencies of  $500$ ,  $1000$  and  $2000$  Hz. Word recognition was based on NU-6 (1/2 list) test materials. This word test could not be performed in subject AN6 because of his non-native English-

speaking status. Auditory brainstem responses were recorded between vertex and the stimulated ear and identified as either absent (no definable waveforms) or abnormal (presence of only wave V). Acoustic reflexes were measured for pure-tone stimuli at  $500$ ,  $1000$ ,  $2000$  and  $4000$  Hz, presented ipsilaterally and/or contralaterally to the stimulated ear using a Grason-Stadler GSI 33 middle ear analyzer. Otoacoustic emissions were measured with a V5 ILO92 OAE system by Otodynamics Ltd. and reported as the dB value above the noise floor. The cochlear microphonic was measured from auditory brain stem responses averaged to separate presentations of condensation and rarefaction clicks. All psychophysical tests used a three-alternative, forced-choice procedure to measure the threshold that resulted in a 70.7% correct response.

## Results

Figure 1A shows pure-tone thresholds as a function of frequency (audiogram) in auditory neuropathy subjects and control subjects. Auditory neuropathy subjects generally had moderate to severe hearing loss at low frequencies and mild to moderate hearing loss at high frequencies. The cochlear-impaired subject had an unusual configuration of low-frequency hearing loss, which was generally within 20 dB of the average neuropathy subject's hearing thresholds.

We first measured a temporal integration function for each subject to test the hypothesis that the speech recognition deficit in neuropathy patients was related to their inability to hear short-duration sounds. Detection thresholds for normal-hearing listeners (shaded area in Fig. 1B) decrease at a rate of about 3 dB per doubling of signal duration for durations up to 100–200 ms. Except for subject AN3, the patients in the original Starr *et al.* study [13], all neuropathy subjects as well as the two control subjects showed normal or nearly normal temporal integration functions (Fig. 1B). Thus, the results from the detection of short-duration sounds apparently could not explain the poor speech recognition in neuropathy patients.

In contrast, detecting short silent intervals, or gaps, in acoustic signals was uniformly impaired in the neuropathy patients (Fig. 1C). In both the normal-hearing listeners and the unilateral control, gap detection thresholds improved from 20 to 30 ms at low sound levels to 2–3 ms at high sound levels. The cochlear-impaired subject had slightly elevated gap detection thresholds at moderate sound levels but reached the normal range of values at the highest sound level, a pattern similar to previous studies employing cochlear-impaired listeners [19–21]. In contrast, all neuropathy subjects still had large

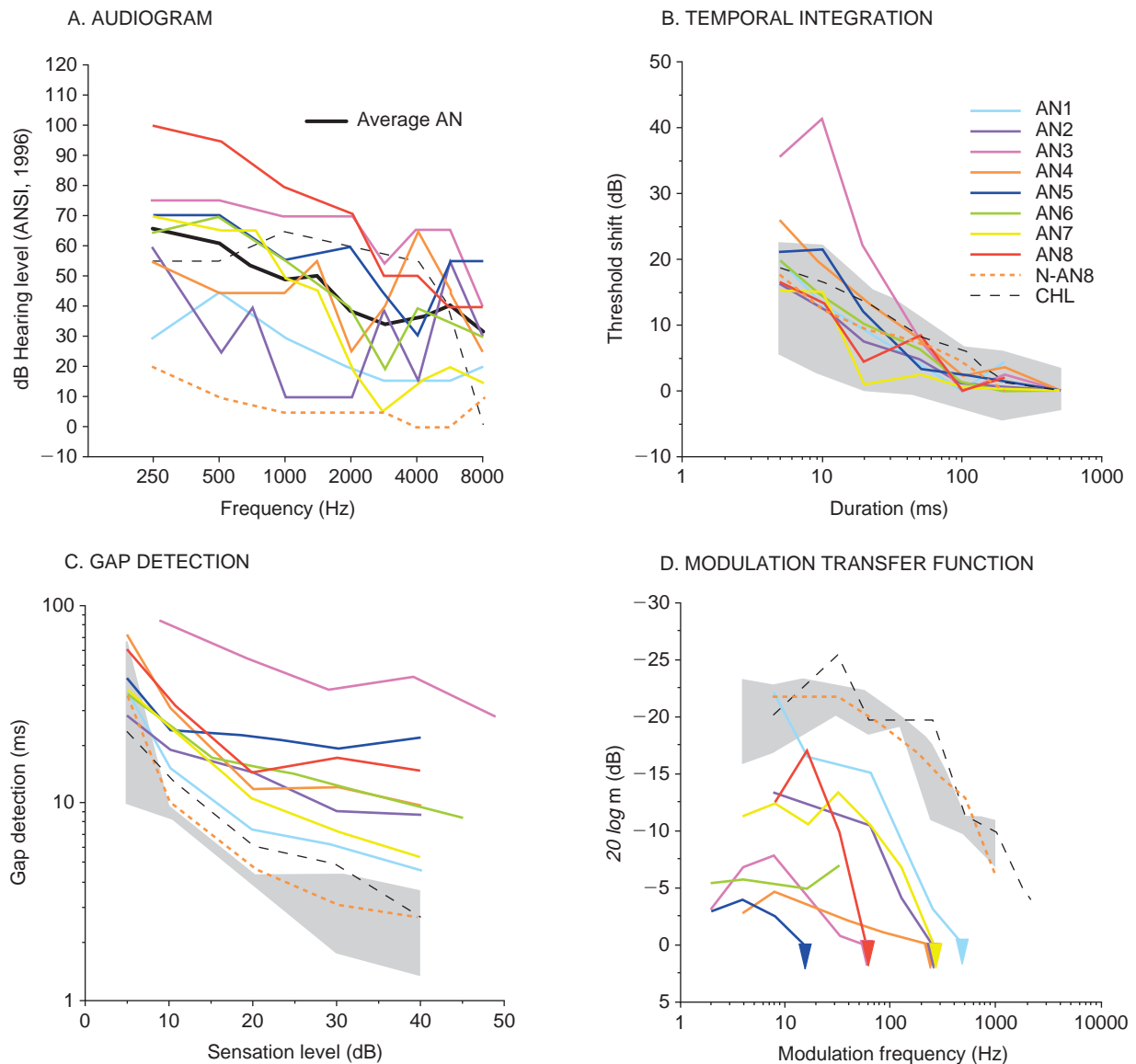


FIG. 1. Psychophysical data. (A) Audiogram. Pure-tone thresholds are plotted as a function of frequency. (B) Temporal integration functions. Threshold shifts (y-axis) refer to the difference in dB between detection thresholds for noise bursts of different durations (x-axis) and that for the longest duration (500 ms). Normal control data are represented as the shaded area (mean  $\pm$  2 s.d.). Neuropathy data are represented by solid lines of different colors. The dashed line represents the cochlear impaired case and the dotted line represents the healthy ear of the unilateral case. (C) Gap detection thresholds. Detection thresholds (y-axis) are plotted as a function of sound presentation level (dB SL). (D) Temporal modulation transfer functions. Modulation detection thresholds (y-axis) represented as  $20 \log m$  are plotted as a function of modulation frequency (x-axis). Arrows represent the fact that subjects could not reliably detect the presence of even a 100% modulated noise.

deficits at the highest sound level; their gap detection thresholds were 2–25 times greater than the normal threshold.

To further characterize the temporal processing impairment in auditory neuropathy, we measured the sensitivity to slow and fast temporal fluctuations, i.e. modulation transfer functions [22]. We modeled the modulation transfer function as a first-order Butterworth low-pass filter (Table 2). The normal-hearing listeners showed a low-pass function (Fig. 1D), being most sensitive (peak sensitivity  $-20.4$  dB) to slow temporal fluctuations and becoming less sensitive as the fluctuation rate was in-

creased (3 dB cutoff frequency = 247 Hz). Both the unilateral and cochlear-impaired controls showed modulation transfer functions that were virtually indistinguishable from the normal low-pass function. In contrast, all neuropathy subjects showed impaired sensitivity to both slow and fast temporal fluctuations. The average peak sensitivity at low modulation frequencies was  $-10.2$  dB and the average 3 dB cutoff modulation frequency was 47.2 Hz. These values were about one-third ( $-10.2$  vs  $-20.4$  dB) and one-fifth (47.2 vs 247 Hz), respectively, the corresponding values obtained for our control listeners.

**Table 2.** Summary of temporal modulation transfer function parameters

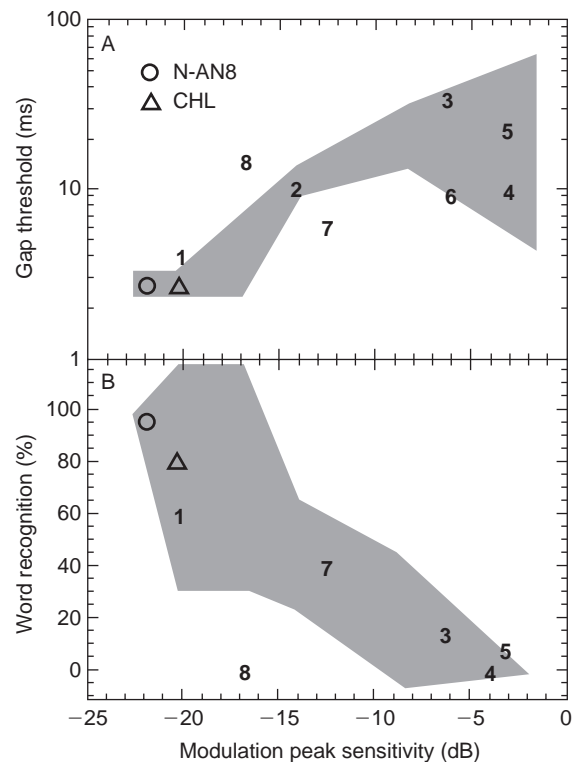
Subject	Sensation level (dB)	Peak sensitivity (dB)	3 dB Cutoff (Hz)	r
Normal individuals	40	-20.4	237.8	0.97
CHL	37	-21.8	234.8	0.95
N-AN8	41	-21.6	175.2	0.99
AN1	40	-20.1	41.7	0.98
AN2	29	-13.8	51.2	0.99
AN3	49	-5.8	32.9	0.79
AN4	40	-3.6	106.6	0.88
AN5	42	-3.6	14.1	0.95
AN6	45	-6.1	44.8	0.82
AN7	39	-12.4	72.3	0.97
AN8	40	-16.4	14.3	0.87

Sensation level refers to the dB value of the noise presentation level above the subject's absolute hearing threshold for the same noise stimulus. Peak sensitivity and 3 dB cutoff frequency were estimated using a first-order Butterworth filter. The coefficient (*r*) reflects the goodness of fit. A different model by Formby and Muir [25] that has a -3 dB per octave slope was also evaluated and yielded generally higher peak sensitivity values (ranging from -3.9 to -23.1 dB) and lower cutoff frequencies (ranging from 4 Hz to 120 Hz). The goodness of the fit of this model (*r*=0.72-0.98) was slightly worse than the first-order Butterworth filter.

The temporal modulation transfer function measured for the neuropathy subjects allowed development of simulations of auditory neuropathy in normally hearing listeners [18]. Figure 2A shows simulation results of gap detection thresholds, which increased monotonically from about 2 to 20 ms as the severity of the simulated auditory neuropathy was increased from mild to profound. The actual individual neuropathy patients' gap thresholds generally were within 2 s.d. of the simulated thresholds. For comparison, the two control conditions are also shown for the healthy ear of the unilateral neuropathy listener (circle) and for the cochlear-impaired listener (triangle). Figure 2B shows simulation results of word recognition, which decreased monotonically to a 50% correct level when the modulation detection threshold was elevated by about 5 dB from the normal value of -20 dB and reached 0% correct level with about 15 dB elevations. Actual word recognition scores from six neuropathy patients and two controls are shown in the same fashion as in Fig. 2A. With one exception (AN8), poor word recognition is consistent with the degree of impaired temporal processing in neuropathy patients. The exceptional subject had the most severe hearing loss, suggesting that additional factors such as audibility may have contributed to the poor speech recognition in this neuropathy patient.

## Discussion

The present tests have revealed a severe temporal processing impairment in auditory neuropathy patients, in contrast to the relatively normal temporal processing often associated with hearing disorders



**FIG. 2.** Simulations of auditory neuropathy in normally hearing listeners. **(A)** Gap detection thresholds at 40 dB SL. The gap detection threshold is plotted as a function of the severity of the auditory neuropathy, represented as the peak sensitivity of the temporal modulation transfer function (x-axis). The shaded area represents the mean  $\pm$  2 s.d. from normally hearing listeners who performed gap detection by listening to temporally smeared waveforms (see text for details). The digits denote gap detection thresholds measured for each of the neuropathy subjects also tested at 40 dB SL (from Fig. 1C). The symbols denote two control subjects (also from Fig. 1C). Because the normal-hearing listeners and the two control subjects all produced peak sensitivity values of about -20 dB, their x-coordinates were shifted by 1-2 dB to avoid overlap. **(B)** Word recognition from normally hearing listeners who listened to both unprocessed words and temporally smeared speech sounds simulating various degrees of auditory neuropathy (see text for details). Symbols as in (A).

due to cochlear damage [19–21,23–26]. Because a lack of audibility could be a confounding factor in measuring the temporal processing abilities in hearing-impaired subjects [23,24] we conducted a correlational analysis between subjects' averaged pure-tone thresholds (column 4 in Table 1) and peak sensitivities to slow fluctuations (column 3 in Table 2). We found only an insignificant correlation ( $r=0.24$ ) between the pure-tone average threshold and the peak sensitivity, suggesting a true temporal processing deficit in auditory neuropathy, rather than a byproduct of hearing loss due to limited bandwidths at low sensation levels. This conclusion received additional support from the simulation results that these degrees of temporal processing impairment can account for the abnormal speech recognition observed in neuropathy patients. The present finding of a close coupling between temporal and speech processing deficits complements the recent emphasis on speech recognition using temporal cues in general [7,27] and amplitude modulations in particular [28,29].

The physiological deficit in auditory neuropathy could involve inner hairs, the hair cell to nerve synapses, and/or the auditory nerve fibers. While the exact mechanism of auditory neuropathy is not clear, there is some evidence linking the observed temporal processing impairment to damaged synapses and demyelination in the auditory nerve. For example, the failure to detect the evoked auditory brain stem responses has been related to the loss of discharge synchrony secondary to demyelination of the auditory nerve [15,16]. Demyelinated nerve fibers have slowed conduction velocities, which vary as a function of the extent of demyelination in each fiber, resulting in disrupted discharge synchrony both within a neuron and across a neural population.

Figure 3 presents a phenomenological model of the disrupted synchronous neural activity and its account for the present psychophysical data. We assume that the main effect of the desynchronous activity is a smeared temporal representation of the acoustic stimulus (see the difference between the sharp waveform in the physical representation and its smeared version in the internal neural representation). If the listening task was merely detection of either presence (top trace) or absence (bottom trace) of a sound, as in the case of temporal integration experiment, then this smeared representation would not present a difficult perceptual problem. However, if the task was discrimination of two different waveforms, one with a gap (top trace) and one without gap (bottom trace), then the smearing in the internal representations would result in a much more difficult perceptual task. A quantitative prediction of the

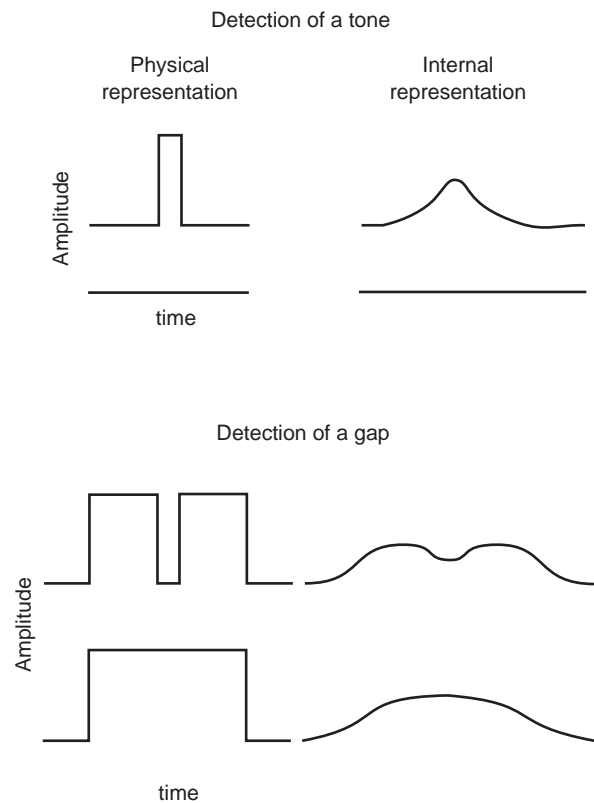


FIG. 3. A phenomenological model of auditory neuropathy. This simple model assumes that desynchronous neural activity results in a smeared internal representation of a physical stimulus. The smearing does not affect the detection of a tone (top panel) because the task requires only an all-or-none decision. However, the smearing can cause a major problem in gap detection (bottom panel) if the task requires finer discrimination of two different waveforms.

psychophysical data is not possible at present and requires much better understanding of the exact physiological mechanisms of auditory neuropathy (see [30] for an animal model of auditory neuropathy). Nevertheless, the present results demonstrate the importance of neural synchrony in human auditory and speech perception and are consistent with previous physiological and behavioral data in animals [1–3,8,9].

Temporal processing deficits have also been observed in elderly listeners [31], patients with multiple sclerosis [32] and children with learning disabilities [33–37]. Similar to the present results, these previous studies also found a close relationship between temporal processing and speech recognition deficits, despite a peripheral origin of the temporal processing impairment in auditory neuropathy and a central origin in the other cases. The present study suggests that simple behavioral gap and temporal modulation detection tasks, when used in combination with other audiological and neurological tests, can distinguish the extent of temporal processing impairment due to auditory neuropathy in those communication disorders. For example, abnormal

temporal processing may reveal the presence of disordered auditory nerve synchrony when there is a concomitant cochlear hearing loss, as occurs in aging.

The present results also bear on the failure of conventional hearing aids to help auditory neuropathy patients, who often complain 'I can hear you but I cannot understand you'. Conventional hearing aids either do not change temporal fluctuations of speech sounds (using linear amplification), or even reduce the fluctuations when a non-linear amplitude-compression circuit is employed [38]. To improve speech recognition in this population, a new type of hearing aid design is needed. This design should not only amplify the sound to overcome the audiometric hearing loss at the threshold level, but also should accentuate temporal envelope fluctuations to compensate for the impaired temporal processing at suprathreshold levels.

## Conclusion

Temporal processing abilities are severely impaired in auditory neuropathy subjects and can account for poor speech recognition that is disproportional to the degree of their hearing loss. While the exact physiological process underlying auditory neuropathy is not clear, the temporal processing deficit may be a result of desynchronous neural activity at the auditory nerve level. The present results provide evidence for the importance of neural synchrony in auditory perceptions and also contribute to better diagnosis and treatment of auditory neuropathy.

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ACKNOWLEDGEMENTS: We thank Neal Viemeister for suggesting the measurement of gap detection using the simulation procedure and John Galvin for technical support. Sid Bacon, Marilyn Flack, Craig Formby, Sandy Gordon-Salant, and Neal Viemeister provided helpful comments on an earlier version of the manuscript. This work was supported by National Institutes of Health (DC02267 and DC02618).

**Received 5 August 1999;  
accepted 20 August 1999**