refinements were performed with X-PLOR (27).

- W. I. Weis, K. Drickamer, W. A. Hendrickson, *Nature* 360, 127 (1992); W. I. Weis and K. Drickamer, *Structure* 2, 1227 (1994).
- 21. Multiple conformers [J. Kuriyan et al., Proteins 10, 340 (1991)] (9) of the sub-MBP-A protein molecules were generated starting with the model that was obtained after single-conformer refinement (19). The water molecules and Yb<sup>3+</sup> were restrained to their initial positions. Conformers of the protein were rendered invisible to each other in terms of chemical interactions. Each conformer in the ensemble contributed equally to the calculated structure factor with the occupancy set to the reciprocal of the number of conformers. Evaluation of the free *R* value as a function of the number of conformers, which were used for subsequent analysis.
- 22. Vector difference electron density maps were computed by taking the vector difference between complex structure factors  $[|F_{obs}| \exp(i\phi_{obs}) - |F_{calc}|]$ exp $(i\phi_{calc})]$ , the experimental structure factor with centroid phases obtained from  $P_{\lambda_A}(\phi)$  (17) minus that

computed from the refined single-conformer model. A conventional (model-phased) difference electron density map consisting of a Fourier synthesis of  $||F_{obs}| - |F_{calc}|$ ) exp( $i\phi_{calc}$ ) is an approximation of the vector difference map [J. Drenth, *Principles of Protein X-ray Crystallography* (Springer-Verlag, New York, 1994), pp. 150–152]. As a consequence, vector difference maps of sub–MBP-A were observed to have less noise than conventional difference maps.

- 23. M. M. Teeter, Proc. Natl. Acad. Sci. U.S.A. 81, 6014 (1984).
- 24. G. M. Clore et al., Structure 2, 89 (1994).
- M. Levitt and R. Sharon, Proc. Natl. Acad. Sci. U.S.A. 85, 7557 (1988); Y. Komeiji et al., Proteins 16, 268 (1993); M. Karplus and G. A. Petsko, Nature 347, 631 (1990); P. J. Steinbach and B. R. Brooks, Proc. Natl. Acad. Sci. U.S.A. 90, 9135 (1993); V. Lounnas et al., Biophys. J. 66, 601 (1994).
- D. C. Rees and M. Lewis, *Acta Crystallogr.* **A39**, 94 (1983); E. Arnold and M. G. Rossmann, *ibid.* **A44**, 270 (1988); L. M. Rice and A. T. Brünger, *Proteins Struct. Funct. Genet.* **19**, 277 (1994).
- 27. A. T. Brünger, X-PLOR. Version 3.1. A System for

## Temporal Processing Deficits of Language-Learning Impaired Children Ameliorated by Training

## Michael M. Merzenich,\* William M. Jenkins, Paul Johnston, Christoph Schreiner, Steven L. Miller, Paula Tallal

Children with language-based learning impairments (LLIs) have major deficits in their recognition of some rapidly successive phonetic elements and nonspeech sound stimuli. In the current study, LLI children were engaged in adaptive training exercises mounted as computer "games" designed to drive improvements in their "temporal processing" skills. With 8 to 16 hours of training during a 20-day period, LLI children improved markedly in their abilities to recognize brief and fast sequences of nonspeech and speech stimuli.

Experiments conducted in human (1) and monkey (2) neurological models of perceptual learning have demonstrated that the capacity for segmentation of successive events in sensory input streams can be sharpened, apparently throughout life, by practice. Electrophysiological studies of learning-induced plasticity conducted in the neocortices of monkeys have provided a growing body of evidence about the neural processes that underlie practice-based improvements in both temporal segmentation and spectral (spatial) discrimination performances (3-5). These studies have shown that the ability of an adult animal to make fine distinctions about the temporal or spectral features of complex inputs can be sharply improved, or degraded, by a period of intensive behavioral training (2-4, 6).

In parallel with animal and human mod-

els of temporal sequence learning, earlier studies of the receptive deficits of LLI children (7) had shown that they have a "temporal processing deficit" expressed by limited abilities at identifying some brief phonetic elements presented in specific speech contexts and by poor performances at identifying or sequencing short-duration acoustic stimuli presented in rapid succession (8). Consistent with a temporal processing deficit hypothesis, LLI children can distinguish these brief speech features and can correctly reconstruct stimulus input sequences if stimuli are presented in slower forms or at slower event rates (8).

Taken together, these experimental findings led us to hypothesize that the deficits underlying the phonetic reception limitations of a LLI child might arise in early life as a consequence of abnormal perceptual learning that then contributes to abnormal language learning (3, 4). For example, a child might simply make more-limited-than-normal use of temporal information as he or she learns to make distinctions about speech inputs as a learning alternative, or a child might generate a representation of phonetic information under early

X-ray Crystallography and NMR (Yale Univ. Press, New Haven, CT, 1992); developmental version of X-PLOR, available on request.

D. T. Cromer, J. Appl. Crystallogr. 16, 437 (1983);
 \_\_\_\_\_\_ and D. L. Liberman, J. Chem. Phys. 53, 1891 (1970).

29. W. A. Hendrickson and W. I. Weis, unpublished data.

- L. M. Gregoret, S. D. Rader, R. J. Fletterick, F. E. Cohen, Proteins Struct. Funct. Genet. 9, 99 (1991).
- 31. We thank P. Gros for assistance in designing the X-PLOR crystallographic language for phasing; V. Agrawal, S. Shah, and M. Willis for help with data collection; C. Ogata for beamline support; and P. Adams, M. Gerstein, M. Levitt, and L. Rice for critical reading of the manuscript. The coordinates and the diffraction data have been deposited with the Brookhaven Data Bank (accession number 1YTT). Supported by the Howard Hughes Medical Institute (A.T.B.), NSF (DIR9021975, A.T.B.), and NIH (GM50565, W.I.W.). W.I.W. is a Pew Scholar in the Biomedical Sciences.

8 September 1995; accepted 1 November 1995

childhood conditions (for example, in the presence of middle ear disease) under which acoustic inputs are consistently muffled. Cortical plasticity studies indicate that temporal processing deficits like those that emerge in LLI children would be expected from these learning scenarios, if they were to be undertaken in a training regime applied in a monkey model (3, 4).

Visual psychophysical studies have already shown that very great improvements in the recognition of brief, successively presented stimuli can be achieved with practice in adult humans (1). In this study, we asked: Can we substantially alter the deficient temporal processing capacities of young, school-age LLI children by similar acoustic practice?

For training tools, we produced two audiovisual (AV) "games" designed around a circus theme to engage 5- to 10-year-old children at high levels of attention and enthusiasm within highly repetitive learning tasks. The first AV game (Circus Sequence) was a perceptual identification task in which a correct response in the exercise was a faithful reproduction of the order of two-stimuli sound sequences by touchscreen button-press sequences (9). The nonverbal stimuli applied in training were 16 octave-per-second upward- or downward-gliding (U and D, respectively) frequency-modulated (FM) tonal pairs (U-U, U-D, D-U, or D-D). Stimuli in each FM pair swept across the same frequency range. These stimuli were in the range of sweep frequencies and speeds that apply for the formant transitions of English consonants that LLI children have difficulty recognizing (7, 8). The interstimulus intervals (ISIs) and FM frequencies were adaptive parameters.

The second game was a phonetic element recognition exercise implemented as a two-alternative forced-choice task in which the child was presented two consonant-

M. M. Merzenich, W. M. Jenkins, P. Johnston, C. Schreiner, W. M. Keck Center for Integrative Neurosciences and Coleman Laboratory, University of California, San Francisco, CA 94143–0732, USA.

S. L. Miller and P. Tallal, Center for Molecular and Behavioral Neuroscience, Rutgers University, 197 University Avenue, Newark, NJ 07102, USA.

<sup>\*</sup>To whom correspondence should be addressed.

vowel (CV) stimuli with contrasting consonants (for example, [bɛ] versus [dɛ] presented in rapid sequence) (10). The child's task was to identify the sequence position of a target CV (in this example, of either a precued [bɛ] or [dɛ]). The main variables in this exercise were (i) the durations of synthetically produced consonants (and reciprocally, of the following vowels; the total CV duration was constant), (ii) the magnitudes of a 0- to +20-dB amplification of consonant elements versus vowel intensity, and (iii) the ISIs between presented CV pairs.

These two games were begun with stimuli that LLI children could easily distinguish and recognize: They had long nonverbal stimulus (60 ms) or consonant transition (65 to 70 ms) durations, were presented with long ISIs (500 ms), and for CV stimuli, were presented with a maximum differential amplification of the consonant transition (+20 dB). These variables were then altered adaptively in training, trial by trial, to drive each child in the direction of normal performance levels.

Correct performances at both of these exercises were rewarded in several ways. The children received feedback about their



**Fig. 1.** Game performance functions at the sequence recognition game for three of the four stimulus sets (9) for one LLI child, recorded near the beginning (open dots) and in the final week (filled dots) of 4 weeks of testing (study 1). All children in both studies who worked under response control at these games showed substantial, progressive gains in their abilities to sequence these fast, brief stimuli. The symbols represent changes in performance level; for positive changes in level (decreasing ISIs) a dot may represent from one to three correct responses. After eight reversals in difficulty level, the child progressed to training with another FM stimulus set.

trial performances by an audio and visual signaling of a correct response and by a point accumulator that advanced for "hits" but not "misses." Entertaining reward animations were presented at frequently achieved performance benchmarks. Children were also rewarded for their progress by working in a token economy in which earned points could be traded for prizes.

The first trial of these temporal processing games was conducted with seven 5.9- to 9.1-year-old LLI children (11). Training at the nonverbal Circus Sequence temporal training exercise was applied for 19 to 28 training sessions of 20 min each conducted over a 4-week training period. Five of these LLI children benefited from the reinforcement contingencies used in the game and progressed regularly for extended periods of training across the daily sessions of adaptive training. For the four children who were under the best psychophysical control, performances over successive daily practice sessions asymptoted at progressively higher performance levels (Fig. 1). Two of these four children reached or exceeded normal performance levels at this task; that is, after adaptive training they could consistently order stimuli that were presented in immediate or nearly immediate succession. Note that normal children can reliably identify 75-ms-duration stimuli that are separated by  $\sim 10 \text{ ms}$  (12). Three other children made severalfold improvements in task performance with practice, operating with ISIs at or below 100 ms for some or all FM stimulus categories. One child never displayed a consistent response pattern during this exercise and never progressed to ISIs shorter than  $\sim$ 300 ms. Another child showed a clear progression in performance, but that performance achievement was limited to stimuli separated by  $\sim$ 200 ms for all stimulus categories.

A benchmark test of temporal processing ability, the Tallal Repetition Test (12), was conducted before and after training. It revealed statistically significant improve-

Fig. 2. Performance of study 1 and study 2 children before and immediately after the conclusion of training, as evaluated with a benchmark measure of temporal sequence recognition ability, the Tallal Repetition Test. Bars are standard errors. The Tallal Repetition Test measures (A) threshold ISIs at which the sequence or ments in the temporal event recognition and sequencing abilities for tonal stimuli centered at 1.2 kHz, for all children (study 1 in Fig. 2). Specifically, there were significant performance improvements in these children's abilities to sequence both stimuli of shorter durations and stimuli separated by shorter ISIs, although all training for the latter was conducted with stimuli of a fixed (60-ms) duration.

For the Phoneme Identification game, all children in study 1 performed at nearchance levels when they attempted to identify stop consonants presented with brief formant transitions in the initial sessions. All reliably identified the same brief consonant transitions with a high performance reliability in some later sessions. A benchmark test of phonemic reception (13) conducted before and after training showed that six of seven children made significant improvements at phonetic element identification. Their average gain translated to  $\sim$ 1.5 years in language development age. Because stimulus delivery in this training exercise was relatively slow and because the stimulus categories were not changed in a fixed pattern, performance improvements at this game were somewhat erratic and were not easily compared between children.

A second study was conducted to determine if these results could be replicated in a larger, independent sample of LLI children (14). The games were modified in an attempt to increase performance consistency and to more strongly maintain the attention of LLI children on these tasks (15). Children progressed at the task of identifying rapidly successive stimuli (the Circus Sequence game) more reliably and under better response control than in the initial game version, with 10 of 11 children systematically improving their performances over the majority of time spent at this exercise. With extended stimulus sets that included stimulus duration as a parameter and with more reliable on-task behavior, LLI children were also driven to higher



ders of rapidly sequenced tonal stimuli pairs of 0.8 and 1.2 kHz are correctly identified with 0.8 probability, and it also measures (**B**) the minimum durations of stimuli that can be sequenced [see (12)]. The effects of training were significant for all pre- and posttraining comparisons. For study 1, pretraining versus posttraining threshold ISIs, ANOVA (repeated measures, two-tailed) F(1,6) = 36.7, P < 0.001; for study 2 ISIs, F(1,6) = 12.8, P < 0.05. For study 1 durations, F(1,6) = 7.3, P < 0.05; for study 2 durations, F(1,6) = 28.9, P < 0.01.

performance levels in this revised game. Despite a highly variable number of total trials for different children (640 to 3739 in 17 to 22, 20-min training sessions), 10 of 11 children showed progressive gains and were able to complete a substantial program of learning within at least two FM stimulus categories; 9 of 11 completed a substantial program of learning and showed progressive gains in all four categories (Fig. 3).

For example, for distinguishing between FM stimuli of 60-ms duration with a starting or ending frequency of 1 kHz, the average performance improved about fourfold (see Fig. 3A), with four children achieving a perfect (ISI = 0) performance level at this task. The initial reversal-defined threshold (9) averaged 268 ms for these children; with training, it dropped to an average ISI of 77



Fig. 3. (A) Average performance differences on the Circus Sequence game for the 11 children in study 2, recorded early and late in a 20-day (20 min/day) training period. "Early" scores were from the first trials in which there was a clear demonstration that the children understood the "rules of the game" (that is, played the game on-task) and reached a stable response level revealed by stimulus reversals within a training session. These initial measures overestimate the early performance abilities of these children in some cases because children often practiced these games for a session or two before any clear stimulus reversals indicating stable performance limits were recorded. (B) Progression in performance at the 1or 2-kHz FM stimulus tasks for 6 of the 11 children in the second experimental series performing the stimulus sequence recognition (Circus Sequence game) exercise (9). The highest difficulty levels reached on every trial day on which children worked at these particular stimulus sets are shown. Similar progressive learning functions were recorded for nine other children in these two studies (that is, in 15 of 18 trained LLL children) More difficult stimuli had progressively shorter ISIs and durations.

ms. Three children also progressed to a perfect (ISI = 0) performance level when the duration of the FM stimuli was lowered to 40 ms, and one child mastered the task for 20-ms-duration FM stimuli in this category. Differences between early and late training performance levels were statistically significant [ANOVA (analysis of variance) repeated measures, two-tailed: F(1,18) = 54,  $P \le 0.0001$ ; see Fig. 3]. Although some individual performance differences by category were recorded, overall, performance gains did not significantly vary by FM stimulus category (16).

Again, the performance gains measured in these training experiments were mirrored by results obtained before and after training on the benchmark Tallal Repetition Test (12). All 11 children showed gains by this performance measure (see study 2, Fig. 2). The pre- and posttraining group differences were again significant. On the average, minimal ISIs dropped to  $\sim 1/15$  of their pretraining values. The mean ISI threshold of about 20 ms achieved after training approaches normal performance abilities (8).

Similarly, trained children could identify much briefer stimulus tones presented in almost immediate succession (Fig. 2). After training, children could distinguish the sequence order of almost immediately successive tonal stimuli that were, on the average, 18 ms in duration, which was about onefifth the pretraining value. This performance ability again approaches that of normal children (8). These training effects on the ability of study 2 LLI children to identify the sequence order of briefer sound stimuli was significantly greater than those for study 1 children, possibly because they were trained with stimuli that varied in duration. In contrast, 11 matched LLI children who were undergoing classical lan-

Fig. 4. Performance levels achieved early and late in training in five LLI children working at the Phoneme Identification game. The bottom of each colored bar marks a stable performance level achieved during the first five to six training days; the top of each colored bar marks the performance level achieved during the final days of training. Note that in this exercise, training began with differentially prolonged and amplified consonants guage training and equivalent periods of nonadaptive video game playing per day over the 20-day training period (7) did not significantly improve in their sequencedstimulus recognition abilities, as measured by this benchmark test (17).

The phoneme recognition game was also revised for testing in the 11 study 2 LLI children. Six of the 11 children progressed to stimulus categories for several CV contrasts at which they could identify the briefest consonants (35 ms) at the fastest ISIs (10 ms) (see examples in Fig. 4). Two other children also learned to reliably identify the fastest forms of natural (nonamplified) consonants. Two others showed significant improvements but, with this limited training, did not achieve normal recognition abilities for CV stimuli in which consonants were presented in very fast and nonenhanced forms. The 11th child, again, never consistently performed above chance at this game. Notably, performance gains were again mirrored by improvements in a phonetic element recognition benchmark test (13). Analyses of results from these tests indicated that with training at these exercises supplemented (i) by two other games designed to promote speech perception generalization (18) and (ii) by special language training with acoustically modified speech (7), temporal processing improvements applied generally to these children's language comprehension abilities [see (7)].

It is likely that performance at these adaptive training tasks could be further improved by additional practice in almost every tested LLI child (19). The five children who had the lowest performance results played the game for the least number of sessions and trials. Moreover, the number of training sessions and training trials completed by different children were directly



delivered initially in CV stimuli presented at slow repetition rates. Every child could initially identify these synthetically disambiguated CV stimuli. As the child's performance at the task improved with training, task difficulty was progressively increased (see right margin of the graph). The ISI was first decreased in 100-ms steps to initially stabilize at 200 ms; then the consonant duration was decreased progressively to natural fast transition rates (35- to 40-ms durations) in seven steps; then the differential consonant versus vowel amplification (consonant "emphasis") was faded in seven steps; then the ISI between CVs were further incrementally decreased in eight nonlinear steps to an ISI of 10 ms.

correlated with a benchmark measure of language outcome (20) for both study 1 [n = 7; r (correlation coefficient) = 0.85;  $P \le 0.01$ ] and study 2 LLI children (n = 11; r = 0.73;  $P \le 0.01$ ) (21).

These experiments once again confirm that LLI children have major temporal processing, fast-speech-element recognition deficits (8). Those deficits have presumably been in place for most of the prior years of the speech reception histories of these children (22). With a total of 5 to 10 hours of intensive practice at each of these two tasks in brief daily sessions extended over only 20 days, a substantial remediation of these deficits was achieved in nearly all the LLI children studied. These studies strongly indicate that the fundamental temporal processing deficits of LLI children can be overcome by training.

These studies also strongly indicate to us that there may be no fundamental defect in the learning machinery in most of these children, because they so rapidly learn the same skills at which they have been defined to be deficient. That finding suggests in turn that the physical differences and distributed functional response differences revealed in evoked potential and imaging studies of the brains of LLI individuals (23) may substantially be effects of the learning histories of these special children. Furthermore, it may also imply that inherited factors contributing to LLI origin (24) may relate to the initiation of a scenario that embeds, through learning, a defective representation of speech phonetics-and does not necessarily mean that these children have irreversible defects in the molecular and cellular elements of the learning machinery of their brains.

## **REFERENCES AND NOTES**

- A. Karni and D. Sagi, *Proc. Natl. Acad. Sci. U.S.A.* 88, 4966 (1991); *Nature* 365, 250 (1993); M. Ahissar and S. Hochstein, *Proc. Natl. Acad. Sci. U.S.A.* 90, 5718 (1993).
- G. H. Recanzone, M. M. Merzenich, C. E. Schreiner, *J. Neurophysiol.* 67, 1071 (1992); X. Wang, M. M. Merzenich, K. Sameshima, W. M. Jenkins, *Nature*  378, 71 (1995); G. Bertini, A. Karni, P. De Weerd, R. Desimone, L. G. Ungerleider, *Neurol. Abstr.* 21, 276 (1995); R. Beitel *et al.*, *ibid.*, p. 1180.
- M. M. Merzenich, C. S. Schreiner, W. M. Jenkins, X. Wang, in *Temporal Information Processing in the Nervous System: Special Reference to Dyslexia and Dysphasia*, P. Tallal, A. M. Galaburda, R. R. Llinás, C. von Euler, Eds. (New York Academy of Sciences, New York, 1993), pp. 1–22.
- M. M. Merzenich and W. M. Jenkins, in *Maturational Windows and Adult Cortical Plasticity*, B. Julesz and I. Kovacs, Eds. (Addison-Wesley, New York, 1995), pp. 247–272.
- For reviews of this complex subject, see M. M. Merzenich and W. M. Jenkins, in *Memory Concepts*, P. Anderson, O. Hvalby, O. Paulsen, B. Hokfelt, Eds. (Elsevier, Amsterdam, 1994), pp. 437–451; M. M. Merzenich and C. DeCharms, in *The Mind Brain Continuum*, R. Llinás and P. Churchland, Eds. (MIT Press, Cambridge, in press).
- M. M. Merzenich, G. M. Recanzone, W. M. Jenkins, K. A. Grajski, Cold Spring Harbor Symp. Quant. Biol.

55, 873 (1990); N. N. Byl, M. M. Merzenich, W. M. Jenkins, *J. Neurol.*, in press.

- 7. P. Tallal et al., Science 271, 81 (1996)
- 8. P. Tallal and M. Piercy, Nature 241, 468 (1973); Neuropsychologia 13, 69 (1975); P. Tallal, Brain Lang. 9, 182 (1980); \_ and R. E. Stark, Ann. Dyslexia 32, 163 (1982); \_ ., E. D. Mellits, Brain Lang. 25, 314 (1985); P. Tallal, S. Miller, R. H. Fitch, in (3), pp. 27-47. It has been argued that the fast-element (usually consonant) phonetic recognition difficulty arises because of an inappropriate "integration with or "masking" by following or preceding speech elements (usually vowels). Although parametric psychophysical studies are lacking, this may apply only within frequency channels as these children apparently have less difficulty identifying consonant-vowel pairs with brief consonants in which consonant transitions and vowel formants are within largely nonoverlapping channels
- 9. Cortical plasticity and learning studies conducted in primate and human models had shown that such training (i) had to be applied with a heavy schedule of practice trials, (ii) would be ideally conducted on a series of successive training days, (iii) would require relatively intense practice schedules designed to drive continuous performance improvements, and (iv) would have to be conducted under conditions of high motivational drive. We chose to accomplish these training objectives in LLI children by using entertaining and highly rewarding CD-ROM-mounted exercises disguised as games. The Circus Sequence game was developed with Authorware Professional and Director (Macromedia) software. The FM stimuli were generated with a 22.05-kHz sampling rate and 16-bit processor in Audio Interchange File Format (AIFF) with Matlab (Mathworks) software. Stimuli were ramped on and off to reduce spectral spatter. The compact disks were produced with Sony Hybrid software and a Sony 900 CDR. Games were played on Macintosh computers with CD-ROM drives or with these exercises copied and played off of Macintosh hard disks for convenience. Children received sound stimuli through Sony model MDR-V600 headsets. Four stimulus sets were mounted in this game in version 1: 60-ms-duration FM sweeps with starting or ending frequencies at 0.5, 1.0, 2.0, or 4.0 kHz. Three successive correct responses resulted in a shortening of either the ISI or the stimulus duration. An error resulted in a one-step lengthening of the ISI or stimulus duration. This learning schedule assured that at least 79.3% of the child's responses were correct. When the child achieved a predetermined number of positive and negative task difficulty reversals in any single training session, he or she was advanced to a new FM stimulus set. Training was initiated at a new stimulus set at a performance level established by a prior session's performance achievements.
- 10. The Phoneme Identification game was created with Authorware Professional (Macromedia) software. Synthetic speech stimuli were produced with 16-bit processing and with a 22.05-kHz sampling rate by using SenSyn (Sensimetrics) software, based on a Klatt cascade-parallel formant synthesizer [D. Klatt, J. Acoust. Soc. Am. 67, 971 (1980)]. Children in study 1 were trained with [bɛ], [dɛ], and [gɛ] target and foil stimuli. Children in study 2 were trained with five CV pairs: [ba] versus [da], [bɛ] versus [dɛ], [fa] versus [va], [aba] versus [ada], and [bai] versus [dai] In the initially tested version of this game, children performed trials under given parametric conditions in training blocks of 10. When performance criteria were met, consonant durations were shortened or differential amplification of fast consonant elements was reduced (or both) for another set of CVs through the next trial block. In study 2, an adaptive staircase training procedure identical to that used in the Circus Sequence game (9) was used,
- 11. Seven children (four females, three males) ranging in age from 5.8 to 9.1 years (mean age = 7.3 years, standard deviation = 1.5 years) who had a mean nonverbal intelligence score of 106 (standard deviation = 18.25) participated in the study. The group comprised four whites, two Hispanics, and one African American. The children were from lower and middle socioeconomic status (SES) families. All chil-

dren demonstrated a severe delay in receptive and expressive language development (mean language age = 4.8 years) as well as marked temporal processing deficits. These school-age children also had reading deficits. All were without other primary deficits.

- 12. The Tallal Repetition Test determines the threshold ISI at which sequences of two tonal stimuli (in this case, of 1000 and 1400 or 800 and 1200 Hz) that are 150, 75, 40, or 17 ms in duration are perceived with their delivery sequence reproduced with a 75% accuracy. ISIs vary in the test from 500 to 0 ms. See P. Tallal, in *Non-Speech Language and Communication*, R. Schiefelbusch, Ed. (University Park Press, Baltimore, MD, 1980), pp. 449–467.
- 13. The Goldman-Fistoe-Woodcock Diagnostic Auditory Discrimination Test (American Guidance Service, Circle Pines, MN) was used as a standard benchmark. It was designed to define an individual's ability to identify phonic elements within words.
- 14. In study 2, 22 children (8 females, 14 males) ranging in age from 5.2 to 10.0 years (mean age = 7.4 years, standard deviation = 1.4 years) who had a mean nonverbal intelligence score of 96.4 (standard deviation = 9.7) participated. The group included 18 whites, two Hispanics, one Asian, and one African American. All children were from middle SES families. All children demonstrated a severe delay in receptive and expressive language development (mean language age = 4.9 years; standard deviation = 1.4 years) as well as marked temporal processing deficits. These school-age children also had reading deficits. All were without other primary deficits.
- After initial testing with these training exercises in 15. these seven children, both games were revised, then retested in study 2 in 11 LLI children (14). In the second version of the Circus Sequence game, the number of stimulus variations in each set was extended to 135 by including FM stimuli with durations of 60, 40, and 20 ms. An animated performance barometer was added to the game to further signal performance progress in yet another compelling visual manner, and points were subtracted for response "misses." To further ensure that children were kept on task in these games, five misses in a row resulted in a suspension of a change in difficulty level; task difficulty was then maintained constant until the child again recorded four "hits" in a row. For the Phoneme Identification game, an animated performance barometer was also added to the AV displays, and points were subtracted for incorrect responses. Most importantly, the game was reconstructed as a progressively adaptive exercise in which task difficulty was (i) increased progressively when any three-trial block was completed without error, (ii) decreased by one step in difficulty for any error, and with the drop in game difficulty, (iii) halted whenever a child made five errors in succession. Task difficulty was increased by first reducing the duration of the consonant stimulus elements, then a differential amplification of fast consonant elements progressively faded, then interstimulus ISIs for successive CVs were progressively reduced.
- 16. For the main effect of stimulus category, F(1,18) = 1.7, not significant (n.s.); for the interaction of time and stimulus category, F(1,18) = 2.5, n.s.
- 17. Group B children, who received equivalent language training but with natural speech materials and who played video games rather than these adaptive auditory-speech training games (7), did not improve significantly with respect to either ISI or duration thresholds measured by the Tallal Repetition Test. For ISI, ANOVA (repeated measures, two-tail) F(1,7)= 2.8, n.s.; for duration, F(1,7) = 3.9, n.s. In contrast to the experimental treatment group A, in which everv child improved at this benchmark, the majority of group B children had equal or poorer performances on this test after their 1-month-long training period. Although the mean performance of group B LLI children was modestly better than was that for group A children, children in these groups did not differ in their pretreatment Tallal Repetition Test measures of threshold ISIs or durations.
- 18. Children in study 2 were also trained at two additional games, both designed to facilitate the generalization of training gains from these first two described games to the wider range of temporal sequence

events and phonetic element contexts and contrasts that occur in natural running speech. The third game (Old McDonald's Flying Farm), produced with Director (Macromedia) software, was a limited hold reaction time task in which the child maintained a touchscreen "button" press while repeated stimuli were delivered in regular sequence. The child's task was to release the button when there was a change in phonetic element identity. The durations of a wider array of synthetic consonant elements and the interstimulus times between repeated stimuli were the main exercise variables. The fourth game (Phonic Match), also developed with Director (Macromedia) software, was a sound-matching exercise in which button presses resulted in soundings that the child had to locate a match for, on a 2-by-2 to 5-by-5 touch-screen button array. The button array size and the temporal structure of elements and of element sequences in individual consonant-vowel-consonant stimuli were game variables. Stimuli applied in this exercise were synthetically processed to prolong and differentially amplify brief phonetic elements [see (1)]. Children also played both of these games for approximately 20 min/day throughout the 20-day training period. In general, children's performances at these two games paralleled their progressive achievements at the time order judgment and phonetic element recognition tasks described in this report. All LLI children who were trained at these games also underwent training with acoustically modified speech stimuli, as described by Tallal et al. (7).

- 19. Children were still improving at their game performances when these exercises were arbitrarily terminated at the end of the 4-week training period. Their ultimately achievable performance limits are unknown.
- The Token Test for Children (Teaching Resources Corporation, Boston, MA, copyrighted 1978) is designed to test the ability to follow auditory commands of increasing length and grammatical complexity.
- 21. The intensity of practice at three FM stimulus categories were all significantly correlated with Token Test (language outcome) results. For the 1+ kHz category, trial numbers versus language outcome, r = 0.75,  $P \le 0.01$ ; for 2+ kHz FM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 4+ kHz FM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 4+ kHz FM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 2+ kHz FM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 2+ kHz FM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 2+ kHz FM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 2+ kHz FM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 2+ kHz FM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 2+ kHz FM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 2+ kHz FM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 2+ kHz FM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 2+ kHz fM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 4+ kHz fM stimulus, trial numbers versus language outcome, r = 0.73,  $P \le 0.01$ ; for 4+ kHz fM stimulus, trial numbers versus language outcome,  $r \ge 0.48$ .
- 22. A. A. Benescish and P. Tallal, in (3), pp. 312–314; Infant Behav. Dev., in press.
- A. M. Galaburda, G. F. Sherman, G. D. Rosen, F. Aboitiz, N. Geschwind, Ann. Neurol. **18**, 222 (1985);
  J. P. Larson, T. Hoien, I. Lundberg, H. Odegaard, Brain Lang. **39**, 289 (1990); T. L. Jernigan, J. R. Hesselink, E. Sowell, P. A. Tallal, Arch. Neurol. **48**, 539 (1991); J. M. Flynn, W. Deering, M. Goldstein, M. H. Rahbar, J. Learn. Disabil. **25**, 133 (1992); R. Duara et al., Arch. Neurol. **48**, 410 (1991); J. O. Hagman, F. Wood, M. S. Buchsbaum, L. Flowers, W. Katz, *ibid.* **49**, 734 (1992); A. Kusch et al., Neuropsychologia **31**, 811 (1993); A. M. Galaburda, Neurol. *Clin.* **11**, 161 (1993); A. M. Galaburda, Neurol. *Clin.* **11**, 161 (1993); M. Ras, *Curr. Opin. Neurol.* **7**, 179 (1994).
- P. Tallal, J. Townsend, S. Curtiss, B. Wulfeck, *Brain Lang.* **41**, 81 (1991); B. A. Lewis, *J. Learn. Disabil.* **25**, 486 (1992); \_\_\_\_\_\_, N. J. Cox, P. J. Bayard, *Behav. Genet.* **23**, 291 (1993); B. F. Pennington, *J. Child Neurol.* **10**, S69 (1995).
- 25. We thank T. Jacobson, B. Wright, X. Wang, G. Bedi, and G. Byma for their technical assistance, and C. Checko, N. Reid, and A. Lipski for assistance in programming the animation reward sequences for these AV exercises. T. Realpe, I. Shell, C. Kapelyn, A. Katz-Nelson, L. Brzustowicz, C. Brown, A. Khoury, J. Reitzel, K. Masters, B. Glazewski, A. Rubenstein, and S. Shapeck assisted in the training of these children at Rutgers University. This research was funded by the Charles A. Dana Foundation with supportive assistance by Hearing Research, Incorporated. For further information about this and related subjects, contact: http://www.ld.ucsf.edu/
  - 6 October 1995; accepted 30 November 1995

Language Comprehension in Language-Learning Impaired Children Improved with Acoustically Modified Speech

Paula Tallal,\* Steve L. Miller, Gail Bedi, Gary Byma, Xiaoqin Wang, Srikantan S. Nagarajan, Christoph Schreiner, William M. Jenkins, Michael M. Merzenich

A speech processing algorithm was developed to create more salient versions of the rapidly changing elements in the acoustic waveform of speech that have been shown to be deficiently processed by language-learning impaired (LLI) children. LLI children received extensive daily training, over a 4-week period, with listening exercises in which all speech was translated into this synthetic form. They also received daily training with computer "games" designed to adaptively drive improvements in temporal processing thresholds. Significant improvements in speech discrimination and language comprehension abilities were demonstrated in two independent groups of LLI children.

**E**xposure to a specific language alters an infant's phonetic perceptions within the first months of life, leading to the setting of prototypic phonetic representations, the building block on which a child's native language develops (1). Although this occurs normally without explicit instruction for the majority of children, epidemiological studies estimate that nearly 20% of children fail to develop normal speech and language when exposed to speech in their native environment (2). Even after all other primary sensory and cognitive deficits are accounted for, approximately 3 to 6% of children still fail to develop normal speech and language abilities (3). Longitudinal studies have demonstrated a striking convergence between preschool language delay and subsequent reading disabilities (such as dyslexia). A broad body of research now suggests that phonological processing deficits may be at the heart of these language-learning impairments (LLIs) (4, 5).

Tallal's earlier research has shown that rather than deriving from a primarily linguistic or cognitive impairment, the phonological and language difficulties of LLI children may result from a more basic deficit in processing rapidly changing sensory inputs (6). Specifically, LLI children commonly cannot identify fast elements embedded in ongoing speech that have durations in the range of a few tens of milliseconds, a critical time frame over which many phonetic contrasts are signaled (7). For example, LLI children have particular difficulty in discriminating between many speech syllables, such as [ba] and [da], which are characterized by very rapid frequency changes (formant transitions) that occur during the initial few tens of milliseconds. Interestingly, LLI children are able to identify these same syllables when the rates of change of the critical formant transitions are simply synthetically extended in time by about twofold (8). A strong prediction is suggested by these findings: If the critical acoustic cues within the context of fluent, ongoing speech could be altered to be emphasized and extended in time, then the phonological discrimination and the on-line language comprehension abilities of LLI children should significantly improve.

To test this prediction, we have conducted two studies with LLI children who have been trained with the application of temporally modified speech. These same children also received training at making distinctions about fast and rapidly sequenced acoustic inputs in exercises mounted in the format of computer "games" (9). Modification of fluent speech was achieved by application of a two-stage processing algorithm (10). In the first stage, the duration of the speech signal was prolonged by 50% while preserving its spectral content and natural quality. In the second processing stage, fast (3 to 30 Hz) transitional elements of speech were differentially enhanced by as much as 20 dB. This two-step acoustic modification process was applied to speech and language listening exercises that were recorded on audiotapes, as well as to the speech tracks of children's stories recorded on tapes and on educational CD-ROMs. The differential emphasis of fast elements also resulted in a speech envelope that was more sharply segmented. This processed speech had a staccato quality in which the fast (primarily consonant) elements were exaggerated relative to more slowly modulated elements (primarily vowels) in the ongoing speech stream. We reasoned that amplifying the fast elements should render them more salient, and thus

P. Tallal, S. L. Miller, G. Bedi, G. Byma, Center for Molecular and Behavioral Neuroscience, Rutgers University, Newark, NJ 07102, USA.

X. Wang, S. S. Nagarajan, C. Schreiner, W. M. Jenkins, M. M. Merzenich, W. M. Keck Center for Integrative Neurosciences and Coleman Laboratory, University of California, San Francisco, CA 94143–0732, USA.

<sup>\*</sup>To whom correspondence should be addressed.