teins were digested with pepsin, and the collagenous proteins were extracted with acetic acid, separated by electrophoresis on polyacrylamide slab gels, and visualized by fluorography. Three cell-associated collagens were identified: (i) the typical α_1 and α_2 chains of type I collagen (lane 2 in Fig. 3); (ii) a high molecular weight collagen (above the β region), which was reduced to a lower molecular weight by treatment with dithiothreitol (DTT) (lane 4 in Fig. 3), corresponding to the α_1 chain of type III collagen; and (iii) two collagenase-sensitive, reducible radioactive bands observed in the γ region (top of the lane) on lanes 2 and 6 and an additional band migrating between α_1 (type I) and the β region (lane 2 in Fig. 3, arrow). These three bands are consistent with pepsin-generated fragments of the α_1 chain of type IV collagen (*11*). Type V collagen, if present, would also migrate near the region indicated by the arrow (lane 2). However, it is unlikely that this band (arrow, lane 2) represents type V collagen because when cultures were stained with antibodies specific to type V, only trace reactivity was observed. Moreover, attempts to isolate type V collagen from the cultures with selective salt fractionation procedures have thus far been unsuccessful. The medium from hepatocyte cultures contained type I and type III collagens (lanes 6 and 8 in Fig. 3) and also faint, reducible bands in the γ region (lane 6) consistent with pepsin-generated fragments of the α_1 chain of type IV collagen. Although the hepatocyte cultures were incubated in the presence of β-aminopropionitrile during the period of exposure to radioactive proline and glycine, there is still some evidence for cross-linked collagen in the β region in lanes 2, 4, 6, and 8 (Fig. 3).

These results provide evidence that mature hepatocytes in culture are capable of simultaneously synthesizing at least three types of collagen. That the collagen initially formed by the hepatocyte in culture is a component of basement membrane implies physiologic or pathophysiologic importance. A complete and thickened basement membrane in the sinusoid adjacent to the hepatocyte has been observed in normal regenerated liver and in cirrhosis (*12*). However, the relevance of our findings with cultured hepatocytes to the liver in vivo has been questioned (*1, 13*) in that many types of cells may produce collagen in culture (*14*). To demonstrate that the hepatocyte produces collagen in vivo as it does in culture, we stained slices of pathologic rat liver with the antibodies to collagen. The hepatocytes as well as the adjacent sinusoids uniformly stained positively for type IV collagen (Fig. 2A). Only under pathologic conditions, such as experimental bile duct ligation, does the hepatocyte produce and deposit type IV collagen. This phenomenon cannot be observed under normal physiologic conditions. No staining of the hepatocytes was observed with antibodies to type I or type III collagen. We conclude that among the normal reparative processes in the liver is the production of basement membrane collagen by the hepatocyte.

The conditions used to isolate and maintain the hepatocyte in culture may evoke its collagen-synthesizing potential and thus simulate some of the conditions of liver injury in vivo (*1*). Our study demonstrates that under culture conditions that permit expression of numerous specialized functions of the adult liver, such as albumin or fibrinogen formation or drug-mediated induction of mature forms of cytochrome P-450 (*15*), hepatocytes also sequentially recapitulate the time course of phenotypic expression of collagens associated with liver injury in vivo (*16*). Hence, the sequential appearance of basement membrane collagen, type I collagen, and type III collagen from hepatocytes in culture implies that these cells in vivo may be important contributors to the fibrotic process.

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Specific Reading Disability: Identification of an Inherited Form Through Linkage Analysis

Abstract. *Linkage analysis in families with apparent autosomal dominant reading disability produced a lod score of 3.241. Since the traditionally accepted significance level for linkage is a lod score of 3.0, these results strongly suggest that a gene playing a major etiologic role in one form of reading disability is on chromosome 15.*

Specific reading disability is diagnosed in an individual with severe reading and spelling problems in the absence of neurological, intellectual, emotional, or environmental handicap. Although multiple etiologies are likely within this broadly defined group of affected individuals, a strongly positive family history is frequently reported by educators working with affected children. This suggests that many cases may be primarily genetic in origin. The lack of precise diagnostic criteria and laboratory tests have restricted the ability of investigators to

define specific entities and modes of inheritance within the overall group (*1*), although autosomal dominant inheritance has been reported in some families (*2*). If a trait can be shown to be linked to a known genetic marker locus, it is inferred that a major gene for that trait is located on the same chromosome as the marker locus. Since the available battery of genetic markers and linkage analysis provides a reasonable chance of detecting a linkage, this study was designed to define one or more inherited types of reading disability.

Families were selected in which specific reading disability appeared to be inherited through several generations in an autosomal dominant fashion so that linkage, if present, could be detected. Most were identified through special schools and parents' groups. Minimal requirements were a proband with apparent specific reading disability, full scale IQ greater than 90 (initially determined from school records), and one parent and one of his or her parents with a history of reading disability similar to that of the proband. Both parents and at least one sibling of the proband over 8 years old had to be available for study. All families were Caucasian, and English was their native language. Family, medical, and educational histories were reviewed. Each family member was given a series of standardized achievement tests to detect affected family members and to ensure that the disability was confined to reading and spelling. These tests included the Gray Oral Reading Test, the spelling subtest of the Wide Range Achievement Tests (WRAT), and the Peabody Individual Achievement Tests (PIAT: mathematics, reading recognition, reading comprehension, spelling, and general information). Test results were scored according to age-specific standards available in the respective manuals.

Children were diagnosed as reading disabled if their reading level was at least 2 years below expected grade level. The Gray Oral Reading Test was used as the measure of reading ability, and the average of the PIAT mathematics and general information tests were used to determine the expected level. Children under 7 years were not included in the study unless they could already read and were clearly not affected.

If there was a discrepancy between test results and a history of reading disability in adults, the history was used to determine the status of the individual in the linkage analysis. Misdiagnosis is not likely to result in a spurious linkage result, as discussed by Morton (*3*). This issue is also taken into account through the high level of statistical significance required for the acceptance of a positive linkage and is one of the advantages of this approach.

Studies have been completed in nine families or kindreds. Sample pedigrees are shown in Fig. 1. From these, 84 individuals have been tested: 20 men (over 18 years), 21 women, 25 boys, and 14 girls. Of these, 50 individuals (12 men, 10 women, 19 boys, and 9 girls) were judged to be affected, 32 (8 men, 13 women, 6 boys, and 5 girls) were not affected, and two males were borderline.

As in earlier studies (*1*, *2*) males were more frequently affected. All probands were male. When these were removed, the sex ratio of those affected was 1.44:1, and not statistically significant ($P > .05$, χ^2 test).

Twenty-one routine genotyping markers as well as chromosomal heteromorphisms were used in the linkage analysis which was done with the computer program LIPED (*4*). For the chromosome analysis, sequential Q-to-C banding was performed for 80 family members (*5*). Heteromorphic chromosomes were scored according to the Paris conference criteria and the criteria of McKenzie and Lubs (*6*) and followed through families in the same manner as marker alleles.

The linkage analysis between specific reading disability and chromosome 15 heteromorphisms produced a lod score of 3.241 at $\theta = 0.13$, where θ is the recombination fraction (Table 1). Thirteen sibships from eight kindreds were informative for this test. All other loci tested gave lod scores less than 1.0. It is important to note that the relation between diagnosis and the fluorescence level of chromosome 15 was not statistically significant as indicated by a 2 by 2 contingency table ($\chi^2(1) = 0.422$).

Family or kindred 432 has a particularly high lod score (Table 1). This is the combined score from three families within this kindred and does not indicate a

Table 1. Lod scores for specific reading disability and chromosome 15 heteromorphisms. Scores are given for each family at different values of theta (θ), the recombination fraction. By interpolation, a maximum score of 3.241 is obtained at $\theta = 0.13$.

Family	Lod score for θ =					
	0.00	0.05	0.10	0.20	0.30	0.40
371	0.602	0.535	0.465	0.318	0.170	0.049
372	∞	−0.350	−0.126	0.019	0.043	0.027
375	0.903	0.836	0.766	0.612	0.438	0.237
484	0.602	0.535	0.465	0.318	0.170	0.049
576	0.301	0.258	0.215	0.134	0.064	0.017
491	∞	−1.885	−1.076	−0.377	−0.081	0.026
432	2.755	2.501	2.237	1.673	1.060	0.414
005	0.301	0.258	0.215	0.134	0.064	0.017
Total		2.688	3.161	2.831	1.928	0.836

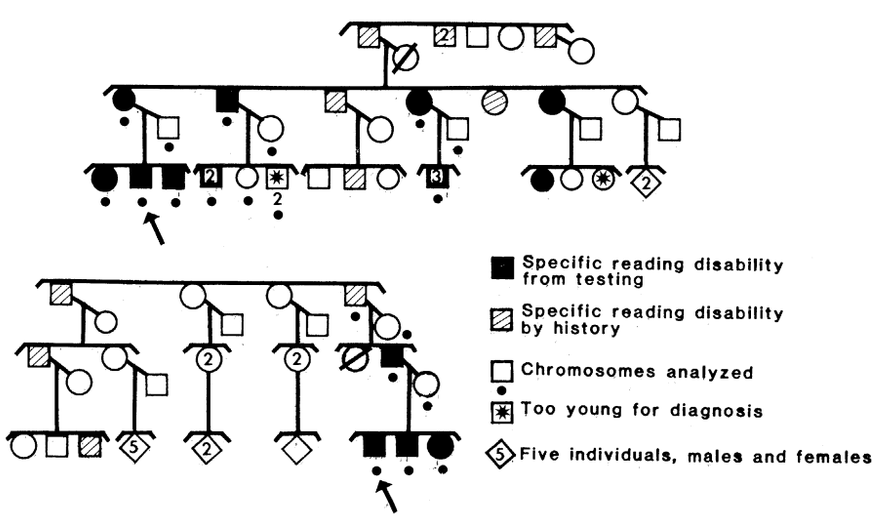

Fig. 1. Two representative pedigrees 432 and 375 showing apparent autosomal dominant transmission of specific reading disability.

biological difference. In contrast, family 491 has a large negative lod score, which could indicate nonlinkage. A test for heterogeneity of lod scores (*7*), however, was not significant, so that elimination of this negative lod score from the total cannot be justified. The possibility remains that this family may have a different type of specific reading disability with the locus being on another chromosome.

A lod score above 3.0 (equivalent to prior odds of 1000 to 1) is normally considered sufficient to establish linkage, thus assigning a gene for specific reading disability to chromosome 15. Because of the complexity of the phenotype and the importance of the linkage studies in providing evidence of a genetic etiology in certain cases of specific reading disability, this study will be continued until a lod score of at least 5 is obtained. Confirmation by a second study is also required before a linkage is considered proven.

An opportunity to study the effects of one gene on information-processing has evolved from these studies. Moreover, the methods are applicable to many other problems in behavior genetics.

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Infant Intermodal Speech Perception Is a Left-Hemisphere Function

Abstract. *Prelinguistic infants recognized structural correspondences in acoustic and optic properties of synchronized, naturally spoken disyllables, but did so only when they were looking to their right sides. This result suggests that intermodal speech perception is facilitated by rightward orientation of attention and subserved by the left hemisphere.*

Research on infants' capacities for intermodal perception has demonstrated that infants are sensitive to correspondences in the acoustic and optic properties that specify an event (*1, 2*). Infants may prefer a natural pattern of structural correspondence between the optic and acoustic dimensions of an event by which, in speech for example, an opening mouth is correlated with a rise in amplitude and with an upward shift in overall spectral structure and a closing mouth with the reverse. Alternatively, infants may simply prefer a temporal pattern of correspondence by which gross points of change in acoustic and optic structure are synchronized (*1*). If infants prefer mere synchrony, they should be satisfied with any arbitrary pattern of acoustic-optic correspondence; thus, in speech they might have no preference for syllable amplitude peaks synchronized with an open mouth over those synchronized with a closed mouth. But if infants prefer natural patterns of structural correspondence, they should look longer at the synchronized video monitor display of a woman producing articulatory patterns that specify the speech they are hearing than at an alternative, synchronized video display of the same woman displaying a different articulatory pattern. We therefore investigated the capacity of infants to recognize acoustic-optic correspondences in speech structure when the synchrony between an acoustic and two competing optic displays was maintained.

Our preliminary analyses suggested that when acoustic and optic speech displays specified the same disyllable, intermodal recognition was enhanced if infants were watching the right, rather than the left, video display. When adults look to the right (or left) as they complete a task, their performance is facilitated if the task demands are better subserved by the hemisphere contralateral to gaze direction (*3*). Such results have been interpreted as evidence that attention, behaviorally manifested by gaze, may selectively activate the hemisphere contralateral to direction of gaze. We therefore expected that only rightward looking would significantly enhance recognition of acoustic-optic correspondences in speech structure.

Table 1. First fixation times in seconds, averaged across six disyllables, to the left and right video display when the display matched or mismatched the audio CVCV. Mean fixation times are summed across 18 infants.

Direction of gaze	Video display	
	Matches audio CVCV	Mismatches audio CVCV
Left	66.0	59.3
Right	81.2	67.0

Eighteen infants, eight males and ten females, 5 to 6 months of age ($\bar{X}$ = 5 months, 25 days) participated in the experiment. We used three pairs of naturally produced consonant-vowel-consonant-vowel (CVCV) disyllables, spoken with equal stress on both syllables: /mama lulu/, /bebi zuzi/, and /vava zuzu/. We enhanced the opportunity to detect acoustic-optic correspondences by making the articulatory dynamics of the contrasting video displays highly discriminable. To prepare the experimental materials, an adult female silently articulated each CVCV in synchrony with either the corresponding or the contrasting spoken disyllables of another adult female. The voice and the articulating face were recorded simultaneously to appear on one side of a 28 cm by 22 cm video monitor screen. The video recording procedure was then repeated so that the articulating face appeared on the other half of the split video screen, silently articulating the second CVCV in the pair in synchrony with the audio playback of the original disyllable. Deviations in acoustic-optic synchrony were below the adult threshold for detecting asynchronies (*4*). The resulting recording of the acoustic signal synchronized with two competing articulatory displays was output to two video monitors.

The infant sat 46 cm from the video monitors on its mother's lap at the open end of a wooden box. The infant viewed a different articulatory display on the split screen of each monitor, one appearing through the right back window of the box and the other through the left. The