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16. The L-6 cells were labeled with FITC under mild conditions (*15*). The FPR measurements were performed only on cells stained peripherally and not on cells in which the cytoplasm was stained. Sparse cultures yielded a greater fraction of damaged cells than confluent populations (*5*). All cells stained with TNBS and rhodamine-labeled antibodies to DNP were stained peripherally. Similar diffusion coefficients were obtained for cells labeled with TNBS and rhodamine-labeled Fab antibodies to DNP indicating that cross-linking between surface proteins via the intact antibody is unlikely.
17. The cells were incubated with 1 ml of TNBS (10 m*M*) in Hanks BSS for 15 minutes at 37°C, then washed three times and incubated for 15 minutes at 37°C with 1 ml (25 μg/ml) of rhodamine-labeled antibodies (sheep, immunoglobulin G) to DNP.
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Developmental Dyslexia: Two Right Hemispheres and None Left

Abstract. *Developmental dyslexia may be associated with (i) bi-hemisphere representation of spatial functions, in contrast to the right-hemisphere specialization observed in normal children, and (ii) typical left-hemisphere representation of linguistic functions, as is observed in normal children. The bilateral neural involvement in spatial processing may interfere with the left hemisphere's processing of its own specialized functions and result in deficient linguistic, sequential cognitive processing and in overuse of the spatial, holistic cognitive mode. This pattern of cognitive deficits and biases may lead dyslexics to read predominantly with a spatial-holistic cognitive strategy and neglect the phonetic-sequential strategy. Such an approach in learning to read phonetically coded languages, such as English, may be inefficient and limited.*

Developmental dyslexia, or specific reading disability, refers to the clinical syndrome of difficulty in reading in intellectually, emotionally, and medically normal individuals. Such a deficit is particularly incapacitating in modern, highly literate societies and frequently results in secondary behavioral and emotional difficulties. Estimates of the incidence of the disorder are as high as 5 percent of school-age children, which makes it a prevalent as well as a serious disorder (*1*).

Numerous etiological hypotheses of dyslexia have implicated various neurological, social, and educational factors (*2*). None, however, has received strong or consistent support. One long-standing neural hypothesis, originally suggested by Orton (*3*), implicates abnormal cerebral dominance or functional asymmetry of the hemispheres. Testing this hypothesis has become possible only within the last decade with the development of a number of experimental techniques; for example, tasks requiring the perception of lateralized stimuli allow inferences about hemisphere specialization in nonbrain-damaged individuals (*4, 5*). Numerous studies using these techniques, particularly dichotic (auditory) stimulation (*6*) and, to a lesser extent, tachistoscopic stimulation in the lateral visual fields (*7*), have been reported with variously defined groups of poor readers. All these studies used linguistic stimuli and addressed themselves to the question of whether the left hemisphere is specialized for linguistic processing in such children; the implicit assumption has been that specialization of the left hemisphere is impaired in dyslexia. This assumption probably arose from the well-established clinical knowledge that acquired alexia or dyslexia is usually associated with lesions in the left (speech dominant) hemisphere (*8*) and from the fact that reading has traditionally been conceptualized as a language skill. The results of these studies (*6, 7*) have consistently indicated right-ear and right-visual-field superiorities and, by inference, specialization of the left hemisphere for linguistic processing in poor readers, as is the case in normal individuals. However, in spite of the data, many of these reports contain unfounded suggestions of a lack of, or less strong, specialization of the left hemisphere in dyslexia.

In contrast, I have investigated (i) specialization of the right hemisphere for spatial processing, (ii) specialization of the left hemisphere for linguistic processing, and (iii) the relative participation of the two hemispheres on a task that requires the specialized functions of both. Performance on the last task may be particularly illuminating for, like reading, it involves both types of cognitive processing (*9*).

The results indicate that in dyslexics, spatial functions are represented in both hemispheres in contrast to the specialization of the right hemisphere in normal children. In addition, and consistent with the previous studies, dyslexics have the typical pattern of left-hemisphere representation of linguistic functions. Although the left hemisphere may mediate the typical cognitive functions, the results suggest that left-hemisphere processing may be deficient in dyslexics. These two possible neural correlates may result in a cognitive pattern of deficits and biases in dyslexia; specifically, a deficiency in the linguistic, sequential, analytic cognitive mode of information processing, and an intact or even overdeveloped use of the spatial, parallel, holistic mode.

A group of 85 right-handed boys (6 to 14 years of age, $\bar{X} = 10.6$), selected as cases of developmental dyslexia on the basis of extensive pediatric, psychiatric, and clinical psychological assessments, were given a battery of four tests considered to reflect hemisphere specialization. Two tests are considered to be indices of right-hemisphere specialization for spatial processing: (i) "dichhaptic stimulation" with meaningless shapes, a relatively new task, in which two different shapes are simultaneously presented one to each hand, to be perceived by active touch alone (*5, 10*), and (ii) a tachistoscopic task, adapted from the test procedures originally developed with adults, in which pairs of identical or different figures of people were presented in either the right or left visual half-field and had to be identified as "same" or "different." Specialization of the left hemisphere for linguistic processing was assessed with a typical dichotic stimulation test that used free recall of series of pairs of digits. The final test involved dichhaptic presentation of letters that were to be named by the subject (*5*). The performance of the dyslexic group on these tests was compared to that of a group of 156 normal, right-handed boys who were matched for age ($\bar{X} = 10.5$ years) and socioeconomic class, who had no history of academic or behavioral difficulty, and who obtained age-appropriate scores on reading and spelling achievement tests.

On the dichhaptic shapes test, the dyslexic group showed no difference in accuracy in recognizing shapes presented to their left and right hands ($\bar{X} = 5.1$ and 5.5, respectively, $t = 1.43$, d.f. = 61), in contrast to the normal group, who obtained higher left- than right-hand scores ($\bar{X} = 5.4$ and 4.6, $t = 3.82$, d.f. = 99, $P < .001$). Greater left-hand accuracy in the normal group is considered to reflect greater participation of the right hemisphere on this spatial task (*5, 10*). The lack of hand asymmetry in the dyslexic group suggests, instead, bilateral processing of spatial functions.

This interpretation is corroborated by the results of the visual test of right-hemisphere specialization. The dyslexic group showed no difference in accuracy in the perception of human figures presented in the left and right visual fields ($\bar{X} = 5.8$ and 5.6, respectively, $t = 0.96$, d.f. = 81). In contrast, the normal group showed greater accuracy for stimuli presented in the left field ($\bar{X} = 6.0$ and 5.5, $t = 2.28$, d.f. = 84, $P < .05$) and, by inference, right-hemisphere specialization for this task. Although the dyslexic and normal groups differed in the pattern of perceptual asymmetry on both the tactual and visual spatial tests, the groups did not differ in total accuracy for either test (tactual test: $\bar{X} = 10.5$ and 10.0; visual test: $\bar{X} = 11.3$ and 11.5, respectively).

On the dichotic test, both groups demonstrated better recall for digits presented to the right than to the left ear. (For the normal group, $\bar{X} = 46.0$ and 42.1, $t = 7.32$, d.f. = 155, $P < .001$; for the dyslexic group, $\bar{X} = 41.1$ and 35.6, $t = 5.15$, d.f. = 84, $P < .001$). These results suggest that the left hemisphere is specialized for linguistic functions in both dyslexic and normal boys. However, total accuracy of the dyslexics was lower than that of the normal group ($\bar{X} = 76.7$ and 88.2; $t = 8.17$, d.f. = 239, $P < .0001$). Such impaired overall performance on this task is similar to that observed for groups of individuals with known dysfunction in the left temporal lobe (*11*); this performance suggests the possibility of dysfunction in the left hemisphere of dyslexics.

On the dichhaptic letters test, the normal group showed only a tendency toward naming more right- than left-hand letters ($\bar{X} = 6.8$ and 5.6, $t = 1.67$, d.f. = 27, $P \doteq .10$), whereas the dyslexic group named significantly more left- than right-hand letters ($\bar{X} = 7.7$ and 6.8, $t = 2.45$, d.f. = 54, $P < .02$). There was no difference in total accuracy between the groups ($\bar{X} = 12.5$ and 14.6, respectively, $t = 1.53$, d.f. = 81). Both spatial and linguistic processing are considered necessary in this task (*5*), and, consequently, it may allow the manifestation of individual differences in the relative use of the two cognitive strategies. In dyslexics the left hemisphere appears to be the main linguistic processor. The necessity for it to process the linguistic requirements of this task, albeit minimal, particularly if, as I have suggested, it has a limited capacity to do so, may force the spatial processing in this case to be mediated predominantly by the right hemisphere. Furthermore, the actual superiority for left-hand letters exhibited by the dyslexics may reflect a predominance of right-hemisphere functioning and of spatial cognitive processing on this task. These procedures and some of these results are discussed in greater detail elsewhere (*12*).

The issue arises as to the possible relationships of the hypothesized bilateral neural representation of spatial processing in dyslexics to (i) their cognitive processing and (ii) their reading difficulty. The available evidence indicates that bilateral representation of a cognitive function that is usually lateralized is not necessarily associated with diminished ability (*13, 14*). Similarly, in this report, in which bilateral spatial representation is hypothesized for dyslexics, there is no evidence that their spatial processing is deficient. Their mean scaled score on the Wechsler Intelligence Scale for Children (WISC) Block Design subtest was 11.3, which indicates at least average ability and is not different from that of 11.9 for the normal group ($t = 1.30$, d.f. = 239). The dyslexic group's mean WISC Performance Intelligence Quotient (IQ), reflecting various aspects of visuospatial processing, was 107, within the average range, and was greater than their Verbal IQ of 97.4 ($t = 5.49$, d.f. = 84, $P < .001$). Furthermore, they were as accurate on the two lateral perception tests involving spatial processing as the normal group. The conclusion that at least most dyslexics have normal or better visuospatial perception was previously drawn by Benton (*15*), in contrast to widespread belief to the contrary, and is further corroborated by a growing body of data (*16*).

Bilateral representation of a cognitive process could, however, affect cognition by overloading one hemisphere and interfering with those functions "native" to it. Levy (*13*) observed that some left-handed individuals have lower spatial than verbal ability and suggested, in a vein similar to that of Lashley concerning the neural localization of function (*17*), that this may be due to the higher incidence of bilateral representation of language in sinistrals and the resultant interference with the right hemisphere's processing of spatial information. In the case of dyslexics, bilateral representation of spatial functions could overload the left hemisphere and interfere or be incompatible with its specialized role in sequential, linguistic processing. Interference with left-hemisphere processing should lead to poor performance on linguistic tasks, as was observed in the present study: the dyslexic group was impaired in overall performance on the verbal dichotic test; the Verbal IQ was significantly lower than the Performance IQ; and the mean scaled score on the WISC Vocabulary subtest was 10.2, which is lower than the normal group's score of 11.4 ($t = 3.44$, d.f. = 239, $P < .001$). The hypothesis of deficient left-hemisphere processing is further supported by the results of many studies which indicate that dyslexics show deficits specifically on cognitive tasks that require sequential processing or verbal encoding of information (*18*), considered to be left-hemisphere functions. Dysfunction per se in the left hemisphere was directly suggested on the basis of the similarity of impaired recall of dichotic stimulation in dyslexics and in patients with known dysfunction in the left temporal lobe.

Deficiency in linguistic, sequential, analytic processing, whether resulting from interference or dysfunction per se in the left hemisphere, could lead to predominant use, wherever possible, of the other cognitive mode, the spatial, parallel, holistic mode, with which dyslexics appear to have no difficulty. The dyslexic group's performance on the dual processing task of dichhaptic letters supports such speculation. In contrast to normal boys, they showed a significant left-hand superiority and, by inference, greater right-hemisphere participation and greater use of spatial, holistic processing. This finding may have relevance for the reading process in dyslexics, since reading also involves dual cognitive processing. In reading, dyslexics may predominantly use a spatial, holistic cognitive strategy and ignore or ineffectively use a phonetic, analytic strategy; such a cognitive strategy bias may be a disadvantage in learning to read. There is evidence compatible with these suggestions. Poor readers appear to make phonetic rather than optical errors (*19*). Children with marked difficulty in learning to read English readily learned to read (that is, associate with English words) Chinese logographs (*20*), which depend on visual, holistic processing and not on phonetic, analytic decoding. However, studies with normal children suggest that phonetic encoding facilitates reading progress (*21*). From the opposite perspective, poor spatial ability is not necessarily associated with reading difficulty.

Individuals with Turner's syndrome (XO karyotype) have well-documented specific deficits in spatial processing but have normal reading ability [reported for the English language, which is phonetically coded (*22*)]. Females, who are generally less proficient on spatial tasks than most men (*23*), have a much lower incidence of reading difficulty (*1*). It has not yet been determined whether reverse observations hold for the reading of ideographic languages.

Thus, at the neural level, developmental dyslexia may be associated with bilateral processing of spatial functions and with deficient left-hemisphere processing of linguistic functions. The left hemisphere may not execute its specialized functions well, but it is not necessarily inactive or ineffectual; it may engage in right-hemisphere types of cognitive processing. This raises the possibility that in dyslexics the left hemisphere does not have focal but, instead, has the right-hemisphere type of diffuse neural organization in terms of Semmes' (*24*) hypothesis of the nature of hemisphere specialization. Moreover, the right hemisphere also seems to be well equipped for spatial processing. This neural substrate may result in the cognitive profile, at least in the majority of dyslexic boys (*25*), of intact and overused spatial, holistic processing combined with deficient linguistic, sequential processing. This pattern of cognitive skills may lead to an inefficient and limited strategy for the reading of phonetically coded orthographies.

The dyslexics were able to perform as well as the normal boys on the dichhaptic letters test in spite of their apparent use of different cognitive strategies. This test is similar to reading in that both necessarily involve both cognitive processes. The good performance of the dyslexics on the dichhaptic letters test suggests that it may be possible to design an approach to reading that elicits an optimum balance between linguistic processing (the phonetic approach) and spatial processing ("look-say" method) which may allow dyslexics to progress in reading. Such an approach, however, would be constrained by the requirements of reading English orthography and the cognitive capacities of dyslexics.

In view of the possible existence of right-hemisphere specialization for spatial processing in normal boys of at least 6 years of age (*10*), and in view of the extensive data indicating the presence of many aspects of hemisphere specialization at birth or in the first few years of life (*26*), the evidence for bi-hemisphere representation of spatial functions in dyslexics until at least age 14 supports a theory of a qualitative neural deficit rather than a neural maturational lag (*27*).

I have previously hypothesized that normal girls have bilateral representation of spatial functions (*10*), yet they exhibit no reading difficulty. This is not necessarily paradoxical. If the brain is a sex organ, then what may be satisfactory for one sex may not be for the other. Moreover, dyslexic boys, unlike normal girls, may have a deficient left hemisphere. Sexual dimorphism in neural organization (*10*) plus the relatively lower incidence of dyslexia in females than males (*1, 12*) suggest that the neural substrate of dyslexia in females may be different from that in males. There is some evidence to support this (*28*).

In the present work, I have made no direct study of cognitive deficits of dyslexia. I investigated neural factors in dyslexia and, on the basis of hypothesized neural correlates, predicted a cognitive profile of deficits and biases, which appears to be consistent with other research. Such neural hypotheses allow for further more specific predictions of cognitive deficits in dyslexia, which might not be considered without this neurological framework associated with a large body of knowledge of brain-behavior relationships (*29*).

It may now be possible to define and relabel the disorder of developmental dyslexia more precisely. The syndrome is not so much a specific deficit in reading (as many clinicians well know, since speech, spelling, fine motor coordination, among others are often also deficient) but, rather, a "specific *cognitive* deficit." Different subgroups may have different patterns of cognitive deficits and biases (*30*). If the reading of any orthography depends on the particular cognitive functions that are impaired in the individual, only then will the disorder become manifest with reading difficulty as part of the syndrome.

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