Neuroanatomical Evidence of Dyslexia (III): A Review of Brain Potential and Post Motem Studies

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EP/ERP Studies

Evoked potential (EP) and event related potential (ERP) are methods to examine electrophysiological activities of the brain. One of the advantages of the EP/ERP is that we can examine on-going brain activities to a certain stimulus. They are also risk-free, relatively low cost techniques, so it is possible to examine larger group of subjects as compared with the methods discussed previously. One of the limitations of the techniques is the limitation of the localizability of activities. Another limitation is that the interpretation of a specific wave is not clear. Even for a very consistent wave component such as P300, we can only speculate the meaning of the wave.

The EP/ERP studies are classified in several ways. One is a focus of the components of the wave. Earlier part of the wave, 0 to about 250 ms post on-set, is called exogenous wave, which reflects the sensory/perceptual process. Each component of the wave is associated with one of the stages of sensory processes. EP studies focus on this process, and researchers use this technique to investigate if the sensory/perceptual processes of their subjects is intact. Later part of the wave is called endogenous wave and associated with cognitive processes. ERP studies usually focus on this component, and various cognitive tasks have been employed to elicit the wave. Interpretation of the components of the wave is somewhat ambiguous, but there are some components such as P300 and N400 that are replicated consistently. EP/ERP studies are also classified by the types of stimuli such as auditory and visual EP/ERP.

Earlier Components of the Wave

Dool, Stelmack, and Rourke (1993) summarized earlier EP/ERP studies on exogenous wave and concluded that the wave forms of the LD and control groups are not qualitatively different, and the group differences were found as slight differences of amplitude and latencies. Not many studies focused on earlier components among recent studies reviewed here. Normal subjects showed L > R asymmetry for N1 in the temporal area (Brunswick & Rippon, 1994) and P110 in the occipital area (Brandeis, Vitacco, &

This is the concluding part of this series of review articles. The text related to Tables 1 and 2 is shown in the second part of this series of review articles appeared in the previous issue of this journal.

Steinhausen, 1994), whereas these asymmetries are absent in the dyslexic group. These results in conjunction with those of earlier studies suggest that individuals with dyslexia have some sensory/perceptual dysfunctions especially in the left hemisphere.

Later Components of the Wave-P300

Although earlier studies focused on sensory or exogenous components of the wave, recent researchers shifted their focus to later endogenous components of the wave. P300 is considered a good index of attention and processing speed (Pritchard, 1981). Although some studies showed smaller amplitude and longer latency among dyslexics, there are also studies which failed to find this difference (reviewed in Dool, Stelmack, & Rourke, 1993 ; Duncan, Rumsey, Wilkniss, Denkla, Hamburger, & Odou-Potkin, 1994).

Types of the task may be one of the reasons of the inconsistency. Language tasks tend to yield L > R asymmetry among normals and non-verbal tasks yield opposite asymmetry. subjects with dyslexia showed lack of these asymmetry or reversed asymmetry in some studies (Segalowitz, Wagner, & Menna, 1992 ; Mazzotta & Gasllai, 1992), but some studies report the same asymmetry (or symmetry) pattern across groups (Taylor & Keenan, 1990). These inconsistency may be stemmed from task difficulty and heterogeneity of dyslexic groups (Duncan, et al., 1994). For example, Duncan, et al. (1994) replicated the lower amplitude on P300 and lack of L < R asymmetry in dyslexic group. However, this result is only found in the group with dyslexia and high ADHD tendency during childhood, but not in dyslexia without ADHD.

Later Components of the Wave-N400

N400 is a negative wave that is elicited by a semantically incongruent word in the ending of a sentence (Kutas, & Hillyard, 1980). Amplitude of this wave is reduced in subjects with dyslexia, suggesting attenuated semantic processing as well as sensory/perceptual deficit among subjects with dyslexia (Brandeis, Vitacco, & Steinhausen, 1994).

Late negative waves elicited by other types of task have also been reported. For example, Stelmack and Miles (1990) studied a late negative wave with a peak latency of about 450 ms (N450) elicited by a recognition memory task. This negative wave is reduced if a target word is preceded by a semantically related picture (prime) among normal subjects, but this priming effect was smaller in dyslexic group. They divided the dyslexic group into three subgroups [reading and spelling impaired (RS) ; reading, spelling, and arithmetic impaired (RSA) ; and arithmetic impaired (A)] and compared the priming effects of word and picture prime (Miles, & Stelmack, 1994). They found that the picture prime could not reduce N450 in the groups of RSA and A, and word prime could not reduce N450 in the groups of RSA and RS. This result suggests that there is a picture processing deficit in group A, word processing deficit in group RS, and both processings are attenuated in RSA.

EP/ERP Study and Other Techniques

In sum, EP/ERP studies have provided the evidence that there are differences between dyslexic and normal groups in their electrophysiological activities of the brain. However, the meaning of such differences is not necessarily clear, because the meaning of each component (especially the later part) is not fully understood. How can we use the information then?

Combination of EP/ERP technique and other techniques will be a promising method to examine the characteristics of the dyslexic brain. For example, Wood, Flowers, Buchsbaum, and Tallal (1991) measured rCBF while collecting ERP. Converging results from different methods are more reliable and they allow researchers to make conclusions with more certainty.

Post Motem Studies

Post motem study is the only way to examine cytoarchitectonical abnormality and the exact measurement of each structure. Because of the limited availability of the samples, it is difficult to find large homogeneous samples and a well matched control group. Also, behavioral measures are usually obtained long before the examination, and they are not always the same across samples. Thus, generalizability of the results are limited. Earlier studies are comprehensively reviewed in Hynd and Semrud-Clikeman (1989), and Hynd, Marshall, and Gonzalez (1991), only two studies have been reported since 1991.

These studies focused on specific structures, that is, lateral geniculate nucleus (LGN) and medial geniculate nucleus (MGN). Since the focus of these studies is specific to the abnormality of the magnocellular system, the results are reviewed in conjunction with the ones from EP/ERP studies in the next section.

Deficit in Magnocellular System in Dyslexia

Magnocellular Defect in Visual System

There are some studies specifically designed to test the hypothesis that individuals with dyslexia have deficit in the visual pathway which is responsible for the temporal processing, namely, magnocellular system. Converging evidence in different experimental paradigm such as flicker contrast sensitivity, metacontrast masking, and motion detection supports this hypothesis (reviewed in Stein, 1994). EP studies showed that flickering low spatial frequency, low contrast stimuli increase latency and/or reduce the amplitude of the wave (Lehmkuhle, Garzia, Turner, Hash, & Baro, 1993; Livingstone, Rosen, Drislane, & Galaburda, 1991; Maddock, Richardson, Stein, 1992).

Livingstone, et al. (1991) added another consistent piece of evidence with post motem

study. They examined lateral geniculate nucleus (LGN) and found that magnocellular layers areas are significantly smaller in dyslexics than in normals. Neurons in the area are disorganized and cell bodies of neurons are smaller in the sample of the subjects with dislexia.

Magnocellular Defect in Auditory System

A similar abnormality found in visual system was also found in auditory system. Galaburda, Menard, and Rosen (1994) showed that the left medial geniculate nuclei (MGN) in brains of subjects with dyslexia contained fewer large neurons than normal brains. This group difference was not found in the right MGN. This result suggests auditory temporal processing deficit in the left hemisphere among subjects with dyslexia, which is assumed to be related to phonological deficit among individuals with dyslexia.

Magnocellular Deficits and Dyslexia

As reviewed in this section, research findings regarding magnocellular deficit seem highly consistent across studies. These results are also consistent with other abnormalities related to left hemisphere in dyslexia, because the left hemisphere receives more magnocellular input than the right, from both the auditory and visual systems (Stein, 1994). Thus, it is very likely that both hemispheric abnormality and magnocellular deficits share the same cause. The cause of this deficit is not known. Stein (1994) speculated the autoimmune attack in utero is a cause of the abnormality.

Conclusions

Neurophysiological and Anatomical Basis of Dyslexia

In spite of the development of the technology, better description of the subject groups, and carefully matched control groups, the results reported during the past 6 years are still far from converging. At this point, there is some convergent evidence from different techniques which suggest lack of left hemisphere lateralization of language function at least in some subtypes of dyslexia. Magnocellular deficit is probably the most consistent finding in the research field of dyslexia. Most of the other findings need further replication.

Neurological mechanisms underlying dyslexia may be hypothesized in several ways. Abnormalities of dyslexic brain may not be limited to a specific structure but a combination of many abnormal structures or abnormal networkings. This assumption is supported by the fact that normal and dyslexic group differences are found in almost everywhere in the brain in EP/ERP and rCBF studies. Also, autopsy studies revealed that cytoarchitectonic abnormalities spread out the most surface areas of the dyslexic brain. These multiple abnormalities can be independent or related each other.

Three Models of the Relationship Among Multiple Abnormalities

I propose three hypothetical models that can explain the formation of the multiple abnormalities.

The first model is that there is a common genetical or acquired cause that yields a combination of several anatomical, functional abnormalities, which results in a specific reading problem. High correlation among several abnormality will support this model.

The second model is that there are several independent anatomical, functional abnormalities which cause similar behavioral symptoms. either one (or more than one) of the abnormalities can result in dyslexia. If the correlation among the multiple abnormalities is low, several independent causes should underly the behavioral indicators of dyslexia. Inconsistency of the results may be explained by this model.

The final model is a combination of the first two models. There are several genetical or acquired causes exist, each of which causes several anatomical, functional abnormalities. Different sources produce different combinations of functional anatomical abnormalities. These different patterns of abnormalities share some common behavioral manifestation (e.g., reading-IQ discrepancy), but also create some unique characteristics of behavior. Thus, when we select subjects with dyslexia using a criterion such as IQ-reading discrepancy, the group is heterogeneous in terms of behavioral and anatomical characteristics that it yields inconsistent results.

Recommendations

We do not know the real nature of individuals with dyslexia, but there are some ways to make the studies more informative. First, combination of two or more different techniques will make the data from each method more meaningful and reliable. Second, breaking a dyslexic group down into more homogeneous subtypes will yield more consistent results. Traditional diagnostic process may not be enough to produce homogeneous groups. More specific cognitive abilities should be taken into consideration for the classification of dyslexia.

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Table 1 Summary of the Characteristics of the Subjects in Functional Imaging Studies

	diagnostic criteria	exclusion of subjects	other neurological disorder	selection of control		N (m / f)	Age	Handednes:	IQ	Reading
Flowers, et al. 1991	Subjects who were referred to Orton Reading Center when they were a child. Reading Quatient ≤ 82 reading disabled, > 91 nondisabled, others are borrderlin	major psychopathological conditions, hearing or other sensory impairment, and chronic pulmonary dysfunction		no reading remediation or repeated grades	Measures			self-report	WAIS, WISC	Task accuracy
					Dyslexia	83 (72/11) (a) RD (33), (b) border-line (27). (c) non-disabled (23)	(a) 33.8, (b) 33.8, (c) 32.2	LH 7, ambi-dextrous 6	(a) FSIQ 96.0, VIQ 94.5,	
					Control	69 (39/30)	29.8	all RH		
Gross-Glenn, et al. 1991	childhood history of reading and spelling problem, severe enough to warrant remedial treatment, normal intelligence	no neurological, sensoryor psychiatric disorder	No	no history of the problems mentioned above	Measures			EHI	WAIS-R	(a) GORT, (b) WRAT-S
					Dyslexia	11 (11/0)	30.3	all RH	FSIQ 113.6, VIQ 112.3, PIQ 111.0	(a) 9.5, (b) 6.9
					Control	14 (14/0)	27.6	all RH	NR	(a) 12, (b) NR
Hagman, et al. 1992	IQ-reading discrepansy 2SD	NR		age, sex, handedness matched	Measures			NR	WAIS (?)	WRAT, GORT
					Dyslexia	10 (9/1)	33	LH 1	VIQ 96, PIQ 103	
					Control	10 (9/1)	34	LH 1	VIQ 106, PIQ 106	

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	diagnostic criteria	exclusion of subjects	other neurological disorder	selection of control	N (m / f)	Age	Handednes:	IQ	Reading
Rumsey, et al. 1994	VIQ or PIQ ≥ 89, meet DSM-III-R criteria for developmental reading disorder, *Finucci criteria for* severe dyslexia in adults	poor educational opportunities, non-English or bilingual backgrounds, neurologic disease or seizures, head injury, severe *psychiatric disorder, chronic* substance abuse, uncorrected visual or hearing impairment	ADHD during childhood (2)	age, sex, handedness, FSIQ, educational level, *matched*	Measures		PNESS (%)	WAIS-R	(a) WRAT-R, (b) WRAT-S, (c) WRAT-M, (d) GORT, (e) GFW-RS
					Dyslexia	15 (14/0) 27	96	FSIQ 105, VIQ 101, PIO 111	(a) 80, (b) 66, (c) 86, (d) 5.3, (e) 39
					Control	18 (14/0) 26	98	FSIQ 115, VIQ 114, PIQ 113	(a) 110, (b) 107, (c) 109, (d) 12, (e) 49.5
Rumsey, et al. 1994	VIQ or PIQ ≥ 89, meet DSM-III-R criteria for developmental reading disorder, Finucci criteria for severe dyslexia in adults	poor educational opportunities, non-English or bilingual backgrounds, neurologic disease or seizures, head injury, severe psychiatric disorder, chronic substance abuse, uncorrected visual or hearing impairment	ADHD during childhood (2)	age, sex, handedness, FSIQ, educational level, matched	Measures		PNESS (%)	WAIS-R	(a) WRAT-R, (b) WRAT-S, (c) WRAT-M, (d) GORT, (e) GFW-RS
					Dyslexia	15 (15/0) 27	96	FSIQ 105, VIQ 101, PIO 111	(a) 80, (b) 66, (c) 86, (d) 8, (e) 39
					Control	20 (20/0) 26	98	FSIQ 116, VIQ 115, PIQ 114	(a) 110, (b) 108, (c) 109, (d) 12, (e) 50
Rumsey, et al. 1992	VIQ or PIQ ≥ 89, meet DSM-III-R criteria for developmental reading disorder, Finucci criteria for severe dyslexia in adults	poor educational opportunities, non-English or bilingual backgrounds, neurologic disease or seizures, head injury, severe psychiatric disorder, chronic substance abuse, uncorrected visual or hearing impairment	hyperactive during childhood (1)	age, sex, handedness, FSIQ, educational level, matched	Measures		PNESS (%)	WAIS	(a) WRAT-R, (b) WRAT-S, (c) WRAT-M, (d) GORT, (e) GFW-RS
					Dyslexia	14 (14/0) 27	96	FSIQ 105, VIQ 102, PIO 110	(a) 81, (b) 67, (c) 86, (d) 5, (e) 39
					Control	14 (14/0) 26	99	FSIQ 111, VIQ 110, PIQ 110	(a) 109, (b) 106, (c) 103, (d) 12, (e) 51
Wood et al. 1991	a subset of subjects from Flowers, et al. (1991)	NR		a subset of subjects from Flowers, et al. (1991)	Measures		NR	NR	NR
					Dyslexia	18 (18/0) NR	NR	NR	
					Control	29 (29/0) NR	NR		

Table 2 Summary of the Results in Functional Imaging Studies

	Technique	linguistic measure	Result (Activation Pattern)	Relation between reading and blood flow
Flowers, et al. 1991	rCBF with xenon inhalation techinque (133Xe) (Novo Cerebrograph 32 system)	spelling analysis (finger lift response to four-letter words)	normal: activation in L temporal site; dyslexia: activation in L posterior temporoparietal region	normal: accuracy of the task was related to Wernicke's area; dyslexia: childhood reading ability correlates with activation in posterior temporoparietal region
Gross-Glenn, et al. 1991	rCMRglc with PET (PET V scanner)	word reading (read aloud a word per 5 sec.)	prefrontal region: group x hemisphere interaction (normal L << R, dislexia L < R); lingual region: dislexia (L < R) > normal (L > R)	
Hagman, et al. 1992	F-fluorodepoxy-2-glucose uptake with PET (NeuroEcat)	Auditory version of CPT (phoneme detection)	higher metabolic rates in medial temporal region in dyslexia; no group difference in lateral area	
Rumsey, et al. 1994	rCBF (^{15}O-labeled water) with PET (Scanditronix positron emission tomograph scanner)	tonal memory task (decide if the sequences in a pair are identical)	(a) R middle temporal region: dyslexia (±) < normal (++); R frontal region: dyslexia (±) < normal (++)	

Table 2 Summary of the Results in Functional Imaging Studies

	Technique	linguistic *measure*	Result (Activation Pattern)	Relation between reading and blood flow
Rumsey, et al. 1994	rCBF (^{15}O-labeled water) with PET (Scanditronix positron emission tomograph scanner)	syntax task (dicide if paired sentences have the same meaning)	Rest: dyslexia showed reduced blood flow in L parietal region; Syntactic Task: normal activation of L middle to anterior temporal and inferior frontal cortex in both groups	
Rumsey, et al. 1992	rCBF (^{15}O-labeled water) with PET (Scanditronix positron emission tomograph scanner)	(a) rhyme detection, (b) auditory attention task (detection of target tone)	(a) L temporoparietal regions (near the angular gyrus): dyslexia (±) < normal (++); L anterior temporal region: dyslexia (++) > normal (±); R temporal region: dyslexia (++) > normal (±); (b) L anterior temporal region: dyslexia (++) > normal (±)	(a) dislexia: VIQ and L parietal activation (r=.53); VIQ-PIQ descrepancy (r=-.47); Digit span and R middle temporal activation; (b) dislexia: VIQ and L anterior temporal activation (r=-.63)
Wood et al. 1991	rCBF with xenon inhalation techinque (133Xe) (Novo Cerebrograph 32 system)	Auditory version of CPT (phoneme detection)	NR	normal: accuracy of the task was related to lower flow at the L superior temporal site; dyslexia: accuracy of the task was related to the greater L temporal activation

Note.
ADD = Attention Deficit Disorder without hyper activity, *ADHD* = Attention Deficit Disorder with Hyper activity, *AEP* = Auditory Evoked Potential, *AHQ* = Annett Handedness Questionnaire, *BAS-WRT* = British Ability Scale Word Reading Test, *CC* = Corpus Callosum, *CNV* = Contingent Negative Variation, *CPT* = Continuous Performance Task, *DSM-III-R* = Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition , *EHI* = Edinburgh Handedness Inventory, *ERP* = Event Related Potential, *FSIQ* = Full Scale IQ, *GFW-RS* = Goldman-Fristoe-Woodcock Reading of Symbols (non-words), *GORT* = Gray Oral Reading Test, *LAC* = Lindamood Auditory Conceptualization Test, *MGN* = Medial Geniculate Necleus, *MR* = Mental Retardation, *MRI* = Magnetic Resonace Imaging, *NPRE* = Nonsense Passage Reading Error, *NPRT* = Nonsense Passage Reading Time, *NR* = Not Reported, *OHI* = Oldfield Handedness Inventory, *PINV* = Post Imperative Negative Variation, *PIQ* = Performance IQ, *PNES* = Physical and Neurological Examination for Subtle signs, *PT* = Planum Temporale, *RD* = reading dificulties, reading disabilities, ROI = Region of Interest, VEP = Visual Evoked Potential, *VIQ* = Verbal IQ, *WAIS* = Wechsler Adult Intelligence Scale, *WISC* = Wechsler Intelligence Scale for Children, *WJL* = Woodcock-Johnson Letter-Word Identification, *WJP* = Woodcock-Johnson Passage Comprehension, *WJR* = Woodcock-Johnson Reading Cluster, *WJW* = Woodcock-Johnson Word Attack, *WRAT-M* = Wide Range Achievement Test Revised, Math, *WRAT-R* = Wide Range Achievement Test Revised, Reading, *WRAT-S* = Wide Range Achievement Test Revised, Spelling, *WRAT* = Wide Range Achievement Test, *WRMT-PC* = Woodcook Reading Mastery Test-Revised, Passage Comprehension, *WRMT-T* = Woodcook Reading Mastery Test-Revised, WRMT-WA = Woodcook Reading Mastery Test-Revised, Word Attack

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