Autism and Unfavorable Left-Right Asymmetries of the Brain¹

Daniel B. Hier, Marjorie LeMay, and Peter B. Rosenberger²

Massachusetts General Hospital and Harvard Medical School

Utilizing computerized brain tomography, left-right morphologic asymmetries of the parietooccipital region were judged in 16 autistic patients, 44 mentally retarded patients, and 100 miscellaneous neurological patients. In 57% of the autistic patients the right parietooccipital region was wider than the left, while this pattern of cerebral asymmetry was found in only 23% of the mentally retarded patients and 25% of the neurological patients. It is suggested that unfavorable morphologic asymmetries of the brain near the posterior language zone may contribute to the difficulties autistic children experience in acquiring language.

INTRODUCTION

Although superficial inspection of the brain suggests that the cerebral hemispheres are exact mirror images, detailed examination reveals numerous left-right morphologic asymmetries (Blinkov & Glezer, 1968). Geschwind and Levitsky (1968) have drawn particular attention to left-right asymmetries in the vicinity of the posterior language zone. In from 60 to 90% of brains the left temporal plane is larger than the right. Only about 10% of brains show a reversed morphologic asymmetry with the right temporal plane larger than the left (Geschwind & Levitsky, 1968;

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²Address all correspondence to Dr. Peter B. Rosenberger, Massachusetts General Hospital, Boston, Massachusetts 02114.

Witelson & Pallie, 1973; Wada, Clarke, & Hamm, 1975). Morphologic asymmetries of the temporal planes cannot currently be judged during life. LeMay (1976, 1977) has utilized computerized brain tomography to demonstrate radiologically morphologic asymmetries of the parietooccipital region near the posterior language zone. She found that the left parietooccipital region is generally wider than the right with approximately 9% of dextrals and 27% of sinistrals showing a reversal of this asymmetry.

The full significance of these morphologic asymmetries is unknown. It has been suggested that morphologic asymmetries favoring the left posterior region of the brain may underlie left hemisphere dominance for language (Galaburda, LeMay, Kemper, & Geschwind, 1978). Since aberrant language acquisition is one of the cardinal features of infantile autism (Rutter, 1972; Churchill, 1972), we have used computerized brain tomography to study morphologic asymmetries of the cerebral hemispheres near the posterior language zone in 16 autistic patients.

METHODS

Autistic Patients

The 16 autistic patients in this study met three major diagnostic criteria: social aloofness, delayed language acquisition, and onset of abnormalities before 2 years of age. Additional autistic features present in many of the patients included gaze aversion, resistance to change, bizarre and ritualistic behaviors, preoccupation with objects, and atypical responses to sensory input (Table I). The mean age of the autistic patients was 14 ± 7 years. All but three were male. Nine of the autistic patients were righthanded, two were left-handed, and five were of indeterminate handedness. They were further characterized by the following features: delayed motor milestones (6/16), seizures (5/16), abnormal electroencephalogram (7/16), preserved nonverbal intelligence (3/16), a history of perinatal complications (10/16), and self-injury (4/16). Patients 14 and 15 are siblings, patient 9 has an autistic brother, patients 3, 8, and 16 have family histories of developmental dyslexia, and patients 1 and 10 have family histories of mental retardation.

Mentally Retarded Control Group

Forty-four mentally retarded patients served as one control group. All of these patients had undergone computerized brain tomography to eval-

	Atypical response	to sound	1	1	+	1	I	ı	1	I	1	1	1	I	1	+	+	+
avioral Characteristics of the 16 Autistic Patients	Preoccupation	with objects	+	+	÷	+	1	1	+	+	+	÷	1	l	+	+	+	+
	Resistance	to change	1	÷	÷	I	÷	I	÷	+	I	÷	1	I	÷	÷	÷	+
	Ritualistic	behavior	I	+	+	+	+	+	÷	Ι	+	+	+	÷	ţ	+	+	+
	Gaze	aversion	÷	+	+	+	+	+	+	t	+	+	÷	+	÷	+	÷	+
	Delayed	speech	+	+	÷	+	+	+	+	+	+	+	+	+	÷	+	+	+
Table I. Beh	Social	aloofness	+	+	+	÷	+	+	+	+	+	+	+	÷	+	+	+	+
	Handed-	ness	D I a	L	R	L	I	R	R	R	R	R	R	I	R	R	Я	I
		Age/sex	7/F	7/F	17/F	9/M	25/M	15/M	21/M	6/M	M/6	24/M	M/6	27/M	16/M	15/M	16/M	4/M
		No.	Ţ	6	n	4	S	9	7	8	6	10	11	12	13	14	15	16

a Abbreviations: R = right; L = left; I = indeterminate; + = present; - = absent.

uate moderate to severe mental retardation. None of these patients met the diagnostic criteria for autism as described above.

Neurological Patient Control Group

A second control group was made up of 100 consecutive neurological patients without space-occupying lesions who underwent computerized brain tomography for a variety of indications.

Assessment of Cerebral Asymmetry

Cerebral asymmetry was judged by examination of the computerized brain tomograms of the 16 autistic patients, the 44 mentally retarded patients, and the 100 neurological patients. Horizontal sections of the brain were examined on self-developing pictures (Polaroid), which showed the brain reduced in size by a factor of 3.3 times. Using either the falx or the interhemispheric fissures as a midline structure, the widths of the posterior parietooccipital regions were measured at a point approximately 5 mm anterior to the inner table of the vault (Figure 1). Brains were classified as wider in the left parietooccipital region if the left measurement exceeded the right by 1 mm or more, wider in the right parietooccipital region if the right measurement exceeded the left by 1 mm or more, and equal in the parietooccipital regions if the two measurements were within 1 mm of each other.

Statistical Methods

The χ^2 test was used to ascertain the level of statistical significance.

RESULTS AND DISCUSSION

None of the computerized brain tomograms of the 16 autistic patients revealed evidence of focal or diffuse brain injury.

As shown in Table II, a majority of the mentally retarded patients (59%) and the miscellaneous neurological patients (57%) had a left parietooccipital region wider than the right. In contrast, only a minority of the autistic patients exhibited this usual pattern of cerebral asymmetry. Nine of the 16 autistic patients (57%) had a reversed pattern of cerebral asymmetry (right parietooccipital region wider than left), whereas only 23% of the mentally retarded patients and 25% of the neurological patients had a reversed pattern of cerebral asymmetry (difference significant, p < .05).



Fig. 1. Computerized brain tomogram of autistic patient No. 4. The brain is shown in horizontal section with the frontal horns of lateral ventricles anteriorly and the occipital horns posteriorly. The white arrows indicate the interhemispheric fissure in the posterior parieto-occipital region. The tomogram illustrates the reversed cerebral asymmetry pattern (right parietooccipital region wider than left) found in 9 of the 16 autistic patients. A reciprocal structural asymmetry exists in the frontal region so that the left frontal region is wider than the right (see Results section).

Since infantile autism is rare (occurring in .01 to .05% of children) and reversed cerebral asymmetry of the parietooccipital region is common (occurring in 10 to 25% of miscellaneous neurological patients), a reversal of cerebral asymmetry cannot be considered directly causative of infantile autism. On the other hand, the observation that a reversal of the usual morphologic asymmetry of the parietooccipital region occurs with greater frequency in autistic patients than in either mentally retarded or miscella-

	L > R	L = R	R > L
Autistic group $(N = 16)$	5	2	9
Mentally retarded group $(N = 44)$	26	8	10
Neurological patients $(N = 100)$	57	18	25

 Table II. Patterns of Cerebral Asymmetry of the Parietooccipital Region

neous neurological patients suggests this reversal may be a risk factor in autism. In this respect, reversed cerebral asymmetry may be similar to male sex (Treffert, 1970), a family history of delayed speech (Bartak, Rutter, & Cox, 1975), perinatal complications (Knoblock & Pasamanick, 1975), an abnormal electroencephalogram (Small, Milstein, DeMyer, & Moore, 1977), and cerebral damage (Hauser, DeLong, & Rosman, 1975; Aarkrog, 1967), all of which serve as risk factors for autism.

A reversal of the usual left-right morphologic asymmetry of the parietooccipital region may be particularly relevant to the delayed language acquisition (Rutter, 1972; Churchill, 1972) and verbal disability (Bartak et al., 1975) that regularly accompany infantile autism. If the left hemisphere is indeed anatomically specialized to acquire language (Galaburda, LeMay, Kemper, & Geschwind, 1978; Galaburda, Sanides, & Geschwind, 1978), then a reversal of the usual left-right asymmetry of the brain near the posterior language zone might leave the left hemisphere anatomically illsuited to subserve language functions. A mismatching between functional asymmetries of brain (the left hemisphere remaining dominant for language) and morphologic asymmetries (the right parietooccipital region larger than the left) might produce circumstances particularly unfavorable for language acquisition. We have previously noted that a reversal of the usual left-right morphologic asymmetry of the parietooccipital region is more common in children with developmental dyslexia (Hier, LeMay, Rosenberger, & Perlo, 1978), supporting the suggestion that unfavorable asymmetries may in fact be associated with a greater risk of experiencing difficulties in language acquisition. Further, the dyslexic children with a reversed pattern of cerebral asymmetry of the parietooccipital region were noted to have lower verbal IQs and were more likely to experience delayed speech acquisition than the dyslexic children with the more usual pattern of cerebral asymmetry.

Reversal of the usual left-right asymmetry of the parietooccipital region appears to be more prevalent among autistic and dyslexic children than among the general population of neurologic patients. Both autism and

dyslexia are characterized by abnormal language development as well as verbal disability (Bartak et al., 1975; Warrington, 1967). A reversal of the usual left-right asymmetry of the parietooccipital may put some children at added risk to experience left hemisphere dysfunction for the acquisition of language.

REFERENCES

- Aarkrog, T. Organic factors in infantile psychoses and borderline psychoses. Danish Medical Bulletin, 1967, 15, 283-288.
- Bartak, L., Rutter, M., & Cox, A. A comparative study of infantile autism and specific developmental receptive language disorder: I. The children. *British Journal of Psychiatry*, 1975, 126, 127-145.
- Blinkov, S. M., & Glezer, I. I. The human brain in figures and tables. New York: Basic Books, 1968.
- Churchill, D. W. The relation of infantile autism and early schizophrenia to developmental language disorders of childhood. *Journal of Autism and Childhood Schizophrenia*, 1972, 2, 182-197.
- Galaburda, A. M., LeMay, M., Kemper, T. L., & Geschwind, N. Right-left asymmetries in the brain. *Science*, 1978, 199, 852-856.
- Galaburda, A. M., Sanides, F., & Geschwind, N. Human brain: Cytoarchitectonic left-right asymmetries in the temporal speech region. Archives of Neurology, 1978, 35, 812-817.
- Geschwind, N., & Levitsky, W. Human brain: Left-right asymmetries in temporal speech region. Science, 1968, 161, 186-187.
- Hauser, S. L., DeLong, G. R., & Rosman, N. P. Pneumographic findings in the infantile autism syndrome. *Brain*, 1975, 98, 667-688.
- Hier, D. B., LeMay, M., Rosenberger, P. B., & Perlo, V. P. Developmental dyslexia: Evidence for a subgroup with a reversal of cerebral asymmetry. *Archives of Neurology*, 1978, 35, 90-92.
- Knobloch, H., & Pasamanick, B. Some etiologic and prognostic factors in early infantile autism and psychosis. *Pediatrics*, 1975, 55, 182-191.
- LeMay, M. Morphological cerebral asymmetries of modern man, fossil man, and nonhuman primates. Annals of New York Academy of Sciences, 1976, 280, 349-366.
- LeMay, M. Asymmetries of the skull and handedness: Phrenology revisited. Journal of Neurological Sciences, 1977, 32, 243-253.
- Rutter, M. Childhood schizophrenia reconsidered. Journal of Autism and Childhood Schizophrenia, 1972, 2, 315-337.
- Small, J. G., Milstein, V., DeMyer, M. K., & Moore, J. E. Electroencephalographic (EEG) and clinical studies of early infantile autism. *Clinical Electroencephalography*, 1977, 8, 26-35.
- Treffert, D. A. Epidemiology of infantile autism. Archives of General Psychiatry, 1970, 22, 431-438.
- Wada, J. A., Clarke, R., & Hamm, A. Cerebral hemispheric asymmetry in humans: Cortical speech zones in 100 adult and 100 infant brains. Archives of Neurology, 1975, 32, 239-246.
- Warrington, E. K. The incidence of verbal disability associated with reading retardation. Neuropsychologia, 1967, 5, 175-179.
- Witelson, S. F., & Pallie, W. Left hemisphere specialization for language in the newborn: Neuroanatomical evidence of asymmetry. *Brain*, 1973, *96*, 641-646.