

New Directions in the Neurobiological Research of Infantile Autism (II): Laterality and Changing Views on Neurophysiological Mechanisms

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Introduction

Once, infantile autism was considered a primary psychopathological disease of emotional involvement and social communicative deficits in the family environment (Kanner, 1943, 1944; Bettelheim, 1959, 1967). It was hypothesized that this disorder with affective contact primarily contributes to the disturbances of social relating and communication in unusual families. However, most psychopathological investigation could not provide clear evidence of parental characteristics of abnormal interactions with autistic children. About 30 years ago, B. Rimland (1964) and E. M. Ornitz et al. (1965a, 1965b) presented the earliest detailed hypothesis that autism is not primarily a disorder of psychopathological origin, but rather neurophysiological or neurobiological origin in human brain functioning. Since that time, although many neurobiological investigations have tried to find the etiological factors and biological markers in autistic syndrome, we still have little understanding of interaction between the unique behavioral abnormalities and the neurobiological factors. However, more recent work which included study of genetics, neurotransmitter, brain evoked potentials, and the use of positron emission tomography (PET), magnetic resonance imaging (MRI), and magnetoencephalography (MEG) might elucidate this enigmatic syndrome in the not-too-distant future (Campbell and Green, 1985; Courchesne et al., 1987, 1988, 1989, 1992; Rumsey, 1992; Ritvo et al., 1985, 1989, 1990; Hari, 1990; Naruse et al., 1987, 1992; Erwin et al., 1991; Tsai et al., 1992; Makela et al., 1994). Nowadays, autism cannot be considered one etiology with a single pathologic mechanism producing a specific set of symptoms, but it is associated with multiple etiologies, since there are numerous pathological conditions, each of which could potentially cause central nervous system (CNS) dysfunction.

This report mainly reviews the laterality research and the recently changing views on neurophysiological mechanisms in infantile autism, and presents new

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findings in recognizing the causes of autistic symptoms.

1. Language Disorders in Autism

It is well known that language skills (including inflectional, phonological, syntactic, morphological, grammatical, semantic and vocabulary) are always more severely impaired in autism than perceptual skills. There is now considerable support for the theory that a severe and global language deficit underlies autism, so that autism is considered to be primarily a disorder of language development. In particular, mean verbal IQ has been reported to be lower than mean performance IQ in most widely used IQ tests. G. Dowson et al. mentioned that the autistic child's relative strength in performing visuo-spatial tasks, identifying complex visual forms and patterns such as Block Design, Form Boards, and Object Assembly, might suggest relative right hemisphere intactness (Dowson et al., 1983, 1986, 1989). On the other hand, the particular pattern of language developmental disorders in autistic children may constitute the deficits of general abstractive, symbolic thought and cognitive functioning as major symptoms of early infantile autism. M. Rutter et al. have explicitly developed this position (Rutter et al., 1978, 1983), although the latter no longer espouses this hypothesis that autism is considered to be primarily a disorder of language and cognitive development (Hobson, 1986a, 1986b; Ornitz, 1983, 1992). The hypothesis in considering language deficits to be primary in autism should be rejected, because other language-impaired clinical patients, deaf, aphasic, and retarded children all suffer delayed language development, but they do not suffer from the symptoms that autistic children exhibit, and they can use and comprehend gesture in their attempts to communicate, unlike autistic children. Differentiation between primary and secondary etiological causes is important for the focus of treatment. The language deficits in autism are a secondary consequence of their corresponding lack of coordinated reference with other people and difficulty interpreting affective signals (Hobson, 1986a, 1986b).

2. Handedness in Autism

An increased incidence of left-handedness or mixed-handedness in autistic children has been cited as evidence for the hypothesis of left-hemisphere disorders in autism. Increased left-handedness is taken to indicate that insults to the left hemisphere have caused a switch in manual dominance from the injured left hemisphere (controlling the right hand) to the intact right hemisphere (controlling the left hand).

Normal children usually show inconsistent handedness until age 4, and

handedness shows a fluctuation course in early childhood. It has been reported that mixed hand preference might appear to be at a lower developmental level than the children with dominance established, and a lower score on cognitive tasks for these children might result, than children with established hand preference.

We investigated characteristics of handedness in autistic and age-matched mentally retarded children (Table 1), and analyzed the longitudinal data in evaluation (ten items: such as cutting with a scissors, throwing a ball, forefinger pointing, cutting with a knife, eating with a spoon, shoveling, unscrewing a bottle cap, tracing a circular figure, picking up small objects, and rubbing out with an eraser) concerned with left- or mixed-handedness versus established hand dominance (Table 2). We found that left-handedness or mixed-handedness is found more often in autistic children than in mentally retarded samples (Fig. 1), and autistics with established hand preference were older than autistic children with mixed-handedness according to the longitudinal data analysis. Although left- or mixed-handedness has an elevated frequency in autistic children compared with mentally retarded subjects, it is revealed only in younger autistic subjects (Fig. 1). There were no significant differences between the older two groups in degree or direction of hand dominance, although the autistic group showed a significantly greater variance in hand preference. This suggests that left- or mixed handedness in these samples can not be related to incidence of certain left hemisphere damage. It is difficult to draw conclusions based on a comparison of the two groups, because the finding indicates a developmental delay rather than left-hemispheric impairment.

Table 1. Test scores of handedness in autistic and mentally retarded children

Autistic subjects	Age	Vocabulary age *	Handedness quotient **
1. T. S.	(m) 6-10	2- 0	R 5
2. K. Y.	(m) 7- 7	2- 0	R 6
3. T. K.	(m) 7- 7	3- 8	R 7
4. #M. F.	(f) 7- 8	4- 5	R10
5. #T. S.	(m) 8- 5	3- 0	R 7
6. S. T.	(m) 8- 5	5-10 (IQ67)	L10
7. T. K.	(m) 8- 6	4- 0	R 6
8. S. S.	(m) 8- 7	5- 7	R 9
9. #I. S.	(m) 8-11	2- 8	L 3
10. S. T.	(f) 9- 4	6- 0 (IQ68)	L 7
11. M. I.	(f) 9- 5	2- 0 (IQ40)	R 4
12. #S. T.	(m) 9- 7	3-10	R 8
13. #H. I.	(m) 9- 8	7- 2 (IQ69)	R 7
14. #H. O.	(m) 9- 9	6- 7	L 6
15. K. H.	(m) 9-11	3-10 (IQ47)	R 5
16. #H. K.	(m)10- 3	3- 4	R 5

17. H. Y. (m)	10- 6	3- 0	L 2
18. Y. A. (m)	10- 6	6- 6 (IQ65)	R 6
19. M. N. (m)	10- 7	3-10 (IQ42)	R 6
20. H. Y. (m)	11- 4	2- 0	L 3
21. #H. N. (m)	11- 5	12- 0 (IQ92)	R 9

Average 9- 3 4- 4 (IQ61.3) 6.24

Mentally retarded	Age	Vocabulary age	Handedness quotient
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1. #M. C. (f)	6- 8	5- 6	R 8
2. M. O. (f)	7- 8	3- 8 (IQ55)	L 6
3. T. K. (m)	7-11	4- 4 (IQ70)	R10
4. Y. M. (f)	8- 3	4- 0 (IQ50)	R10
5. #M. O. (f)	8- 6	4- 0	L 8
6. M. Y. (f)	8- 9	4- 2 (IQ40)	R 1
7. H. I. (m)	8- 9	5- 7 (IQ69)	R 8
8. #Y. K. (f)	8-10	6- 0	R 8
9. #T. K. (m)	8-10	7- 6	R10
10. H. O. (m)	8-11	5- 7	R 9
11. #Y. M. (f)	9- 2	4- 2 (IQ60)	R10
12. H. K. (m)	9- 5	3-10	R 9
13. #M. Y. (f)	9- 7	3-10	R 8
14. K. S. (m)	10- 1	12- 0 (IQ72)	R 8
15. #K. O. (m)	10- 2	7- 4	R 7
16. A. N. (f)	10- 4	3-10 (IQ50)	R10
17. #C. T. (m)	11- 1	9- 8 (IQ73)	R 7
18. Y. K. (f)	11- 3	9- 8 (IQ74)	R 9
19. Y. K. (f)	12- 0	8- 9	R10
20. M. A. (m)	12- 3	5- 9	R 9

Average 9- 3 6- 1 (IQ61.3) 8.25

Table 2. Longitudinal handedness data in autistic and mentally retarded children

Autistic subjects	Age	Vocabulary age	Handedness quotient
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1. M. F. (f)	12- 8	6-10	R10
2. T. S. (m)	13- 5	3-10	R10
3. H. I. (m)	13- 8	12- 0	R 6
4. H. O. (m)	13- 9	7- 4	R 9
5. I. S. (m)	13-11	6- 1	R 9
6. H. K. (m)	14- 3	10-10	R10
7. S. T. (m)	14- 7	3- 8	R10
8. H. N. (m)	15- 5	12- 0 (IQ91)	R 9

Average 13- 8 7- 8 9.13

Mentally retarded	Age	Vocabulary age	Handedness quotient
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1. M. C. (f)	10-10	7-10	R 7
2. M. O. (f)	12- 8	5- 6 (IQ55)	R 8
3. Y. K. (f)	12-10	8- 9 (IQ70)	R 8

4. T. K. (m)	12-10	10- 0 (IQ70)	R10
5. Y. M. (f)	13- 2	5- 6	R10
6. M. Y. (f)	13- 7	4-11	R10
7. K. O. (m)	15-11	11-10 (IQ72)	R10
8. C. T. (m)	16- 1	12- 0	R10

Average 13- 7 8- 2 9.13

#: Longitudinal subjects

*: PVP (Picture Vocabulary Test by K. Ueno et al. 1979)

** : Evaluation of Preference Handedness (ten items: cutting with a scissors, throwing a ball, fore-finger pointing, cutting with a knife, tracing a circular figure, picking up small objects, and rubbing out with an eraser).

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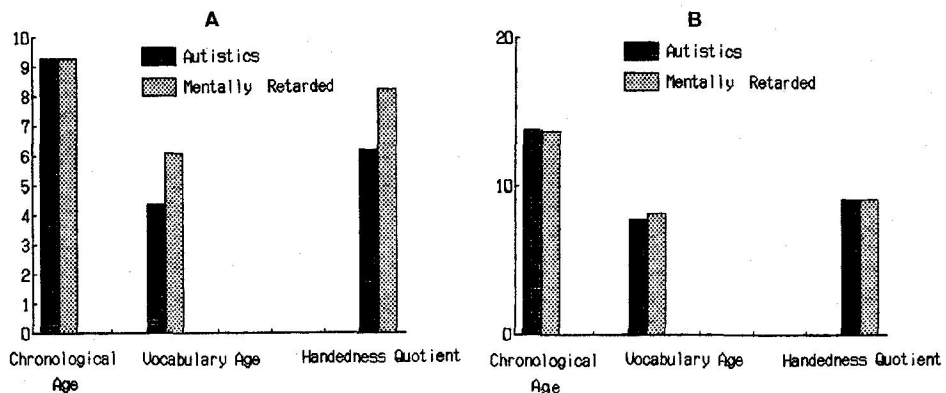


Fig. 1 A: Mean handedness quotients and vocabulary ages in autistic (n=21) and mentally retarded (n=20) children. B: Longitudinal handedness quotients in each group.

3. Theories of Left-hemisphere Impairment

Various central nervous system loci have been suggested as possible sites of impairment in infantile autism. The possibility of a cognitive defect has stimulated a number of investigations of possible pathology of telencephalic linguistic processing, so that most theorists focus heavily on language impairment as implicating left hemisphere deficit in autism. About twenty years ago, Hauser et al. (1975) initially reported the pathological enlargement of the left temporal horn and general widening of the left lateral ventricle by

pneumoencephalographic (PEG) findings in 15 of 18 children exhibiting some autistic behavior, which in these cases included dilatation of the third ventricle, cortical atrophy, epilepsy, increased height of the fourth ventricle, neglect of the right visual field, dilatation of the left temporal horn, and distorted frontal lobes. Eight patients were left-handed, and 3 autistics had failed to establish preferred handedness. However, other investigators could not confirm the evidence of the left temporal lateral cleft enlargement presented by Hauser et al. Since that time, it has been hypothesized that left hemisphere impairment underlies the autistic syndrome (e.g. B. S. McCann et al., 1981), because on the surface, the theory of left cerebral hemisphere dysfunction might account for the language deficits and cognitive symptoms of autism. Autistic children apparently are proficient in tasks usually attributed to right hemisphere functioning. Dowson et al. also reported a higher degree of left rather than right hemisphere dysfunction in autistics in a comparison of retardates, autistics, and bilaterally impaired neurological patients. Autistic children showed lower left-hemisphere functioning than the control group, but their right hemisphere performance was equal to retardates and higher than the performance of neurological patients (Dowson et al., 1983). It is important to note that this pattern is not specific to the autistic children and that most cases exhibit bilateral involvement rather than isolated left-sided damage.

D. Fein et al. (1984)'s critical review suggested that the hypothesis of left-hemisphere impairment overestimates the importance of linguistic abnormalities in autistic patients. They argued that the left hemisphere impairment is not primary, and that attentional, motivational or organizational defects of autism are primary for the first several years of life.

A. Question of Right-Hemisphere Intactness

There is some evidence suggesting that the right hemisphere is specialized for the directed attention and the perception of negative emotion, whereas the left hemisphere is biased toward positive emotional stimuli (Natale et al., 1983; Rueter-Lorenz et al., 1983). The right hemisphere may be dominant for mediation an attention-arousal response, because patients with right hemisphere disease show emotional indifference and dramatically smaller arousal responses than do patients with left hemisphere disease. Bear (1983) has described patients with right-hemisphere lesions who fail to detect and sustain attention to emotionally significant stimuli, and therefore fail to develop appropriate emotional responses. Intact right hemisphere has the capacity to recognize the components of certain types of emotional facial expression, but autistic patients show a deficiency to direct attention toward emotionally relevant stimuli in their environment. The right hemisphere attends to both contra- and ipsilateral

stimuli, whereas the left hemisphere is more limited to contralateral attention. Directed attention can be considered as an element of both sensory processing at lower subcortical structures and information processing at higher levels. It is a complex neuropsychological construct, but neglect occurs more often after right hemisphere lesions (Toshima et al., 1994). Margulies (1985) has attributed the attentional component of directed attention almost exclusively to the hippocampus and the intentional component to the nucleus accumbens. Thus, these data can not support the theory of right-hemisphere intactness in autism.

B. Preference for Auditory Stimuli

E. Blackstock (1978) maintained that autistic children usually do not show the normal right-ear advantage, and prefer nonverbal (music) to verbal auditory stimuli in a dichotic listening task. When the experiment was designed to show ear preference for verbal or musical stimuli by placing a child in a room with two speakers, one playing music and one playing various speech stimuli, both at a very low volume to demonstrate asymmetric hemispheric dominance, the subjects put one ear up to the speaker in order to hear it. The autistic children showed a left-ear preference (right-hemisphere advantage) for both melody and story speech stimuli, whereas normal children showed a slightly left-ear preference for melody and a right-ear preference (left hemisphere superiority) for the speech stimulus. However, Blackstock's data have not at all been confirmed in the recent sophisticated studies that were designed in a dichotic listening task. Autistic children generally exhibit various abnormal patterns of prosodic skills, whereas prosodic disturbances have been related to right-hemisphere functioning. They are also deficient at reading emotional expression (flat, monotonic, emotionless quality of autistic speech is reflected in the faulty use of intonation) which may be specifically depressed, but this deficiency can be attributed to right-hemisphere impairments (Weintraub et al., 1981; Ross, 1981, 1984). Abnormalities in prosodic and pragmatic (social) aspects of language, as well as other emotional behavioral features, suggest analogies to not only left-hemisphere impairment, but also to right-hemisphere disorder patients.

C. Cortical and Subcortical Hypotheses

The autistic syndrome consists of two major clusters of behavioral disturbances: language, communication and relation to people; and relating to objects and sensory-information processing. The emphasis on the disturbances of social relation, language and communication has attempted to identify the specific areas of cortical dysfunction, notably involving the cognitive left-hemisphere, although the evidence for an abnormality of hemispheric lateralization is inconsistent. There is a controversy concerning neurophysiological evidence f

for both cortical (cognitive and linguistic) and subcortical (brainstem) pathophysiology in autism. An older hypothesis of left-hemisphere dysfunction in autism was based on a too-limited clinical picture of autism as a language and cognitive disorder. The view that disturbances of relation, language and communication could be explained as the result of a specific cognitive defect (Rutter, 1978, 1983) may fail to account for the primary components of the autistic syndrome. M. Sigman et al. (1984a, 1984b) regarded a developmental disorder of emotional information processing and nonverbal communication as one of the first important social-developmental deficits to emerge in early autistic behaviors.

On the other hand, in the subcortical investigations, E. Ornitz et al. (1992) presents the assumption that the cognitive disorder hypothesis (Rutter, 1978, 1983) cannot explain the disturbances of social relation, and the primacy of the social, emotional dysfunction or the special cognitive deficit can be considered consequences of inconstancy of perception due to faulty modulation of sensory input. He assumes that distorted sensory input, when transmitted to higher centers, rostrally becomes distorted information, and that this in turn becomes the basis of the deviant language and social communication. Autistic dysfunction could be conceptualized as occurring at an interface between information processing and sensory processing involving brainstem and other subcortical mechanisms. Thus distorted sensory processing can induce distorted information processing, while cortical centers and the neostriatum can caudally (inferiorly) modify midbrain and diencephalic function. Again, distortions of information processing at cortical levels might elaborate the emotional disturbance and the distorted sensory input at the diencephalic structures where sensory input is gated.

4. Conclusion

In very early life, all mammals can share affective experiences with their parents which is necessary to develop subsequent sharing experiences and learning of social meaning (Klinnert et al., 1983; Hobson, 1986a, 1986b). Zentall and Zentall (1983) noted that all organisms each have biologically determined optimal arousal levels for input stimuli, efficacy of information processing, and sharing affective experiences. However, autistic children "come into the world with innate inability to form the usual, biologically provided affective contact with people" (Kanner, 1943).

Why can not the autistic child share affective experiences and social meaning? Recent empirical investigations suggest that the telencephalic theories based on a cognitive hypothesis (left-hemisphere disorder, right-hemisphere disorder, or

failure of hemispheric lateralization) could not explain the basic deficiency for the autistic behavioral responses. Thus, autistic behavior should not be understood as a specified cortical impairment but rather as a system disorder of social-affective recognition involving the neurophysiological mechanisms of reticular diencephalic structures between sensory processing and emotional information processing.

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References

- 1) Bear, D. S. : Hemisphere specialization and the neurology of emotion. *Archives of Neurology*, 1983, 40, 195-202.
- 2) Bettelheim, B. : Joey: A mechanical boy. *Scientific American*, 1959, 200, 116-127.
- 3) Bettelheim, B. : The empty fortress: Infantile autism and the birth of the self. Free Press, New York. 1967.
- 4) Blackstock, E. : Cerebral asymmetry and the development of early infantile autism. *Journal of Autism and Developmental Disorders*, 1978, 8, 339-353.
- 5) Campbell, M. and Green, W. H. : Pervasive developmental disorders of childhood. In H. I. Kaplan and B. J. Sadock (Eds.): *Comprehensive Textbook of Psychiatry*. Williams and Wilkins, Baltimore, 1985, pp. 1672-1683.
- 6) Courchesne, E. : Recent advances in autism. In H. Naruse and E. M. Ornitz (Eds.): *Neurobiology of Infantile Autism*. Excerpta Medica, Amsterdam, 1992, pp. 111-128.
- 7) Courchesne, E. : Cerebellar changes in autism. In J. Swan and A. Messer (Eds.): *Disorders of Developing Nervous System: Changing Views on Their Origins, Diagnoses, and Treatment*. Alan R. Liss, Inc., New York, 1988, pp. 93-109.
- 8) Courchesne, E. : Neuroanatomical systems involved in infantile autism: The implications of cerebellar abnormalities. In G. Dowson (Ed.): *Autism*. The Guilford Press, New York, 1989, pp. 119-143.

- 9) Courchesne, E., Hesselink, J. R., Jernigan, T. L., and Yeung-Courchesne, R.: Abnormal neuroanatomy in a nonretarded person with autism: unusual findings with magnetic resonance imaging. *Archives of Neurology*, 1987, 44, 335-341.
- 10) Courchesne, E., Yeung-Courchesne, R., Press, G. A., Hesselink, J. R., and Jernigan, T. L.: Hypoplasia of cerebellar vermal lobules VI and VII in autism. *The New England Journal of Medicine*, 1988, 318, 1349-1354.
- 11) Dawson, G.: Lateralized brain dysfunction in autism: Evidence from the Halstead-Reitan Neuropsychological Battery. *Journal of Autism and Developmental Disorders*, 1983, 13, 269-286.
- 12) Dawson, G., Finley, C., Phillips, S, and Galpert, L.: Hemispheric specialization and the language abilities of autistic children. *Child Development* 1986, 57, 1440-1453.
- 13) Dawson, G. and Lewy, A.: Reciprocal subcortical-cortical influences in autism. In G. Dawson (Ed.): *Autism: Nature, Diagnosis, and Treatment*. The Guilford Press, New York, 1989, pp. 144-173.
- 14) Erwin, R., Van Lancker, D., Guthrie, D., Schwalel, J., Tanguay, P., and Buchwald, J. S.: P3 responses to prosodic stimuli in adult autistic subjects. *Electroencephalography and clinical Neurophysiology*, 1991, 80, 561-571.
- 15) Fein, D., Humes, M., Kaplan, E., Lucci, D., and Waterhouse, L.: The question of left hemisphere dysfunction in infantile autism. *Psychological Bulletin*, 1984, 85, 258-281.
- 16) Hari, R.: Neuromagnetic method in the study of the human auditory cortex. In F. Grandri, M. Hoke, G. Romani (Eds.): *Auditory Evoked Magnetic Fields and Potentials*. Advances in Audiology, Vol. 6, Karger, Basel, 1990, pp. 222-282.
- 17) Hauser, S. L., DeLong, G. R., Rosman, N. P.: Pneumographic findings in the infantile autism syndrome. *Brain*, 1975, 98, 667-688.
- 18) Hobson, R. P.: The autistic child's appraisal of expressions of emotion. *Journal of Child Psychology and Psychiatry*, 1986a, 27, 321-342.
- 19) Hobson, R. P.: The autistic child's appraisal of expressions of emotion: A further study. *Journal of Child Psychology and Psychiatry*, 1986b, 27, 671-680.
- 20) Kanner, L.: Autistic disturbances of affective contact. *The Nervous Child*, 1943, 2, 217-250.
- 21) Kanner, L.: Early infantile autism. *Journal of Pediatrics*, 1944, 25, 211-217.
- 22) Klinnert, M., Campos, J., Sorce, J., Emde, R., and Svejda, M.: Emotions as behavior regulators: Social referencing in infancy. In R. Plutchnik and H. Kellermann (eds.): *Emotion: Theory, research, and experience*. Academic Press, New York, 1983, pp. 57-86.

- 23) Makela, J. P., Hamalainen, M., Hari, R., and McEvoy, L. : Whole-head mapping of middle-latency auditory evoked magnetic fields. *Electroencephalography and Clinical Neurophysiology*, 1994, 92, 414-421.
- 24) Margulies, D. M. : Selective attention and the brain: A hypotheses concerning the hippocampal-ventral striatal axis, the mediation of selective attention, and the pathogenesis of attentional disorders. *Medical Hypotheses*, 1985, 18, 221-264.
- 25) McCann, B. S. : Hemisphere asymmetries and early infantile autism. *Journal of Autism and Developmental Disorders*, 1981, 11, 401-411.
- 26) Nakane, Y., Naruse, H., Takesada, M., and Yamazaki, K. : Clinical effect of RTHBP on infantile autism. In H. Naruse and E. M. Ornitz (Eds.): *Neurobiology of Infantile Autism*. Excerpta Medica, Amsterdam, 1992, pp. 337-349.
- 27) Naruse, H., Hayashi, T., Takesada, M., Nakane, Y., Noguchi, T., Watanabe, Y., and Hayashi, O. : Therapeutic effect of tetrahydrobiopterin in infantile autism. *Proceedings of the Japan Academy*, 1987, 63, 231-233.
- 28) Natale, M., Gur, R. E., and Gur, R. C. : Hemispheric asymmetries in processing emotional expressions. *Neuropsychologia*, 1983, 21, 555-562.
- 29) Ornitz, E. M. : The functional neuroanatomy of infantile autism. *International Journal of Neuroscience*, 1983, 19, 339-352.
- 30) Ornitz, E. M. : A behavioral-based neurophysiological model for dysfunction of directed attention in infantile autism. In H. Naruse and E. M. Ornitz (Eds.): *Neurobiology of Infantile Autism*. Excerpta Medica, Amsterdam, 1992, pp. 89-109.
- 31) Ornitz, E. M., Ritvo, E. R., and Walter, R. D. : Dreaming sleep in autistic twins. *Archives of General Psychiatry*, 1965a, 12, 77-79.
- 32) Ornitz, E. M., Ritvo, E. R., and Walter, R. D. : Dreaming sleep in autistic and schizophrenic children. *American Journal of Psychiatry*, 1965b, 122, 419-424.
- 33) Rimland, B. : *Infantile Autism: The syndrome and its implications*. Appleton Century-Crofts, New York, 1964.
- 34) Ritvo, E. R., Freeman, B. J., Mason-Brothers, A., Mo, A., and Ritvo, A. M. : Concordance for the syndrome of autism in 40 pairs of afflicted twins. *American Journal of Psychiatry*, 1985, 142, 74-77.
- 35) Ritvo, E. R., Jorde, L. B., Mason-Brothers, A., Freeman, B. J., Pingree, C., Jones, M. B., McMahon, W. M., Petersen, P. B., Jenson, W. R., and Mo, A. : The UCLA-University of Uta epidemiological survey of autism: Recurrence risk and genetic counseling. *American Journal of Psychiatry*, 1989, 146, 1032-1036.
- 36) Ritvo, E. R., Mason-Brothers, Freeman, B. J., A., Pingree, C., Jenson, W. R., McMahon, W. M., Petersen, P. B., Jorde, L. B., Mo, A., and Ritvo, A. :

- The UCLA-University of Uta epidemiological survey of autism: The etiologic role of rare diseases. *American Journal of Psychiatry*, 1990, 147, 1614-1621.
- 37) Ross, E. D. : The aprosodias: Functional-anatomic organization of the affective components of language in the right hemisphere. *Archives of Neurology*, 1981, 38, 561-569.
 - 38) Ross, E. D. : Right hemisphere's role in language, affective behaviour and emotion. *Trends in Neurosciences*, 1984, 7, 342-346.
 - 39) Rueter-Lorenz, P. A., Givis, R. P., and Moscovitch, M. : Hemispheric specialization and the perception of emotion: Evidence from right-handers and from inverted and non-inverted left-handers. *Neuropsychologia*, 1983, 21, 687-692.
 - 40) Rumsey, J. M. : Pet scan studies of autism: Review and future directions. In H. Naruse and E. M. Ornitz (Eds.): *Neurobiology of Infantile Autism*. Excerpta Medica, Amsterdam, 1992, pp. 69-84.
 - 41) Rutter, M. : Language disorder and infantile autism. In M. Rutter and E. Schopler (Eds.): *Autism: A reappraisal of concepts and treatment*. Plenum, New York, 1978, pp. 85-104.
 - 42) Rutter, M. : Cognitive deficits in the pathogenesis of autism. *Journal of Child Psychology and Psychiatry*, 1983, 24, 513-531.
 - 43) Sigman, M. and Ungerer, J. : Attachment behaviors in autistic children. *Journal Autism and Developmental Disorders*, 1984, 14, 231-244.
 - 44) Sigman, M. and Ungerer, J. : Cognitive and language skills in autistics, mentally retarded, and normal children. *Developmental Psychology*, 1984, 20, 293-302.
 - 45) Toshima, T., Yoshida, H., and Maedoh, S. : Can unilateral neglect patients detect the visual objects in their neglected space ? The 23rd International Congress of Applied Psychology, Madrid, Spain, 1994.
 - 46) Tsai, L. : Computed tomography and magnetic resonance imaging studies. In H. Naruse and E. M. Ornitz (Eds.): *Neurobiology of Infantile Autism*. Excerpta Medica, Amsterdam, 1992, pp. 61-67.
 - 47) Weintraub, S. and Mesulam, M. : Developmental learning disabilities of the right hemisphere: Emotional, interpersonal, and cognitive components. *Archives of Neurology*, 1983, 40, 463-468.
 - 48) Zentall, S. S. and Zentall, T. R. : Optimal stimulation: A model of disordered activity and performance in normal and deviant children. *Psychological Bulletin*, 1983, 94, 446-471.