MORPHOLOGY AND PATHOMORPHOLOGY

Asymmetry of Human Brain in Early Embryogenesis under Normal and Pathological Conditions

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 130, No. 10, pp. 442-444, October, 2000
Original article submitted October 13, 1999

The effect of some developmental abnormalities on the morphogenesis of human brain asymmetry during early embryonic stages was studied. Insignificant predominance of the left hemisphere (1-3%) was revealed in human embryos.

Key words: *brain; asymmetry; man; embryonic development*

Lateralization of human brain (HB) is one of the most studied types of asymmetry. P. Broca first attracted attention to verbal HB asymmetry and connected it with the left and right hand asymmetry [5]. Possible relations between brain asymmetry and various disorders such as aphasia, agnosia, dyslexia, agraphia, sleep and dream disturbances [8] were extensively studied. Some authors point to a role of HB asymmetry in the development of epilepsy and schizophrenia [13].

At present, there is no theory on the mechanisms of development of morphological asymmetry of HB. In light of this, asymmetry of HB during ontogeny is still a very important problem. Structural lateralization of HB is poorly studied because obtaining of human embryonic and fetal material is fraught with complexities of ethical nature. However, there is evidence that morphological asymmetry of HB appears during early embryogenesis [2,4].

The aim of the present study was to examine early embryonic development of HB asymmetry and to evaluate the effect of some developmental abnormalities on its morphogenesis.

MATERIALS AND METHODS

The study was carried out on 8 human embryos (5-7 weeks gestation) with or without embryonic abnormalities obtained from 17-36-year-old healthy women during medical abortions.

Several methods were used to determine embryonic age. Since whole embryos were used in the study, embryonic age at early stages was determined by the number of somites. This method is accurate, because the intervals between somites are strictly determined [9]. Simultaneously, the number of spinal ganglia and the dynamics of sclerotome formation were studied. These 3 quantitative parameters strictly correlate, which allows determination of the age of 7-8-week-old embryos with an accuracy of 2-3 days. Apart from axial organs, the state of the limbs, thyroid gland, and thymus, the level of trachea branching, the development of the heart and diaphragm (stable markers) were evaluated [9]. Maternal history was also analysed. To obtain additional information on HB asymmetry, we examined an embryo with hypotelorism (crown-rump length CRL=10 mm; Fig. 1, *a*) and a hypertrophic embryo developing in the fallopian tube (CRL=19 mm; Fig. 1, *b*).

For histological procedures whole embryos were fixed in 10% acid paraformaldehyde within 1 h after abortion.

The material was embedded in paraffin-wax mixture, 10-μ serial sections were stained with hematoxylin and eosin and according to Mallory. The total volume and the surface of telen-, dien-, and mesencephalon were measured using a Wacom Ultra Pad computer

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0007-4888/00/0010-991$25.00

system (Wacom Computer Systems GmbH). The areas of telencephalon, diencephalon, and mesencephalon were estimated using Canvas 5.0.2 software (Deneba systems Inc.). This approach reveals relatively small quantitative differences. Asymmetry coefficient was calculated by the formula:

$$R\text{-}L/R\text{+}L\times 100\%,$$

where R and L are the sizes of right and left structures, respectively.

The data were processed statistically using Wilcoxon paired test.

RESULTS

Studies of HB asymmetry during embryogenesis are mainly associated with examination of the asymmetry of brain regions controlling verbal functions. However, it is known that early damage to the left hemisphere does not result in aphasia, because its functions are compensated by the right hemisphere due to brain plasticity [1]. No data on the formation of other types of morphological asymmetry were reported. G. Rosen *et al* [12] explained the differences in homologous architectonic fields by a decrease in the number of neurons in the smaller structure without changes in cell density. These differences are probably predetermined by some events occurring in early corticogenesis: early and late cell proliferation, effects of talamocortical and cortico-cortical afferents, and cell death during ontogeny.

Our study revealed an insignificant (by 1-3%) prevalence of the left hemisphere over the right one (Table 1). Hypertrophic embryo also showed insignificant prevalence of the left hemisphere, while the embryo with hypotelorism demonstrated the prevalence of the right hemisphere.

TABLE 1. Asymmetry of Telencephalon, Mesencephalon, and Diencephalon during Early Human Embryogenesis

Experimental series	CRL, mm	Asymmetry coefficient
Healthy embryos	7	0
	9	-0.6
	10.5	-5.34
	13	0.5
	14	-0.79
	19	-3.27
Pathology	10	1.89
	19	-0.4

Note. Positive values correspond to predominance of the right hemisphere.

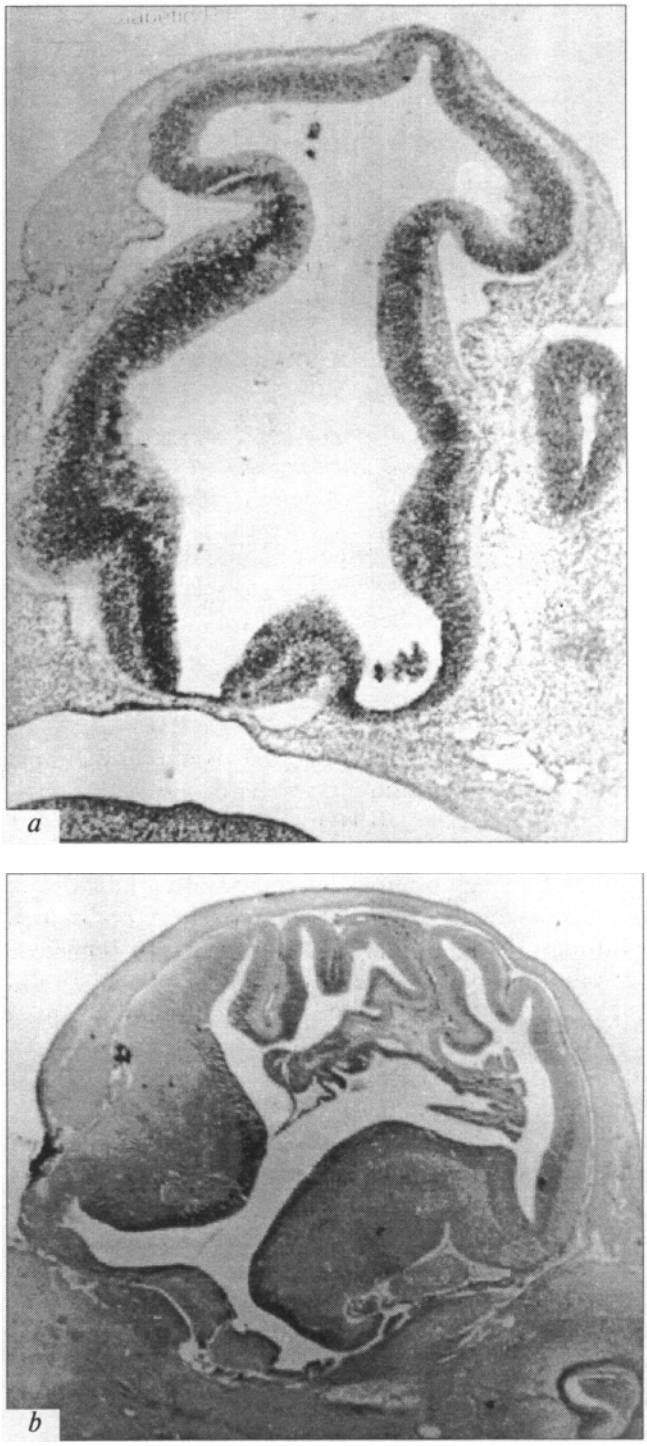

Fig. 1. Cross-sections of the heads of a hypoteloric embryo (*a*; crown-rump length 10 mm) and hypertrophic embryo (*b*; crown-rump length 19 mm) developing in fallopian tube. Mallory staining, ×88 (*a*), ×35.2 (*b*).

On later terms, the right hemisphere prevail over the left one [7,10,14]. Interestingly, three different methods were used in these studies: weighing [7], total study of 5-mm serial sections [14], and nuclear magnetic resonance [10]. Nuclear magnetic resonance

studies revealed similar pattern of asymmetry of the grey matter (*i.e.* its predominance in the cortex and subcortex in the right hemisphere) in 5-17-year-old boys and girls [11].

Our findings suggest that early embryogenesis is characterized by more rapid development of the left brain hemisphere [3].

REFERENCES

1. F. Bloom, A. Lazerson, and L. Hofstadter, *Brain, Mind, and Behavior* [in Russinan], Moscow, 1988.
2. Sh. Kh. Zhalilov, *Anatomy and Topography of Sulci and Gyri, and Cytoachitectonics (fields 8, 44) of the Brain Frontal Lobe during Postnatal Ontogenesis*, Abstract of Cand. Med. Sci. Dissertation, Tashkent (1994).
3. S. Springer and G. Deutsch, *Left Brain, Right Brain* [in Russian], Moscow (1983).
4. R. Achiron, S. Lipitz, S. Mashiach, *et al., Obstet. Gynecol.*, **89**, No. 2, 233-237 (1997).
5. P. Broca, *Bull. Soc. Antrophol. (Paris)*, No. 6, 337-393.
6. E. Bullmor, M. Ron, I. Harvey, and M. Brenner, *Psychiatry Res.*, **61**, No. 2, 121-124 (1995).
7. I. Crichton-Brown, *Brain*, **2**, 137-146 (1880).
8. C. M. Filley, *Neurobehavioral Anatomy*, Niwot (1995).
9. R. O'Rahilly, F. Muller, G. M. Hutchins, and G. W. Moore, *Am. J. Anat.*, **182**, 295-317 (1988).
10. N. Raz, J. D. Acker, and I. Torres, *J. Neurobiol. Learn. Mem.*, **63**, No. 2, 133-142 (1995).
11. A. L. Reiss, M. B. Denckla, J. L. Ross, *et al., Brain*, **119**, No. 5, 1763-1774 (1996).
12. G. D. Rosen, *Neurosci. Biobehav. Rev.*, **20**, No. 4, 607-615 (1996).
13. M. D. Stefan and R. M. Murrey, *Acta Pediatr.*, **422**, Suppl., 112-116 (1997).
14. Q. Xuehua and J. Junben, *Acta Anat. Sin.*, **26**, No. 4, 337-340 (1995).