Structural Basis of the Developmental Plasticity in the Human Cerebral Cortex: The Role of the Transient Subplate Zone

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We correlated neuroanatomical developmental parameters with sequential ultrasonography scans to reveal the structural basis of functional recovery after early focal hypoxic lesions of the human frontal lobe in premature infants. We studied the transient fetal subplate zone in the premotor and prefrontal cortex in premature, newborn, infant, and young adult brains by acetylcholinesterase (ACHE) histochemical, Golgi, and immunocytochemical methods. The structural in vivo rearrangements of the cerebral wall after perinatal lesions were studied on serial real-time sector scans (5-MHz transducer). The subplate zone contains "waiting" axons and randomly oriented fetal neurons, its developmental peak is between 22 and 34 weeks of gestation, and it is present in the frontal cortex of newborns and disappears after the sixth postnatal month, but individual subplate-like neurons remain until adulthood. Ultrasonography revealed remarkable structural rearrangements of the cerebral wall when the hypoxic lesion occurred during the developmental peak of the subplate zone: anechoic cavities ("cysts") develop rapidly (within 3 weeks) in premature brains, the rebuilding of these lesions continues after birth, and cavities disappear around the 11th month. We propose that the transient population of "waiting" axons and cells of the subplate zone participate in the structural and functional plasticity of the human cerebral cortex after perinatal brain damage.

KEY WORDS: transient subplate zone; plasticity; perinatal hypoxic lesions; human frontal cortex.

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INTRODUCTION

Remarkable plasticity and regenerative properties of the immature brain (Goldman-Rakic, 1987) have been attributed largely to the specific growth-related phenomena of the developing brain (Cowan et al., 1984; Purves and Lichtman, 1985). Little attention has been paid to the role of transient populations of fetal neuronal elements. We discovered the subplate zone, transient compartment, which is the thickest zone of the prenatal primate cortex (Kostović and Molliver, 1974; Kostović and Rakic, 1980) and contains fetal neurons, “waiting” axons, and synapses (Kostović, 1986, Kostović and Rakic, 1984; Molliver et al., 1973; Rakic, 1977). It is logical to assume that the variety of transiently arranged, growing neuronal elements and transmitter-related substances of the subplate zone participates in the plastic changes and reconstructive processes after perinatal brain damage in humans. In this paper, we approach this important problem by the correlative analysis of postmortem neuroanatomical parameters and structural rearrangements as revealed by in vivo real-time ultrasonography in low-birth-weight and term infants, a population characterized by an extremely high incidence of hypoxic and hemorrhagic lesions and the most remarkable percentage of neurological recovery (Levene, 1987; Volpe, 1981).

MATERIALS AND METHODS

Human brains (11 prematures aged 22–34 weeks of gestation, 4 newborns, 22 infants, and 6 young adults) obtained at autopsy were fixed in 4% paraformaldehyde–1.25% glutaraldehyde in 0.15 M phosphate-buffered saline (PBS) (pH 7.4), and the prefrontal and premotor cortex was processed for acetylcholinesterase (AChE) histochemistry (Kostović, 1986), somatostatin immunocytochemistry (Kostović and Fučić, 1985), Golgi (Mrzljak et al., 1988), and electron microscope (EM) analysis (Molliver et al., 1973). In 17 premature [26–34 weeks of gestation (wg)] and 56 near-term (37–40 wg) infants admitted to Clinical Hospital Center “Firule” in Split, we detected the perinatal hypoxic lesions characterized by an echogenic focus, using a real-time sector scanner (5.0-MHz transducer) and the anterior fontanelle as an acoustic window. All patients underwent sequential scanning during the postnatal period.

RESULTS

The Developmental Peak of the Subplate Zone in the Lateral Frontal Cortex. Between 22 and 34 wg the subplate zone, a wide compartment situated between the developing layer VI and the fetal “white matter,” contains the following neuronal elements: (1) plexiformly arranged growing axons revealed by AChE histochemistry (Fig. 1A); (2) randomly oriented, loosely arranged, strongly AChE-reactive (Fig. 1B) and somatostatin-like-immunoreactive (Fig. 1D) polymorphic neurons (Golgi impregnation; Fig. 1C); and (3) synapses as well as the prominent extracellular space