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SUSCEPTIBILITY OF THE OCULOMOTOR NUCLEUS TO PERINATAL HYPOXIA IN HUMANS: INCREASED CELL DEATH MEDIATED BY APOPTOSIS INDUCING FACTOR.

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Aims: Epidemiological studies indicated that perinatal hypoxia/ ischemia (PHI) -the main underlying mechanism for most obstetric complications- is a major risk factor for the development of neurological and psychiatric disorders later in life. Our previous studies on autopsy material from neonates with neuropathological lesions of prolonged PHI indicated a dramatic reduction of tyrosine hydroxylase expression (first and limiting enzyme of dopamine synthesis) in the dopaminergic neurons of the substantia nigra (SN) with reduction of their cellular size. The question raised was therefore, whether these observations indicate an early stage of SN degeneration or a developmental defect.

Methods: We used mesencephali from 22 autopsied neonates (total corrected age ranging from 34 to 46.5 gestational weeks) after written parental consent. We immunohistochemically studied the expression of Apoptosis Inducing Factor (AIF), the main effector protein in caspase-independent death pathway, in relation to the severity/ duration of PHI, as estimated by neuropathological criteria.

Results: Although only a limited number of dying neurons were found in the SN of the human neonate under PHI, increased incidence of neuronal death was observed in the oculomotor nucleus, which in some cases with acute PHI reached 40% of neurons.

Conclusions: Our results may represent an underlying mechanism implicated in visual impairments, including defective coordination of saccades, frequently described in individuals who survived after PHI.

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