LPS administration and oxygen-glucose deprivation synergistically induce neuronal damage in hippocampal slices

Peeters-Scholte CMPCD, Vliem MJ*, Groenendaal F, Heijnen CJJ, Van Muiswinkel FL*, Bär PR*, Van Bel F
Department of Neonatology, Wilhelmina Children's Hospital UMCU Utrecht, Utrecht, *Department of Neurology, University Medical Center Utrecht, Utrecht

Background: Preterm neonates are at increased risk for the development of periventricular leukomalacia, which is thought to be caused by the presence of 3 interacting pathogenic factors: the vulnerability of the cerebral white matter; the effects of intrauterine inflammation and cytokine release; and the low anti-oxidant in hypoxia-ischemia. The relative attribution of these factors to the subsequent brain damage is, however, unknown. An organotypically-cultured model of hippocampal slices of a 7-day-old rat, exposed to oxygen-glucose deprivation (OGD) can simulate the preterm brain, subjected to hypoxia-ischemia.
Objective: We hypothesized that cytokine release, elicited by LPS administration, would synergistically induce the amount of brain damage after OGD in the hippocampal slice model.
Design/Methods: Hippocampal slices from 7-day-old Wistar rats were cultured for 7 days. Slices were treated with either LPS (3 μM) 3 hours before OGD was instituted (n=27) or were vehicle-treated (n=21). 14 LPS-treated slices, and 10 vehicle slices were exposed to 50 min of OGD. The remaining slices were used as controls. At 48 h after OGD the amount of injury was assessed with propium iodide staining in the CA1 area of the hippocampus. To compare individual experiments, cell death was assessed as percentage of damage of LPS slices subjected to OGD (=100%).
Results: Vehicle and LPS-treated slices showed little cell death (12±6%). The amount of cell death was significantly increased in the vehicle-treated OGD slices to 61±11%($P<0.005$ vs vehicle), but in the LPS-treated slices subjected to OGD to 100±6%($P<0.005$ vs vehicle OGD).
Conclusions: LPS administration synergistically induced the amount of CA1 brain cell injury in hippocampal slices after OGD. This observation underlines that an interaction exists between the pathogenic factors contributing to periventricular leukomalacia. The release of reactive oxygen species and the low amount of anti-oxidant defenses in the preterm brain might play a key role in this process.

Cacha MPCD Peeters-Scholte, Department of Neonatology, Wilhelmina Children's Hospital- UMCU Utrecht, P.O. Box 85090, 3508 AB Utrecht, The Netherlands t 030-2763193, e-mail cpeeters@azu.nl

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