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MEETING ABSTRACT Open Access

Neuroprotective effects of hypothermia and levetiracetam after hypoxia-ischemia in the neonatal mouse brain

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Aims

Hypoxic-ischemic injury (HI) to the developing brain remains a major cause of morbidity. Hypothermia is currently the only established neuroprotective treatment available for term borns with hypoxic-ischemic encephalopathy, saving one in eight infants from developing severe neurological deficits. Therefore, additional treatments with clinically applicable drugs are indispensable. Furthermore, the pathophysiological mechanisms of hypothermia-induced recovery are not clearly understood. This study examines a potential additive neuroprotective effect of hypothermia combined with levetiracetam in neonatal mouse HI.

Methods

9-days-old C57BL/6-mice were subjected either to a sham-operation or to HI (modified Rice-Vannucci-model). After HI, the pups were randomized into six groups: 1) no treatment, 2) hypothermia (whole body-cooling, 4 hours, 32° C), 3) high-dose levetiracetam intraperitoneal (70 mg/kg body weight), 4) hypothermia combined with high-dose levetiracetam intraperitoneal, 5) low-dose levetiracetam intraperitoneal (7 mg/kg body weight), 6) hypothermia combined with low-dose levetiracetam intraperitoneal. Parameters of apoptosis (cleaved Caspase-3, TUNEL) and myelination (myelin basic protein) were analyzed 24 hours after HI by protein analysis and immunhistochemistry. From P28 to P60, cognitive and sensorimotor function was assessed via different tests.

Results

Hypothermia only and combined with low-dose levetiracetam was associated with a decrease of apoptosis and an increase of myelinated cells, but without additive effects. Intraperitoneal treatment with high-dose levetiracetam caused an increase of apoptotic factors. Behavioural testing demonstrated improved cognitive and sensorimotor outcome after treatment with hypothermia.

Conclusion

Whole-body cooling provides neuroprotection in the neonatal mouse brain by reducing apoptosis and preservation of myelination. However, treatment with levetiracetam after hypoxic-ischemic injury has no additive effects.

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