学位論文審査結果の要旨

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（学位論文審査結果の要旨）

Therapeutic Effect of Nicotinamide Mononucleotide for Hypoxic–Ischemic Brain Injury in Neonatal Mice

【主論文審査結果の要旨】

著者らは論文において下記の内容を述べている。

A clinical challenge remains in the treatment of hypoxic–ischemic brain injury in newborns. Nicotinamide adenine dinucleotide (NAD+) has beneficial effects in animal models of adult stroke. Here, we aimed to understand the short- and long-term neuroprotective effects of NAD+-promoting substance nicotinamide mononucleotide (NMN) in a well-established brain injury model in neonatal mice. Postnatal day (PND) 9 male and female mice were subjected to cerebral hypoxia–ischemia and treated with saline or NMN (50 mg/kg) immediately after hypoxia–ischemia. At different time points after hypoxia–ischemia, hippocampal NAD+, caspase-3 activity, protein expression of SIRT1, SIRT6, release of high mobility group box-1(HMGB1), long-term neuropathological outcome, short-term developmental behavior, and long-term motor and memory function were evaluated. Neonatal hypoxia–ischemia reduced NAD+ and SIRT6 levels, but not SIRT1, in the injured hippocampus, while HMGB1 release was significantly increased. NMN treatment normalized hippocampal NAD+ and SIRT6 levels, while caspase-3 activity and HMGB1 release were significantly reduced. NMN alleviated tissue loss in the long-term and improved early developmental behavior, as well as motor and memory function. This study shows that NMN treatment provides neuroprotection in a clinically relevant neonatal animal model of hypoxia–ischemia in mice suggesting as a possible novel treatment for

neonatal brain injury. .

新生児低酸素性虚血性脳症に対するNicotinamide mononucleotideの有効性についてマウスモデルを用い評価した論文で有り、学術上極めて有益で有り、学位論文として価値あるものと認めた。

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