

## **Knock out of P75<sup>NTR</sup> does not protect against NMDAR – mediated excitotoxic brain injury in newborn mice**

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**Background:** Periventricular leukomalacia (PVL) is a major cause of neurological handicap in preterm born infants. The role of neurotrophin receptor P75 (P75<sup>NTR</sup>) in the pathogenesis and repair of perinatal excitotoxic brain injury is unknown. Beside its trophic function P75<sup>NTR</sup> can also induce apoptosis.

**Hypothesis:** Since the excitotoxic cascade might induce the secretion of neurotrophins and their precursors by microglial cell activation and subplate neurons, which are damaged by hypoxia-ischemia, highly express the P75<sup>NTR</sup>, we hypothesized that P75<sup>NTR</sup> knock out mice (KO) have a significant less lesion size upon excitotoxicity compared to wildtype mice (WT).

**Methods:** To test this hypothesis we used an animal model of neonatal excitotoxic brain damage mimicking several key aspects of human PVL (Gressens, 2001). We subjected 5-day-old WT and KO mice to excitotoxic brain injury by a single intracranial ibotenate injection (N-Methyl-D-Aspartat agonist) into one brain hemisphere. Lesion size and number of Caspase-3 positive cells were determined as outcome parameters.

**Results:** Lesion size in white (WM) and gray matter (GM) did not significantly differ between KO and WT animals 24 and 120 hours after the insult. Excitotoxicity significantly increased the number of activated Caspase-3 positive cells in WM and GM at 24 hours after injury in WT. In KO significant less apoptosis occurred upon NMDA receptor activation in WM compared to WT ( $p < 0.01$ ,  $n = 7-8$ ).

**Conclusion:** To the best of our knowledge we show for the first time a potential role of P75<sup>NTR</sup> in perinatal brain injury. Further studies analyzing the role of P75<sup>NTR</sup> in developmental brain injury are mandatory.