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Hypothermia suppresses inflammation via NFκB and pSTAT3 signalling pathway in stimulated microglial cells

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Background:
Deep Hypothermia is a standard method for neuroprotection during pediatric cardiac surgery. Today, the most serious risk factors affecting the long-term neurological outcome are neurological complications occuring during and after corrective surgery. However, the cellular mechanisms which are induced by deep hypothermia have not been clearly understood. Therefore, we investigated the effects of deep hypothermia and rewarming on BV-2 microglial cells.
Methods:
BV-2 microglial cells are exposed to 17°C for 2 hours, slowly rewarmed to 37°C within 2 hours and observed under normothermic conditions for an additional 24 hours. For stimulation cells were treated with 1µg/ml Lipopolysaccharid (LPS). Cells were stained with DAPI and IB4 to detect morphological changes during cooling and rewarming. The viability of BV-2 microglial cells was quantified using a MTT assay. The pro-inflammatory cytokine IL-6 and chemokine MCP-1 secretion was measured by ELISA. The protein expressions of IκBα and pSTAT3 were analyzed using western blotting.
Results:
Cell viability was observed to be temperature independent in the unstimulated group during the experimental period (24 hours). However, deep hypothermia led to morphological changes from a ramified and resting status under 37°C to amoeboid shaped cells under 17°C, even without LPS stimulation. The IL-6 secretion was significantly decreased 4 hours after the start of the experiment in the hypothermic group. Interestingly, after 24 hours the IL-6 secretion was equal for the hypothermic and normothermic group. Additionally, MCP-1 release was significantly decreased after 4, 6 and 24 hours under hypothermic conditions. Under hypothermia the degradation of IκBα was delayed and pSTAT3 remained down regulated at 24 hours.
Conclusion:
Deep hypothermia had no influence on the cell viability but led to morphological changes in BV-2 microglial cells. The IL-6 and MCP-1 secretion was significantly decreased under hypothermic conditions. The regulation of the transcriptional factors pSTAT3 and IκBα were temperature dependent. Hypopthermia significantly reduced the inflammatory response in stimulated microglial cells. Intervention in the inflammatory process of immunomodullatory microglial cells by hypothermia offers an interesting therapeutic option to prevent neurons from cell death.