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MEETING ABSTRACT

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Hyperbaric oxygen protects neurotrophic activity of carbon monoxide-exposed astrocytes

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Background: Carbon monoxide (CO) poisoning causes neuronal and glial apoptosis that can result in delayed neurological symptoms. The damage of brain cells can be prevented by oxygen therapy. Recently we reported that CO/normoxia caused a progressive decline of viability and mitochondrial function accompanied by caspase and calpain activation. Impairment in astrocyte function was time-dependently reduced by hyperbaric, but not normobaric, oxygen. Due to the central role of astrocytes in maintaining neuronal function by offering neurotrophic support we investigated toxic effects of CO/normoxia on intrinsic neurotrophic activity in these cells and evaluated possible protective influence of oxygen treatment against CO poisoning.

Methods: Cultured rat astrocytes were exposed to 3.000 ppm CO in air for different time periods (0.5–24 h) followed by 24 h of normoxia. Following an 8-hour exposure to CO that significantly affected astrocytic cellular function the cultured cells were exposed during 24 h of normoxia for 1 h in different time periods (0–7 h) after CO to 100% normobaric oxygen (NBO) or 100% oxygen at a pressure of 3 bar (HBO). Real-time PCR was performed to examine the expression of nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3). Specific two-site enzyme immunoassays were utilized to determine protein synthesis and secretion of the examined neurotrophins.

Results: CO/normoxia caused a progressive decline of gene expression, synthesis and secretion of NGF, BDNF and NT-3 with different intensity. A maximal response was seen after 8 h in CO. Subsequent 1-hour treatment with oxygen disclosed pressure- and time-dependent efficacy in restoring astrocytic neurotrophic activity. The protective effect was evident when the cells were exposed to HBO 1–5 h after CO but not if they were exposed to HBO immediately after incubation in CO. A diminished efficiency of HBO in enhancement of neurotrophin synthesis was observed 7 h after CO exposure. In contrast, NBO showed no protective influence on CO-poisoned cells.

Discussion: The neuroprotective role of oxygen therapy in CO-exposed astrocytes is pressure- and time-dependent. In addition to preventing mitochondrial dysfunction and apoptotic processes our present results indicate that HBO, but not NBO, restores astrocytic neurotrophic support that may possibly dictate the short- and long-term neuronal survival as well as the maintenance and retraction of synaptic connections. In order to prevent the occurrence of late neuropsychological sequelae our study opens the way to consider time and pressure regimens of oxygen therapy in the clinical management of CO poisoning.

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