

## **Aquaporin 4 (AQP4) expression and blood brain barrier damage in an experimental model of neurodegeneration induced by trimethyltin**

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Trimethyltin (TMT) is well known to produce a distinct pattern of selective neuronal degeneration in the rodent CNS. TMT intoxication is also an important factor linked to induction of brain edema. Aquaporin-4 (AQP4), a water transporting protein, is thought to be the primary route through which water moves in and out astrocytes, is over-expressed in some pathological conditions, and is considered a marker of vascular permeability. The aim of our study was to investigate the integrity of the blood brain barrier (BBB), and the expression of AQP4 in astrocytes, after TMT intoxication. The brains of adult female Wistar rats, treated and untreated with TMT, were isolated and consecutive coronal sections obtained with a vibratome were incubated with primary fluorescent antibodies AQP4-Ig goat and GFAP-Ig rabbit. Imaging of fluorescence was performed on a confocal laser scanning microscope (Zeiss). In addition, dissected hippocampi and cortex were homogenized and the proteins were separated by SDS-PAGE. Although data in literature document absence of alterations of the BBB in TMT treated rats, our preliminary published data of the MRI investigation with Gd-DTPA suggested the presence of such alterations that concur with the passage of contrast into the damaged tissue. We have analyzed the AQP4 expression 7, 14, 21 and 35 days after TMT exposure. Immunofluorescence and Western Blotting analysis have showed an upregulation of the AQP4 in astrocytes after TMT intoxication., the expression levels of which progressively increased after TMT exposure, both in hippocampus and in brain cortex. All the data suggest that the astrocytes and their AQP4 protein are involved in the brain edema formation and in the possible alteration of the vascular permeability, in this TMT model of neurodegeneration.

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Key words

TMT (thrimethyltin); hippocampus; blood-brain barrier; vascular permeability; aquaporin-4