A NON-SELECTIVE CALCIUM CHANNEL BLOCKER, *BEPRIDIL*, DECREASES SOLUBLE Aβ AND CALCIUM LEVELS IN THE THALAMUS AFTER MIDDLE CEREBRAL ARTERY OCCLUSION IN RATS

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Introduction: Alzheimer’s disease and cerebral ischemia share similar features in terms of altered amyloid precursor protein (APP) processing and β-amyloid (Aβ) accumulation. Related to this, we have previously observed that Aβ and calcium deposition are robustly increased in the ipsilateral thalamus after transient middle cerebral artery occlusion (MCAO) in rats. Importantly, these changes coincided with altered β-secretase levels and activity in the ipsilateral thalamus.

Aims: Here we have investigated whether chronic treatment with bepridil, a non-selective calcium channel blocker, affects Aβ and calcium levels in the thalamus and in turn functional recovery after transient MCAO in rats.

Methods: Twenty-four male Wistar rats were subjected to sham-operation or transient MCAO. Twenty-six-day administration of bepridil (50 mg/kg/day, per os) or the vehicle was started two days after MCAO. Cylinder and tapered/ledged beam walking tests were used as behavioural outcome measures. After the follow-up, animals were sacrificed for analysis of Aβ40, Aβ42, and calcium levels in the contra- and ipsilateral thalami.

Results: Bepridil treatment improved forelimb use in MCAO rats in the cylinder test, which coincided with decreased calcium and soluble Aβ40 and Aβ42 levels in the ipsilateral thalamus when compared to vehicle-treated MCAO rats. Bepridil treatment did not affect astrogliosis or TNFα expression in the ipsilateral thalamus.

Conclusions: These findings suggest that bepridil treatment of MCAO rats decreases soluble Aβ and calcium levels in the thalamus, which coincide with improved sensorimotor recovery.