2.05

Role of Epac in the pathogenesis of ischemic stroke

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Exchange proteins activated by cAMP (Epac1 and Epac2) belong to a family of cAMP-regulated guanine nucleotide exchange factors (cAMPGEFs) for the small GTPases, Rap1 and Rap2. By using the Epac analogue, 007, various biological function including maintenance of endothelial tight and adhesion junctions are attributed to Epac. Previously, we have shown that Epac1 and Epac2 are highly induced on the ipsilateral hemisphere of mouse brain after transient middle cerebral artery occlusion (tMCAO). It is possible that both Epac1 and Epac2 may be involved in maintaining the blood-brain barrier (BBB) and protection of brain from ischemia and reperfusion (I/R) brain injury. Previously, Epac1 KO mice were exposed to tMCAO to determine the significance of Epac1 induction in the endothelial cells and degenerating neurons. Importantly, we observed that Epac2 is significantly upregulated in the ipsilateral side of Epac1 KO brain. Therefore, Epac2 KO mice were also exposed to similar I/R condition to understand the significance of Epac2 upregulation in the ipsilateral side of brain after tMCAO. Epac2 KO mice showed larger infarct size, hemispheric swelling and more severe neurological deficits compared to those of Epac2 wild type mice, suggesting that Epac2 may protect the brain against the pathogenesis of I/R neuronal injury. Currently, the detailed mechanisms of protective role of Epac2 in I/R brain injury is being further investigated.

Reference(s)

1. Please enter references here (e.g. Didder D.K., Churcill W.S, Cheng A.B. (1997) LANCET 83:123-125.)

2.06

Absolute Quantitation of Metabolites in Normal Aging Human Brain

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Objectives: Proton magnetic resonance spectroscopy (MRS) was obtained from twenty-nine healthy subjects to investigate the relationship between aging and metabolite levels in Chinese using 3T magnetic resonance imaging (MRI).

Materials and methods: Twenty-nine subjects were examined (mean=56.8± 18.13 years). Single voxel spectroscopy (SVS) with short echo time(TE)-35ms was employed. Single voxels with size 2cmx2cmx2cm were placed in anterior cingulate, posterior cingulate, 2.5cmx1.5cmx1cm in left and right hippocampi to study any correlation of choline (Cho), creatine (Cre) and N-acetylaspartate (NAA) with age by bivariate linear regression using SPSS version 18.0. Absolute quantitation was done using internal water as reference.

Results: In anterior cingulate, mean absolute Cho is 2.95±0.75 millimoles per kilogram per brain tissue (mmol/kg), Cre is 5.58±1.07mmol/kg and NAA is 8.05±1.12mmol/kg. In posterior cingulate, mean absolute Cho is 2.24±0.48mmol/kg, Cre is 6.25±0.51mmol/kg and NAA is 9.72±0.89mmol/kg. In left hippocampus, mean absolute Cho is 3.19±0.48mmol/kg, Cre is 5.53±0.74mmol/kg and NAA is 8.81±0.92mmol/kg. In right hippocampus, mean absolute Cho is 3.26±0.52mmol/kg, Cre is 5.58±0.91mmol/kg and NAA is 9.26±0.88mmol/kg.

Using bivariate linear regression, anterior cingulate revealed a significant correlation of absolute concentration of Cho (r=0.376; p=0.044) and Cre (r= 0.379; p=0.043) with age. In posterior cingulate, it was also revealed that there is significant correlation of absolute concentration of Cre (r=0.422; p=0.023) and NAA (r=0.604; p=0.001) with age. In right hippocampus, absolute concentration of NAA (r=0.376, p=0.044) significantly correlates with age. Other SVS results show no significance.

Conclusion: The finding that Cr increases with age in anterior cingulate agrees with a previous study.[1] However, the positive correlation of NAA with age in anterior and posterior cingulate differs from another study. [2]

Keywords: MRS, SVS, Aging, 3 Tesla

Reference(s)

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2. Brooks JCW, Roberts N, Kemp GJ, et al. A proton magnetic resonance spectroscopy study of age-related changes in frontal lobe metabolite concentrations. Cerebral Cortex 2001; 11 (7): 598-605.