Detection of 1,2-Propanediol in Rat Brain Microdialysates by High Resolution NMR Spectroscopy

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Abstract

We used high resolution (9.4 T and 17.6 T) NMR spectroscopy to study rat brain microdialysates at baseline, during periods of middle cerebral artery occlusion (MCAO) and reperfusion. Relatively high levels (~100 uM) of 1,2-propanediol (1,2-PD) were detected in all dialysates. During MCAO and reperfusion periods 1,2-PD levels decreased and lactate levels increased significantly. While the source of brain 1,2-PD is not clear, it appears to be a significant and consumable component of rat brain extracellular fluid.

Introduction

A few studies have demonstrated the presence of 1,2-propane diol (1,2-PD) in human cerebral spinal fluid.[1,2] The authors of these previous studies attributed the presence of 1,2-PD to exogenous administration as an intravenous drug vehicle. Microdialysis is a technique whereby brain extracellular fluids may be sampled in vivo. Here we studied rats that, to our knowledge, had not been exposed to 1,2-PD. In previous studies, we performed liquid chromatography on microdialysates to assay the extracellular concentrations of excitatory amino acid accumulation during focal cerebral ischemia and reperfusion. Prior to chromatographic studies, we ran non-destructive high resolution NMR to assay extracellular lactate concentrations. To our surprise, we detected high levels of 1,2-PD in the dialysates. In this study we attempt to investigate whether 1,2-PD can act as a brain energy substrate. Previous studies have demonstrated moderate glycogenic action of 1,2-PD in rats.[3]

Materials and Methods

Eight male Sprague-Dawley rats (320-380g) were studied. Each animal was artificially ventilated with 0.5-1.0% isoflurane in a mixture of 30% O_2 and 70% N_2 after endotracheal intubation. The right femoral artery and vein were catheterized. After craniotomy, a cuprophan microdialysis fiber coated with a thin layer of silicone except for a 5mm dialysis zone located in the ischemic hemisphere, was inserted laterally through the caudate putamen and parietal region of the brain. Artificial cerebrospinal fluid (ACSF) containing was infused at a rate of 2.5µl/min through a micro-pump connected to the fiber. The MCAO was induced by using an intraluminal suture insertion method for 120 min, followed by 3 hours reperfusion. Brain dialysates were collected every 30min for 1h prior to MCAO and during the period of MCAO and reperfusion.

Results

At baseline, brain extracellular 1,2-PD was in equal or higher in concentration than lactate, but following MCAO the lactate level surpassed that of 1,2-PD.

Fig. 1: Example 400 MHz proton NMR spectra of brain microdialysates from one rat in this study, in this case showing only 1,2-PD at baseline (top). By 1-2 h into MCAO, the 1,2-PD level appears to decline and an appreciable amount of lactate is detected.

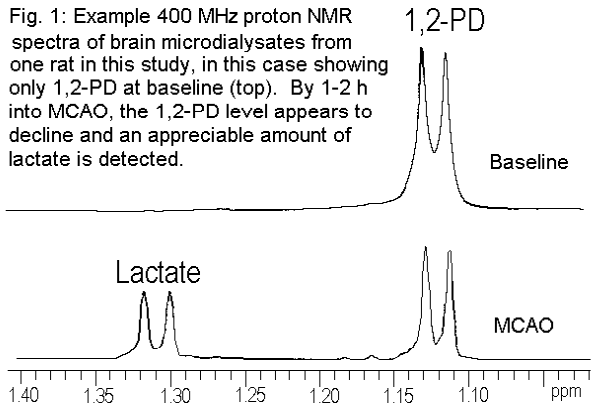
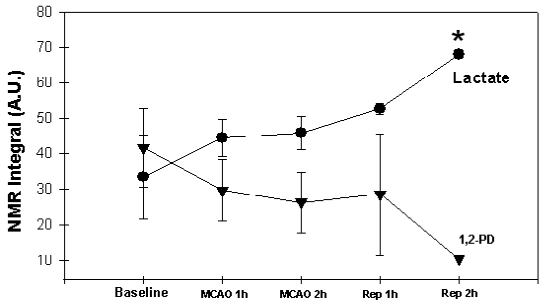


Fig. 2: Mean and standard error NMR integrals (arbitrary units) of 1,2-PD and lactate in microdialysates during periods before and after MCAO. * p<0.05 lactate compared to 1,2-PD.



Discussion

The present study demonstrates the presence of a substantial amount of 1,2-PD in brain microdialysates of rats that had not been previously treated or fed 1,2-PD. This finding begs the question of whether 1,2-PD is being synthesized by the rat. These results also suggest that 1,2-PD may be consumed and possibly converted to lactate in the brain under conditions of ischemia/reperfusion.

References

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