INCREASE OF NADH LEVELS IN THE RAT CORTEX FOLLOWING PERIPHERAL ADMINISTRATION OF NADH

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Nicotinamide adenine dinucleotide (NADH) plays a central role as a co-substrate for energy transfer in the respiratory chain and is therefore an important parameter of cellular metabolism. NADH can be detected by its fluorescence. The NADH molecules bound to proteins of the mitochondrial membranes can be used as an indicator for changes in the metabolic activity of cells and tissues. Several clinical studies showed the positive effect of peripherally given NADH on diseases such as Morbus Parkinson, Morbus Alzheimer and major depression.

Aim of our study was the assessment of the central availability of NADH after peripheral administration.

In vivo-measurement of NADH was performed using laser-induced fluorescence spectroscopy. A two-fibre optic (Ø100 μm) was inserted 2 mm into the brain. The emission of NADH was induced by pulses of a N_2-laser (8 = 337 nm). The resulting NADH fluorescence (sample depth 0.5 mm) was measured using a fluorescence detector with spectral (450±5 nm) and temporal (2 ns) gating of the signal.

Anaesthetised male Shoe:Wist rats (200∀20g) received either vehicle or NADH in doses of 10 and 50 mg/kg i.v. and i.p. Another group received vehicle or NADH or nicotinamide (50 mg/kg) orally. Group size n=10.

Killing the animals and therefore stopping the utilisation of NADH caused a maximum increase in NADH fluorescence.

An i.v. injection of NADH (10 and 50 mg/kg) caused an immediate rise (14% of maximum increase) in the intensity of the cortical NADH fluorescence, which returned to basal level after 4-7 minutes. Following i.p. administration of 50 mg/kg NADH, the cortical NADH fluorescence was increased (10% of maximum increase) for about 20 minutes. NADH given orally increased the NADH fluorescence at the start of the experiment, an indication for the intestinal resorption of NADH. The relatively small changes may be caused by the long period between the application and the measurement of the fluorescence of approx. 60 minutes.

The rise of the measured NADH fluorescence intensity indicates an increase of the NADH concentration in the CNS of the rat after peripheral application of NADH. The changes observed are relatively small but in comparison to the maximum increases even these small changes in NADH concentration could be important. Up to now it is not known, whether NADH given peripherally reaches the brain directly. However, the measured increases in cortical NADH may help to explain the clinical effects reported.

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