Plzeň. lék. Sborn., 84, 2018: 17–19

# THE EFFECT OF CAFFEINE ON THE HEART ACTIVITY OF MICE WITH INBORN CEREBELLAR DEGENERATION

P. Sobotka, F. Vožeh

Department of pathological physiology Faculty of medicine in Pilsen, Charles University, Czech Republic

Lurcher mutant mice are natural model of inborn celebellar degeneration characterized by postnatal rapid loss of Purkinje cells, granule cells and inferior olive neurons (1). From the healthy wild type mice (W) the Lurcher mutant mice (L) differ in their motor abilities and in parameters of higher nervous aktivity etc. (2). We described their increased brain excitability after parenteral application of caffeine (3). Besides its main action on brain functions and behavior caffeine has also cardiovascular effects (4). In this paper we examined the reaction of the heart activity to the application of caffeine in L and W mice.

## MATERIAL AND METHODS

Adult L and W mice were anesthetized with pentobarbitale (60 mg/kg body weight). The EKG was registered by means of needle electrodes in the 2nd limb lead. Caffeine (30 mg/kg body weight) was applied intraperitoneally every 5 minutes. Constant body temperature of animals was monitored.

## RESULTS

The average resting heart rate of L mice was 516/min and of W mice 468/min (tab. 1). After the first application of caffeine the heart rate increased in all animals, in L mice by 20%, in W mice by 30%. Moreover the R wave voltage increased simultaneously in both groups of animals. In W mice the second application of caffeine did not change the heart rate significantly. The dose of 180 mg/kg elicited expressive heart arrhythmia. The dose of 270 mg/kg derranged already the heart activity, the lethal dose being 330 mg/kg. Contrary, in L mice even the second application of caffeine was manifested by disturbance of the hearth rhythm and was intesified by the dose of 120 mg/kg. Severe bradycardia was induced by the dose of 180 mg/kg with lethal termination after the dose of 210 mg/kg.

**Tab. 1** Effect of caffeine application.

| | **Wild** | **Lurcher** |
|---|---|---|
| Heart rate min. | 468.0 | 516.0 |
| T to isoel. EEG (min) | 27.0 | 17.9 |
| T to excitation (min) | 12.4 | 5.2 |
| caffeine (mg) | 3.075 | 1.728 |

## DISCUSSION

Progressive loss of cerebellar Purkinje cells leads to complex disturbances. Besides motor changes, alteration of highe nervous activity and increased brain excitability, L mice have also different reactivity of the cardiovascular system. Higher resting heart rate of L mice may be probably connected with hypertrophy of their adrenal medulla (5). We proved that imitially positive chronotropic and inotropic effect of caffeine has arrhytmogenic consequences after higher doses. The possible mechanism may be the enhanced release of calcium from the sarcoplasmic reticulum (6). Even though the arrhythmogenic consequence of caffeine is analogous both in W and L mice, its effect is achieved in L mice with significantly lower concentration.


## SUMMARY

In 10 Lurcher mutant mice (L) and healthy wild type mice (W) was followed their heart activity after i. p. repeated application of caffeine. Arrhythmogenic as well as lethal effect is expressed in L mice in lower concentrations than in W mice. Experiments proved changed reactivity of the cardiovascular system in L mice.


## *Vliv kofeinu na srdeční aktivitu myší s vrozenou mozečkovou degenerací*


## SOUHRN

U 10 mutantních myší Lurcher (L) a u 10 zdravých myší stejného kmene (W) byla sledována jejich srdeční aktivita po opakované i. p. aplikaci kofeinu. Arytmogenní, stejně jako letální účinek kofeinu je vyvolán u L myší v nižších koncentracích než u W myší. Pokusy prokázaly změnu reaktivity kardiovaskulárního systému u L myší.

## LITERATURA

1.Caddy K. W. T., Vožeh F.: The effect of 3-acetylpyridine on inferior olivary neuron degeneration in Lurcher mutant wild-type mice. Europ. J. Pharmacol. 330, 1997: 137–142. – 2. Vožeh F., Caddy K. W. T., Mysliveček J. et al.: Some characteristic of early learning in cerebellar degeneration model. Studia Psychol. 39, 1997: 279–281. – 3. Barcal J., Sobotka P., Vožeh F. et al.: Brain electrical activity and level of excitability in cerebellar degeneration model. Physiol. Res. 48, 1999, Suppl. 1, 55. – 4. Sobotka P.: The arrhythmogenic effect of caffeine. Plzeň. lék. Sborn. 2001, 68: 5–10. – 5. Vožeh F., Šíma P., Beranová M.: Nervous and endocrine consequences of partial neurodeficiency in an animal model. The European imunology meeting EFIS 2000: 671–676.

Autor's address: P. S., alej Svobody 1655/76, 323 00 Pilsen, Czech Republic