

The motor and cognitive consequences of inborn cerebellar degeneration and some possibilities how to influence it

The cerebellum is traditionally considered to be a coordinator of movements and equilibrium and a regulator of muscular tone. Participation of the cerebellum on the motor learning has been discovered later. Besides that, there is increasing experimental and clinical evidence supporting the idea of an important role of the cerebellum in common cognitive functions.

Increasing number of experimental works - especially those on animals - demonstrate an effect of the the cerebellum on the memory and different types of learning. A suitable model to study the cerebellar degeneration are Lurcher mutant mice. During their lives, there is a progressive loss of Purkinje cells followed by a loss of granular cells and inferior oliva neurons.

We concentrated on the following problems in this work:

- development of motor learning and topical motor skills during the first month of life
- positive and negative changes in NO synthesis and subsequent effect on discriminative learning
- effect of administration of MK-801(non-competitive antagonist of NMDA receptors) on discriminative learning of Lurcher mutants and wild mice derived from two strains (C3H and C57B1/7).

Lurcher mutants and wild mice were put in motor skill tests using four methods once only – in the 15th, 20th, 25th or 30th days of their postnatal lives (PL). The results were compared with those of the animals of both types (Lurcher and wild) in the same days but the latter animals were repeatedly trained in the same methods already in the 3rd, 6th, 9th and 12th days of PL.

Lurcher mutants and wild mice were given every other day (from 2nd to 12th days of PL) either non-specific inhibitor NOS L-NAME or donor of NO Larginin

(20 mg/kg subcutaneously). The controls obtained the saline solution similarly. We followed discriminative learning type inhibition reaction of passive avoidance – in the 3rd, 4th, 6th, and 7th days of PL using the “step through method“ and in the 15th, 16th, 20th and 21st days of PL using the “step down“ method in all animals.

Lurcher mutants and wild mice derived from two strains were administered (from 2nd to 14th days of PL) every other day subcutaneously either noncompetitive

antagonist NMDA MK-801 (0.25 mg/kg) or the saline physiologic solution. The animals underwent methods of discriminative learning of type “step through“ (in the 6th and 7th days of PL) and of type “step down“ (in the 15th and 16th days of PL).

We can summarize our results:

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- motor training is able to influence positively development of the motor skills

in both – the healthy animals as well as (surprisingly markedly) in the animals suffering from inborn neurodeficiency, in spite of their permanent handicaps,

- effect of the drugs in doses used in the experiment is not unambiguous. If it may influence the development of neurodegeneration in some cases, there is a different effect on the healthy animals and the handicaped ones,
- besides the differences caused by neurodegeneration, it is necessary also to know the animals strain. The characteristics of the strains may be so different that significantly same modify the after-effects of the same neurodeficiencies.