EXPERIMENTAL STUDY OF MECHANISMS OF NEURODEGENERATION IN DIFFERENT CONDITIONS – SUMMARY

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The cerebellum is an important structure involved in motor coordination and many other functions including cognitive and emotional processes. Severe cerebellar diseases include a wide group of cerebellar hereditary degenerations with different types of heredity, different pathogenesis and diverse phenotypic manifestation. Many types of mouse models can be used to investigate these diseases and their therapy. These mice carry spontaneous mutations or are genetically modified.

The aim of this work was to analyse the dynamics of morphological changes of cerebellar degeneration in Lurcher mice using fluorescent double staining. We also performed transplantation of embryonic cerebellar tissue suspension in adult Lurcher B6CBA mice, B6.BR mice and wild-type mice of both strains with two-month survival after surgery and transplantation of identical suspension in adult Lurcher B6CBA mice and C3H mice and wild-type mice of both these strains with six-month survival after surgery.

We have confirmed these main characteristics of the degenerating Purkinje cells in Lurcher mutants: the disrupted continuity of the Purkinje cell layer, the presence of dark spots in the cell nuclei, the fragmentation of nuclei and the non-homogenous staining of the cytoplasm. Later, the bodies and the nuclei of the Purkinje cells were deformed, including their shrinkage and disintegration of dendrites.

In neurotransplantation experiments, we have shown that the embryonic cerebellar graft survived very well for two or six months in healthy mice and cerebellar mutants of the pcd and Lurcher type respectively and is also a rich source of Purkinje cells.

The main and most marked difference was found in integration of the graft into the host´s cerebellum. In Lurcher mutants, the graft was mostly sharply limited and separated from the host´s cerebellar tissue, whereas in pcd mutants and healthy mice the grafts exhibited good integration, including fibre sprouting to the cerebellar nuclei. This finding suggested that there are potentially unidentified disease-specific factors significantly limiting development and integration of the cerebellar grafts.

Neurotransplantation therapy did not influence the performance of mutant mice in the rotarod test. Therefore, we failed to demonstrate the functional effect of the cerebellar graft.