Abstract

Amyotrophic lateral sclerosis (ALS) is a progressive neurological disorder of the central nervous system characterized by loss of motor neurons and voluntary muscle degeneration. Astrocytes play a major role in regulation of the disease onset and progression due to their intimate association with neurons. Regulation of ionic homeostasis is one of their key functions and its failure has been linked to several neurological diseases. The aim of this thesis was to explore differences in membrane properties of astrocytes in ALS. To fulfill this aim, a double transgenic mouse strain with ALS-like phenotype and a specific expression of enhanced green fluorescent protein in astrocytes was generated. To phenotype this strain, two sensorimotor tests, wire grid hang test and rotarod test, were conducted. Immunohistochemistry was used to characterize the strain on a cellular level and to explore changes of specific ion channels. Functional properties of astrocytes were explored using the patch clamp technique. The double transgenic strain has the characteristic ALS-like phenotype and is comparable to the original strain with differences in symptom onset and progression between models and sexes. On the cellular level, there are characteristic ALS features, specifically loss of motor neurons and astrogliosis. Mutant cells have higher input resistance and lower membrane capacitance compared to controls, but we observed no changes in membrane potential. Mutants have lower incidence of inwardly rectifying K^+ currents and higher amplitude of delayed outwardly rectifying K^+ currents compared to controls. We also observed decreased immunostaining of Kir4.1 channel subunit in the brain of mutant mice compared to controls.

Key words: amyotrophic lateral sclerosis; astrocytes; membrane properties; electrophysiology; patch clamp; immunohistochemistry; wire grid hang; rotarod