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ALTERED HOMER CELL SIGNAL IN SKELETAL MUSCLE SOLEUS (SOL) OF HEAD TILT (HET-/-) MICE WITH A VESTIBULAR DISORDER

Abstract

Introduction: The molecular mechanisms regulating skeletal muscle structure and function during chronic disuse or under microgravity exposure are not yet fully elucidated. Recently, the role of the vestibular system was proposed. Several evidence suggest the presence of a tonic vestibule-spinal modulation of motor activity, affecting especially antigravity postural muscles. In an attempt to further elucidate such mechanisms, we investigated on Homer subcellular localization and Homer protein-protein interaction in calf SOL and gastrocnemious (GAS) muscles of wild type (WT) and het-/- mice (An autosomal recessive mutation responsible for a vestibular disorder in affected animals). **Hypothesis**: Deconditioning of the vestibular system may result in an altered skeletal muscle structure and function as the results of an altered neuromuscular junction calcium sensitive Homer cell signaling. **Methods**: SOL and GAS from adult WT and het-/- mice were used. Soluble and particulate muscle cell fractions were prepared from the right hind limb muscles and biochemically analyzed by polyacrylamide gel electrophoresis (PAGE) in native experimental conditions and by Western blot (WB) for Homer protein content analysis by using a pan-Homer antibody. Morphological assessment was performed on the contralateral left hind limb muscles. RT-PCR analysis was used to monitor Homer isoforms transcription pattern in het-/- vs. WT. **Results**: In both cell fractions two different Homer immunoreactive bands were detectable. A lower Homer monomer, and a higher Homer dimer immunoreactive band was detected. Both Homer monomer and dimer were quantitatively different between soluble and particulate cell fraction and between muscle type and animal group. Interesting, in GAS particulate cell fraction of het-/- mice no Homer dimer was present, while in SOL soluble fraction there was a twofold increase of Homer dimer when compared to WT. Finally, no Homer monomer was present in both soluble and particulate fraction of SOL WT and het-/- mice suggesting that, major differences were present for Homer monomer and dimer between postural (SOL) and non postural (GAS) muscles. Preliminary results for Homer subcellular localization at the neuromuscular junction (NMJ) showed altered expression in het-/- vs. WT SOL. RT-PCR analysis is still on process. Morphological assessment of het-/- SOL and GAS skeletal muscles myofibers revealed an increase in type-I myofiber cross-sectional area compared to WT. **Discussion**:These results are consistent with the hypothesis that the vestibular system somehow affect skeletal muscle structure and function, and this is, at least in part, translated at the neuromuscular junction by Homer cell signaling.