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Meeting abstract

Ion channel impairments in dystrophic cardiomyocytes

Xaver König[1], Markus Mille[1], Stefanie Kimbacher[2], René Cervenka[1], Péter Lukács[1], Hannes Todt[1], Reginald E Bittner[2] and Karlheinz Hilber*[1]

Address: [1]Institute of Pharmacology, Center for Biomolecular Medicine and Pharmacology, Medical University of Vienna, 1090 Vienna, Austria and [2]Department of Applied Anatomy, Center for Anatomy and Cell Biology, Medical University of Vienna, 1090 Vienna, Austria

Email: Karlheinz Hilber* - karlheinz.hilber@meduniwien.ac.at

* Corresponding author

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Background

Muscular dystrophies comprise a heterogeneous group of inherited diseases that are characterized by progressive muscle weakness and degeneration. Severe forms, e.g. Duchenne muscular dystrophy (DMD), which is caused by a mutation in the dystrophin gene, lead to loss of ambulation, respiratory failure, and premature death. In many types of the muscular dystrophies the cardiac muscle is also affected - cardiomyopathy and/or cardiac arrhythmias regularly represent life threatening complications. The current understanding of the pathomechanisms underlying these cardiac diseases in various muscular dystrophies is still very limited. Here we tested the hypothesis that dysfunctional ion channels may be critically involved in dystrophy-associated cardiac disease.

Methods

The functional properties of voltage-gated sodium and calcium channels in cardiomyocytes derived from normal and dystrophic neonatal mice were studied by using the whole cell patch clamp technique. Besides the most common mouse model for human DMD, the dystrophin-deficient mdx mouse, we also used mice additionally carrying a mutation in the utrophin gene. The mdx-utr double mutant mouse exhibits a more severe disease phenotype than the mdx mouse, and may represent a more suitable animal model for human DMD.

Results

We found that dystrophic cardiomyocytes show reduced sodium current density compared to wild-type cardiomyocytes. In addition, extra utrophin-deficiency altered sodium channel activation and inactivation properties, which was not observed in only dystrophin-deficient (mdx) cardiomyocytes. Preliminary experiments also suggest an impairment of calcium channel inactivation in dystrophic cardiomyocytes.

Conclusion

We found significant impairments in ion channel function in dystrophic cardiomyocytes. These may perturb electrical impulse propagation in the dystrophic heart, and thus contribute to cardiac complications associated with muscular dystrophies.

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