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MEETING ABSTRACT Open Access

Altered sodium channel function in dystrophin/utrophin-deficient cardiomyocytes

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Background

Duchenne muscular dystrophy (DMD), caused by mutations in the dystrophin gene, is an inherited disease characterized by progressive muscle weakness and degeneration. Besides the relatively well-described skeletal muscle degenerative processes, DMD and some other muscular dystrophy types are also associated with cardiovascular complications including cardiomyopathy and cardiac arrhythmias. The current understanding of the patho-mechanisms underlying these cardiovascular complications is still very limited, but recent research points to a contribution of dysfunctional ion channels in dystrophic cardiomyocytes.

Materials and methods

By using the whole cell patch-clamp technique, the functional properties of voltage-gated sodium channels were studied in cardiomyocytes derived from normal and dystrophic mice. In addition, a computer model was used to simulate the effects of altered sodium channel properties on the cardiac action potential. 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 cardiac disease phenotype than the mdx mouse, and is thought to represent a more suitable animal model for human DMD.

Results

We found that dystrophic cardiomyocytes show a reduced sodium current density compared to wild-type cardiomyocytes. In addition, extra utrophin deficiency significantly shifted both the sodium channel activation and inactivation curve to more depolarised potentials, which was not observed in only dystrophin-deficient mdx cardiomyocytes. Computer modelling revealed that the described sodium channel impairments in dystrophic cardiomyocytes suffice to affect the action potential.

Conclusions

Sodium channel dysfunction may perturb electrical impulse propagation in the dystrophic heart, and thus contribute to cardiac complications associated with the muscular dystrophies.

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