AAP10 reverses uncoupling in human cardiomyocytes

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AIM: Ventricular arrhythmia is one of the most important causes of death in industrialized countries and often accompanies myocardial infarction and heart failure. In recent years modification of gap-junctional coupling has been proposed as a new antiarrhythmic principle.

Previous studies showed that AAP10 protects the cardiac gap junctions against acidosis induced uncoupling. We examined whether the gap junction modulator (antiarrhythmic peptide) AAP10 exerts any effects on partially uncoupled human atrial cardiac gap junctions.

Methods and results: We determined the influence of 50 nM AAP10 (H2N-Gly-Ala-Gly-4Hyp-Pro-Tyr-CONH2) on macroscopic gap junction conductance by dual whole-cell voltage clamping in human cardiomyocytes. Cells were partially uncoupled by CO2-mediated acidosis (pH 6.3, T 36 degrees C) or kept at 'normal' conditions (pH 7.4, T 36 degrees C). The conductivity between the two cells rises slighty during the one hour experiment when kept under “normal” conditions. CO2-acidosis-induced uncoupling led to a significant decrease in conductivity wich was completely reversed by AAP10 and elevated over the initial conductivity level.

Conclusion: Our resultes show that AAP10, which improves gap-junctional intercellular coupling, prevents and reverses uncoupling in human cardiomyocytes. The peptide might be useful for antiarrhythmic strategies regarding arrhythmias caused by uncoupling. (supported by DFG grant to S. Dhein).