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The anti-contractile role of vascular smooth muscle calcium-activated potassiumchannels of high conductance

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Potassium channels in the plasma membrane of vascular smooth muscle cells play an important role in controlling arterial smooth muscle function by regulating VSMC membrane potential. The calcium-activated potassium channel of high conductance (BKCa channel) is activated by membrane potential depolarization and increase of the intracellular calcium concentration, both importantly involved in vasoconstriction.

In this thesis, the contribution of the BKCa channel to agonist-induced vasoconstriction and a potential alteration of this contribution in diabetes mellitus were studied.

The contractile responses of intact vessel segments of rat main tail, femoral and saphenous arteries were investigated using isometric wire myography. The content of the intracellular calcium stores were studied with Fura-2 calcium-fluorimetry.

It could be shown that the BKCa channel exerts an anti-contractile effect in agonistinduced vasoconstriction and transforms contractile behavior from phasic to tonic in all three investigated vessels, preventing excessive vasoconstriction. For this effect, ryanodine receptors, sarcoplasmic calcium pumps and L-type voltage gated calcium channels, but not IP3 receptors were found to be important. In diabetic rat tail arteries, an impaired vasomotion after BKCa channel inhibition was observed, indicating an attenuation of BKCa channel activity in diabetes while neither vasoreactivity to a α1- agonist, nor the extent of the anti-contractile effect of the BKCa channel in agonistinduced vasoconstriction was altered.

The results demonstrate the importance of the BKCa channel in the regulation of vascular smooth muscle cell contractility which is essential for a healthy cardiovascular system and of which impairment can lead to a multitude of cardiovascular diseases.