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B/6. MODULATION OF VASCULAR SMOOTH MUSCLE CONTRACTION BY TRANSIENT RECEPTOR POTENTIAL MELASTATIN-4 (TRPM4)

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Keywords: TRPM4, 9-phenanthrol, vasoconstriction, vascular biology, hypertension

INTRODUCTION: The transient receptor potential melastatin-4 (TRPM4) is a calcium-activated monovalent cation channel. TRPM4 has a major role in pressure-induced depolarization and vasoconstriction in intracranial arteries. Our aim was to study the regulatory function of TRPM4 in basilar and mesenteric arteries.

METHODS: Arteries were isolated from Wistar-Kyoto (WKY) rats and experiments were performed in oxygenated Krebs buffer, under isobaric conditions (at 80mmHg) on mesenteric arteries and isometric conditions (preconstriction by about 5mN) on basilar arteries.

RESULTS: Initial diameter of the mesenteric arteries was $325 \pm 18 \mu\text{m}$ ($n=9$). Extracellular K^+ (120 mM) evoked a vasoconstriction (decrease in diameter from $316 \pm 30 \mu\text{m}$ to $155 \pm 40 \mu\text{m}$, $n=4$, $p=0.03$), similarly to norepinephrine (10 μM , decrease from $387 \pm 17 \mu\text{m}$ to $127 \pm 18 \mu\text{m}$, $n=5$, $p<0.01$). Arteries were pre-constricted with norepinephrine and treated with the TRPM4 channel inhibitor 9-phenanthrol (1 μM -300 mM), which evoked a dilation (increase of diameter from $206 \pm 22 \mu\text{m}$ to $390 \pm 10 \mu\text{m}$, $n=5$, $p<0.01$). Extracellular K^+ mediated constriction was also inhibited by 9-phenanthrol. Extracellular K^+ (60 mM) evoked an increase in contractile force in the basilar arteries of the rat (contractile force from $2.6 \pm 0.9 \text{ mN}$ to $9.3 \pm 1.3 \text{ mN}$, $n=4$, $p<0.01$). This extracellular K^+ mediated constriction was also inhibited by 9-phenanthrol (contractile force from $8.3 \pm 1.4 \text{ mN}$ to $2.9 \pm 0.9 \text{ mN}$, $n=4$, $p=0.02$).

CONCLUSION: Our data suggest that TRPM4

has a major role in the modulation of contraction followed by various agonist stimuli in different arteriolar beds of the rat. TRPM4 may participate in pathological conditions characterized by increased arteriolar tone, such as hypertension.

B/7. EX-VIVO MODELLING OF VASOACTIVE EFFECTS OF SUBARACHNOIDAL HEMORRHAGE ON ISOLATED CEREBRAL ARTERIES

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Keywords: hemorrhagic stroke, subarachnoid hemorrhage, vasomotor, basilaris, isolated artery

PURPOSE: Previous studies reported that acute hemorrhage (stroke, trauma) is followed by an early and delayed vasospasm which inflicts severe damage to the cerebral blood flow. However, the vasoconstrictor effects of the hemolyzed blood (HB) have not yet been characterized. We hypothesized that the tone of the isolated cerebral arteries are substantially increased by HB.

METHODS: Basilar artery (BA) from male rats was isolated and placed in a pressure-myograph chamber. The diameters of vessels were measured by videomicroscopy. During incubation (80 mmHg) a substantial active vasomotor tone (AD) developed. The effect of extravasated blood was modeled by adding HB directly to the chamber. The vasoactive function of vessels was studied by the responses to acetylcholine (ACh 10-4 M), sodium-nitroprusside (SNP 10-4M), nifedipine (10-6M) and CO₂.

RESULTS: The active diameters of BA were $277.5 \pm 11.5 \mu\text{m}$ ($n=9$). HB (200 μl /chamber) significantly decreased the diameter compared to the control (to $187 \pm 7 \mu\text{m}$; $46.3 \pm 3\%$ of AD). In control conditions significant dilatation was induced by ACh, SNP, nifedipine and CO₂ (+19 $\pm$ 4%, +26 $\pm$ 2%,