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INTRODUCTION

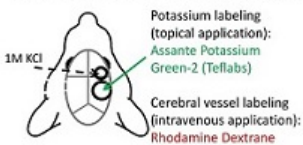
Mild elevation (<20 mM) of extracellular potassium (K_o) due to neuronal activity is one of the most potent vasodilator stimuli in the cerebral vasculature. In contrast, modest increase of brain potassium levels (>20 mM) could rapidly constrict vessels. Spreading depolarization (SD) is a near complete, local depolarization of neurons and glia, which propagates to adjacent cell populations in the cerebral gray matter by means of increasing extracellular K^+ or glutamate concentration. Neuronal depolarization releases a huge amount of K^+ (25-60 mM), which accumulates in the interstitial spaces and further depolarizes the active and the surrounding neurons, resulting a vicious circle that leads to inactivation and reduced excitability in the cortex. In the ischemic brain, recurrent spreading depolarizations are assumed to generate widespread necrosis mediated by insufficient perfusion. Although SD elevates brain K_o to the vasoconstrictive range, its direct impact on the SD-coupled cerebral blood flow (CBF) response is still unclear.

MATERIALS AND METHODS

LIVE BRAIN POTASSIUM IMAGING

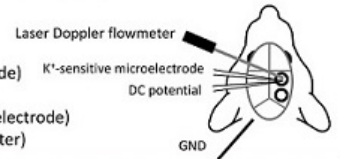
- Animals: C57BL/6 mice (n=6)
- Anesthesia: Avertin (4 mg/kg)
- Two craniotomies
 - Caudal- Imaging (closed)
 - Rostral- SD elicitation (open)
- SD elicitation: 2 μ l 1M KCl

2-photon excitation:
Femto 2D, 690-1024 nm sapphire laser
810 nm: APG-2 and Rhodamine Dextrane



IN VIVO POTASSIUM ELECTROPHYSIOLOGY

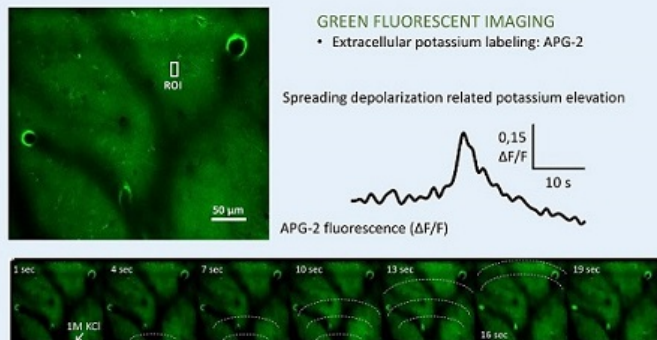
- Animals: C57BL/6 mice (n=8)
- Anesthesia: Isoflurane (1.5-2%) in $N_2O:O_2$
- Two craniotomies
- SD elicitation: 1M KCl
- Acquired parameters:
 - DC potential (microelectrode)
 - extracellular K^+ (potassium sensitive microelectrode)
 - CBF (laser Doppler flowmeter)



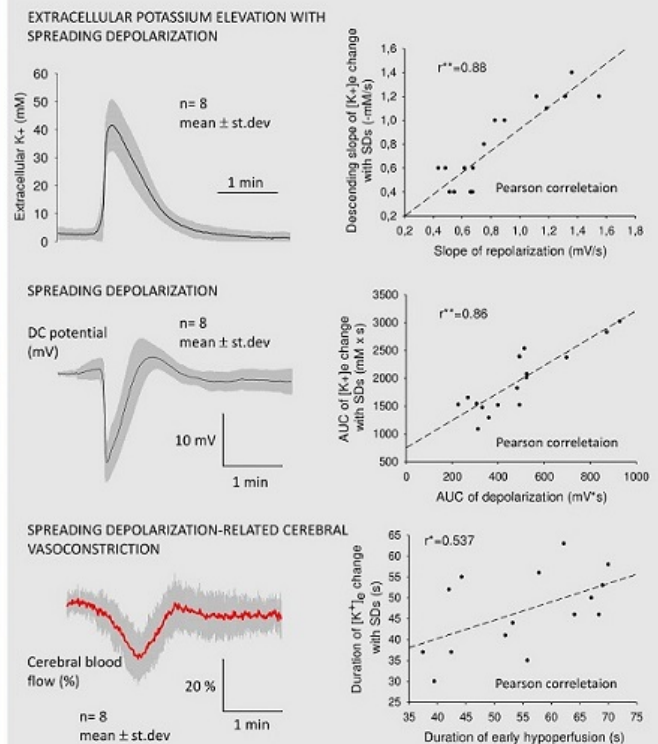
RESULTS

LIVE BRAIN POTASSIUM IMAGING

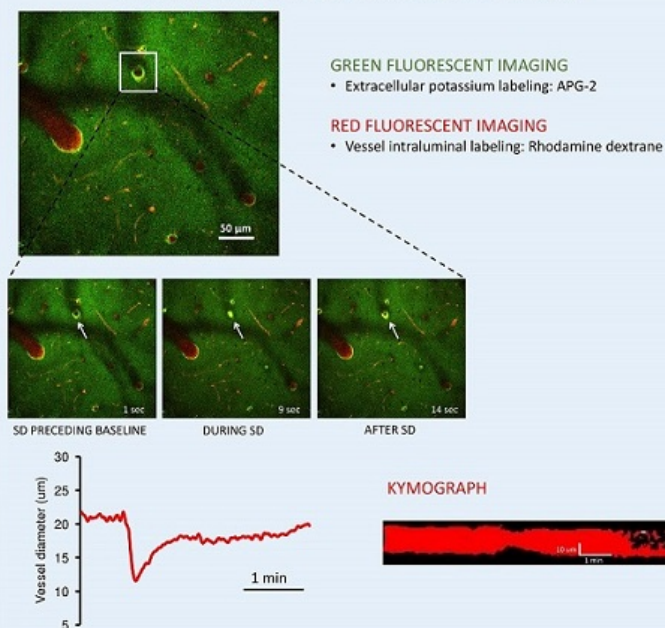
EXTRACELLULAR POTASSIUM WAVE OF SPREADING DEPOLARIZATION



VASOREGULATORY ROLE OF EXTRACELLULAR POTASSIUM LEVELS DURING SPREADING DEPOLARIZATION



MICROVASCULAR EFFECTS OF SPREADING DEPOLARIZATION POTASSIUM WAVE OF SPREADING DEPOLARIZATION CAUSES VASOCONSTRICTION OF CEREBRAL ARTERIOLES



DISCUSSION

We have established a novel technology to assess changes in K_o in the cerebral cortex with two-photon imaging, relying on the fluorescent signal emitted by a K^+ -sensitive dye. Our results indicate that (i) The DC potential signature of SD is strongly dependent on the dynamics of the extracellular concentration of K^+ ; (ii) The extracellular concentration of K^+ elevates over the vasoconstrictive threshold with SD; (iii) SD causes pronounced vasoconstriction in the mouse cerebral cortex; and (iv) The level of interstitial K^+ determines the duration of SD-related vasoconstriction. Overall, the data show the accentuated role of K_o in CBF reductions with SDs, corresponding with vasoconstrictive SD-related CBF responses observed in patients of stroke and traumatic brain injury.

FUNDING

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P41 THE EFFECTS OF ENDOTHELIN-A RECEPTOR ANTAGONISM AND ENDOTHELIN-B RECEPTOR AGONISM IN EXPERIMENTAL SEPSIS

Rutai A, Fejes R, Tallósy S, Poles M, Juhász L, Mészáros A, Boros M, Kaszaki J
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P42 EFFECTS OF ENDOTHELIN-A RECEPTOR ANTAGONISM AND ENDOTHELIN-B RECEPTOR AGONISM ON THE MITOCHONDRIAL FUNCTION IN EXPERIMENTAL POLYMICROBIAL SEPSIS

Tallósy SP, Rutai A, Juhász L, Poles M, Fejes R, Mészáros A, Boros M, Kaszaki J
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P43 KYNURENIC ACID AND ITS NOVEL ANALOGUE SZR-72 DIMINISH THE SEVERITY OF EXPERIMENTAL ACUTE NECROTIZING PANCREATITIS

Balla Z¹, Kui B², Kormányos E², Réka Bálint E², Kiss L¹, Iványi B³, Vécsei L^{4,8}, Fülöp F^{5,9}, Varga G⁶, Harazin A¹⁰, Deli MA¹⁰, Venglovecz V¹¹, Maléth J², Hegyi P^{2,7,12}, Rakonczay Jr. Z¹

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P44 EXCESSIVE ALCOHOL CONSUMPTION INDUCES METHANE PRODUCTION IN HUMANS AND RATS

Tuboly E¹, Molnár R¹, Tókécs T^{1,4}, Turányi RN¹, Hartmann P¹, Mészáros AT¹, Strifler G¹, Földesi I², Siska A², Szabó A³, Mohácsi A³, Szabó G³, Boros M¹

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P45 EXTENDED SYNAPTOTAGMIN 1 MODULATES THE ACTIVITY OF AC8 IN HEK 293 CELLS

Fanczal J¹, Madácsy T¹, Hegyi P^{1,2}, Muellem S³, Maléth J¹

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P46 REMODELING OF CORONARY ARTERY NETWORK DURING QUERCETIN SUPPLEMENTATION

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P47 THE IMPAIRED FUNCTION OF THE PLASMA MEMBRANE CA²⁺ PUMP CAUSES CA²⁺ OVERLOAD AND CELL DAMAGE IN CFTR KNOCK OUT PANCREATIC DUCTAL CELLS

Madácsy T¹, Fanczal J¹, Pallagi P², Rakonczay Z³, Hegyi P^{4,5}, Rázga Z⁶, Gray M⁷, Maleth J¹

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P48 POTASSIUM WAVE OF SPREADING DEPOLARIZATION CAUSES VASOCONSTRICTION IN THE MOUSE CORTEX

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P49 INVESTIGATION OF THE PANCREATIC DUCTAL ION SECRETION IN PANCREATIC DUCTAL ORGANOID CULTURES

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