

Does prostanoid signaling contribute to the evolution of spreading depolarization and the associated cerebral blood flow response?

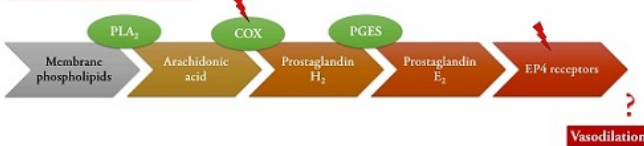
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Conceptual background

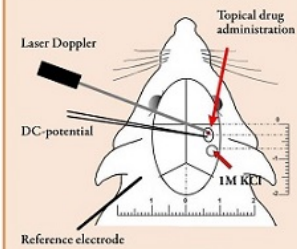
Recurrent spreading depolarization (SD) is a slowly propagating wave of electrical silence in the cerebral gray matter that occurs spontaneously in the ischemic brain. SD is occasionally associated with atypical hemodynamic response, which is thought to contribute to the expansion of the ischemic core by decreasing cerebral blood flow (CBF) and increasing the energy demand of the cells. The significance of prostanoid signaling in neurovascular coupling during somatosensory stimulation is increasingly more appreciated, yet its involvement in mediating the CBF response to SD has remained inconclusive.

Hypotheses driving the study



Experimental approach

Isoflurane-anesthetized Sprague-Dawley rats
Monitoring: MABP and arterial blood gases



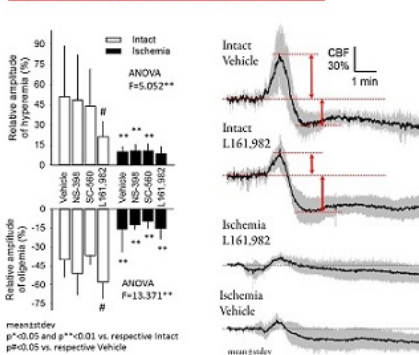
Experimental protocol



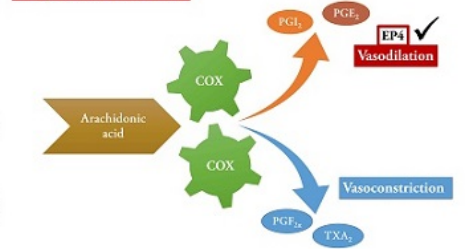
Experimental groups

Experimental group	Pharmacological treatment	Ischemia induction (SHAM or 2VO)	n
1	Vehicle	SHAM	8
2	(1.5% DMSO in aCSF)	2VO	7
3	100 µM NS-398 (COX-2 inhibition)	SHAM	7
4	25 µM SC-560 (COX-1 inhibition)	2VO	6
5	25 µM SC-560 (COX-1 inhibition)	SHAM	7
6	1 µM L161,982 (EP4 receptor antagonist)	2VO	7
7	1 µM L161,982 (EP4 receptor antagonist)	SHAM	6
8	Vehicle	2VO	12

Results: CBF response to spreading depolarization



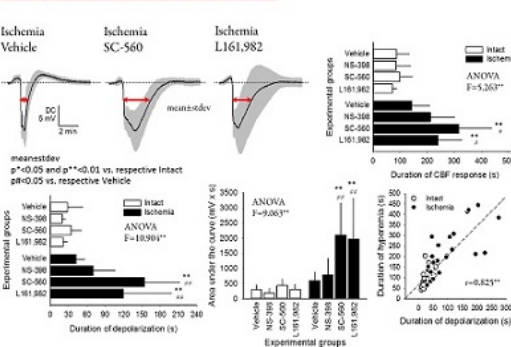
Interpretation: intact cortex



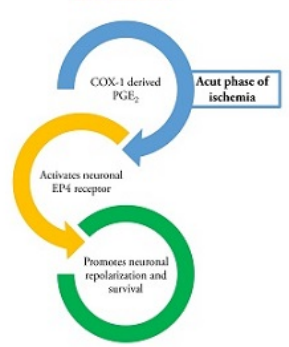
Interpretation: ischemic cortex



Results: kinetics of spreading depolarization



Interpretation



Significance of the results

The restriction of SD evolution in neurological intensive care patients has become a central objective. So far, the inhibition of NMDA receptors by ketamine administration has been the only strategy of promise to decrease the likelihood of SD occurrence. The data presented here demonstrate for the first time that the inhibition of COX-1 or the blockade of the EP4 receptors of PGE₂ remarkably increases SD duration in the early phase of cerebral ischemia. These significant observations may initiate a new line of investigation to dissect specific components of prostanoid signaling that may play a defining role in sustaining or aborting SD in the ischemic nervous tissue.

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SESSION TIME: 09:30 - 13:00
PRESENTATION TIME: 11:30 - 13:00

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