Non-invasive in vivo human model of the involvement of human epidermal mitochondria in the early post-ischaemic preconditioning

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Background
The repetitive ischemia and reperfusion may induce cell and tissue protection against the reperfusion-related injuries. This process, known as the post-ischaemic preconditioning (IPC), can be observed in different tissues and organs, including heart, muscles or skin. During ischemia leading to cellular hypoxia/anoxia, the amount of NADH gradually increases. During the reperfusion and restoration of oxygen, the amount of NADH drops down as it turns to NAD+ in the process of passing both hydrogen and electrons to oxygen within mitochondria. NADH can emit fluorescence light at the length of 460 nm, thus by measuring such fluorescence, it is possible to quantify the amount of NADH. This study aimed to assess non-invasively the presence of IPC in the human skin by quantifying the flow-mediated skin fluorescence at the length of 460 nm (FMSF) at rest, during repeated ischemia and reperfusion episodes.

Methods:
We studied 99 healthy people (23.6±/-7.8 years old; 55 women) who underwent a non-invasive and in vivo measurement of the FMSF at rest, and then three times during 100-second brachial artery occlusions (blood pressure cuff inflated to the pressure 60 mmHg above each subject's systolic blood pressure) producing forearm ischemia (Isch), and the subsequent 10-minute reperfusion (Rep). To study IPC effects on the NADH, we compared the reperfusion related changes in FMSF after the first and third episode of ischemia by measuring: (1) the reperfusion magnitude (RepM), (2) the contribution of the reperfusion to the total change in FMSF during ischemia and reperfusion (RepCont), and (3) the half-time of the recovery of FMSF to the baseline during the reperfusion (tRep). Results were compared by the paired nonparametric Wilcoxon test and presented as median and the 25th-75th percentile (IQR).

Results:
Comparing with the first post-ischaemic changes, the third ischaemia caused a significant increase in the RepM from 14.6 (IQR: 12.3-18.2)% to 17.3 (IQR: 12.7-21.4)% (p=0.0007), the RepCon from 64.0 (IQR: 55.1-80.8)% to 69.1 (IQR: 58.5-81.0)% (p=0.0176), and a shortening of the tRep from 27.2 (IQR: 17.7-41.8) s to 22.1 (IQR: 15.3-40.0) s (p=0.0087).

Conclusions:
We show in an in vivo human model that the short repetitive ischemia and reperfusion episodes may produce acute changes in FMSF corresponding to the post-ischaemic
preconditioning. In more details, the IPC is accompanied by the significantly stronger and faster post-ischaemic recovery of the skin fluorescence to the baseline level. Further physiological and clinical studies are required to explore and better understand this model, including the effects of non-pharmacological and pharmacological treatment.