

SCA 136**TRIGGERING AND MEDIATING ROLES OF MITOCHONDRIA
IN ANESTHETIC PRECONDITIONING**

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Background: Mitochondrial changes that characterize the heart after anesthetic preconditioning (APC), or the mechanisms by which mitochondrial triggering factors lead to protection are unknown. We hypothesized that generation of reactive oxygen species (ROS) during APC is required to initiate the mitochondrial protective effects, and that APC leads to improved mitochondrial electron transport chain function and cardiac function during reperfusion.

Methods: Isolated guinea pig hearts were subject to 30 min ischemia and 120 min reperfusion. Prior to ischemia hearts were either untreated (I/R), or treated with sevoflurane (APC), in the presence or absence of the ROS scavenger tiron (TIR), or the superoxide dismutase mimetic MnTBAP (TBAP). Intracellular ROS were

measured by spectrofluorometry using the fluorescent probe dihydroethidium (DHE). In another series of experiments, using the same protocol, hearts were reperfused for only 5 min and removed for measurement of ATP synthesis by luciferin-luciferase luminometry and ROS generation by dichlorohydro-fluorescein (DCF) fluorescence in isolated mitochondria.

Results: APC improved cardiac function and reduced infarction. Tiron or MnTBAP abrogated the protection afforded by APC. Mitochondrial ATP synthesis was decreased by 70±3% after IR alone, by only 7±3% after APC, by 69±2% after APC+TIR, and by 71±3% after APC+TBAP. Mitochondrial ROS formation (DCF) increased by 48±3% after IR alone, by only 0±2% after APC, by 43±4% after APC+TIR, and by 46±3% after APC+TBAP. ROS generation (DHE) was increased in I/R group at 120 min RP. This was attenuated by APC but this protective effect was abrogated in APC+TIR and APC+TBAP groups.

Conclusions: The results indicate that ROS are central both in triggering and mediating APC, and that the mitochondrion is the target for these changes.