REDOX PROPERTIES OF ATP-SENSITIVE K^+ CHANNELS IN BRAIN MITOCHONDRIA

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Several studies have shown that mitochondrial ATP-sensitive K^+ channel (mitoK$_{ATP}$) opening prevents ischemia/reperfusion injuries in heart, in a manner involving changes in redox state. Brain mitoK$_{ATP}$ channel activation also protects against ischemic damage and excitotoxic cell death. Since these processes are associated with changes in mitochondrial redox state, we studied the redox properties of brain mitoK$_{ATP}$. MitoK$_{ATP}$ activation during excitotoxic cell death prevented cellular accumulation of reactive oxygen species (ROS). Furthermore, mitoK$_{ATP}$ activation in isolated brain mitochondria strongly prevented H_2O_2 release by these organelles. Interestingly, the activity of mitoK$_{ATP}$ was highly dependent on redox state: while thiol reductants prevented mitoK$_{ATP}$ activity, endogenous and exogenous ROS activated the channel. Indeed, the use of substrates that lead to higher levels of mitochondrial ROS release closely correlated with enhanced K^+ transport activity through this pathway. Altogether, our results indicate that brain mitoK$_{ATP}$ is a redox-sensitive channel that controls mitochondrial ROS release, preventing cellular damage promoted by mitochondrial ROS during excitotoxicity.

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