Oxytocin signalling involved in cardiac protection against ischemia-reperfusion

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Abstract
The oxytocin (OT) treatment prevents heart against ischemia. Here we investigated heart-derived H9c2 cells in simulated ischemia-reperfusion (I/R) experiments in order to examine the mechanisms of the OT-induced cardiac protection. I/R was induced in an anesthetized group with 2 hours and followed by 2 hours of reperfusion. I/R was compared to controls. OT was added to cells in the presence of ischemia. OT induced an increase in cardiac troponin T (cTnT) production by H9c2 cells at 60.9 ± 1.7% (RT assay) over control values of 6.3 ± 0.3 ng/mL. OT also induced an increase in cell viability of 32%. These findings suggest that OT may be a potential therapeutic agent for ischemia-reperfusion injury.

Results

OT induces apoptosis in H9c2 cells cultured in simulated ischemia-reperfusion (I/R)

OT induces a short-lived ROS burst in normoxic conditions and prevents ROS formation following I/R

Experiments with specific inhibitors showed that protein kinase G and glycerol-3-phosphate cytosolic OT mediators of cell protection in simulated I/R

Effect of OT and arginine-vasopressin (AVP) agonists and antagonists on Bcl cell viability after simulated I/R

Analysis of phosphorylated ERK2 and NO release in H9c2 cells treated with OT

OT treatment causes Akt phosphorylation and the re-localization of mitochondrial marker OXPHOS III within or around cells' nuclei

Highlights
- We have demonstrated that treatment with oxytocin (OT) prevents the lethal reperfusion injury of H9c2 cardiomyoblasts.
- OT-mediated cardioprotective signals are transferred from the cell surface to mitochondria and nuclei as part of multimolecular complexes containing pro-survival kinases.
- We propose that OT evokes mitochondrial reactive oxygen species generation in H9c2 cardiomyoblasts via Ca2+-dependent mechanism, leading to activation of ERK1/2, PI3K/Akt, and eNOS with rapid NO release.

Mechanisms?