Inhibition of Gi Causes NOS-III Dependent Attenuation of Inotropic and Chronotropic Responses to Beta-Adrenergic Stimulation in Murine Atria In-Vitro

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Methods:

Heart rate and contractile measurements in vitro

- Mice were injected (i.p.) with pertussis toxin (30µg/kg) or saline 3 days before experimentation
- Isolated murine atria in organ bath (3ml, 37°C) to measure heart rate and contraction size (in atria paced at 540bpm)
- Doses of NA (0.5µmol/L) followed by CCh (0.5µmol/L)
- Repeat doses following equilibration with NOS inhibitor (L-NA, 100µmol/L) or ion channel inhibitors nifedipine (L-type calcium channel inhibitor, 0.25µmol/L) or ZD7288 (hyperpolarisation-activated current channel inhibitor, 0.25µmol/L)

Conclusions:

- Cardiac muscarinic signalling requires intact Gi signalling for functional autonomic control (including signals mediated by NO)
- Inhibition of Gi increases atrial NOS-III expression and nifedipine-sensitivity and attenuates the response to noradrenaline by a NO-dependent mechanism

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