Regulation of high voltage-operated Ca^{2+} channels by G_i-protein coupled receptors

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The classic neurotransmitters, dopamine and γ-aminobutyric acid (GABA) are acting through G_i-protein coupled receptors and inhibit α-MSH secretion and Ca^{2+} oscillations of pituitary melanotrope cells in *Xenopus laevis*. The Ca^{2+} oscillations arise from Ca^{2+}-influx through high voltage-operated Ca^{2+} channels (VOCC). Previously, we showed L-, N-, P/Q- and a toxin-insensitive R-type VOCC on *Xenopus* melanotropes. Ca^{2+} current (I_{Ca}) is partly inhibited by activation of D_2- and $GABA_B$-receptors. In this study we determined which types of VOCC are affected. Using the specific VOCC inhibitors, ω-conotoxin GVIA, ω-agatoxin IVA and nifedipine, it is demonstrated that D_2-receptor activation inhibits N-type and R-type currents. In contrast, $GABA_B$-receptor activation inhibits only the R-type current. Both D_2 and $GABA_B$ inhibitions of the R-type current were reversed by pre-pulse facilitation. We therefore conclude that the R-type current is inhibited by D_2- and $GABA_B$-receptor activation through a G_i-protein-β/γ subunit-membrane-delimited pathway. The additional inhibition of the N-type Ca^{2+} current following D_2-receptor activation was not reversed by the pre-pulse facilitation. Most likely, this inhibition is through G_i-protein-α-subunit regulatory pathway.
In conclusion, in *Xenopus* melanotrope cells, either one or more types of VOCC are inhibited, dependent on the type of G_i-protein-coupled receptor that is activated. Depending on the receptor type, inhibition is more or less pronounced.

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Session 16, Wednesday June 2, speaker