Dopamine binds a D1-D2 heteromer coupled to \(G_q\) to activate phospholipase C to increase dendritic branching in the developing Medium Spiny Neuron

Lauren Pelkey Nguyen Lu Neema Moin Afshar Justin Campagna Daniel Tam Lorene Lanier  
Department of Neuroscience

Background

Dopamine (DA) enhances MSN dendritic branching by 19 div (Penrod et al., 2015)

Methods

Modified from Penrod et al. 2011

Results

Fig. 1. 10 \(\mu\)M SKF82958 and 10 \(\mu\)M SKF82958 & 10 \(\mu\)M quinpirole increase dendritic branching proximal to the soma but decrease it at distal ring loci.

Fig. 2. \(G_q\) activation by adding 12.5 nM Clozapine N-oxide to DREADDs expressing MSNs replicates the effects of DA, however, additional controls are necessary to ensure CNO is not being converted to clozapine in vitro (Gomez et al., 2017).

Fig. 3. 100 nM PLC antagonist U73122 doesn’t impact branching. U73122(+)DA effectively blocks DA’s effects

GOAL: Find the mechanism by which DA increases dendritic branching

E16 mouse brain

Sholl Analysis

D1-D2 heteromer MSN

1. \(G_q\) dependent pathway:

Two possible mechanisms for dopamine signaling:

Our data suggest that DA increases branching by a \(G_q\) and PLC dependent pathway

2. \(G_q + G_i\) dependent pathway:

Modified from Molecular Biology of the Cell, 6th edition

Modified from Purves Neuroscience 5th Edition

Modified from Penrod et al. 2011

1. G\textsubscript{q} dependent pathway:

2. G\textsubscript{q} + G\textsubscript{i} dependent pathway:

D1-D2 heteromer MSN

Modified from Molecular Biology of the Cell, 6th edition