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Absence of sGi2 protein role in neuronal apoptosis during rat brain development

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Treatment with dopamine and other dopamine D2 receptor agonists has been shown to induce cell death through activation of caspase-3 pathway. However, initial step that leads to the activation of caspase-3 in D2 receptor-mediated apoptotic pathway remains unclear. Recently, we have shown that a spliced variant of Gαi2 protein (sGαi2) forms intracellular complex with D2 receptors by protein-protein interaction and that D2 drugs treatment causes the liberation of sGαi2 protein from complex. This unbound form of sGαi2 protein was able to activate caspase-3 pathway in baby hamster kidney (BHK) cells. Expression of sGαi2 protein in these cells led to the production of active form of caspase-3 and activation of p38 mitogen-activated protein kinase (p38 MAPK) and extracellular regulated kinase 1/2 (ERK1/2). Co-expression of sGαi2 with either D2 short (D2S) or D2 long (D2L) isoforms of dopamine D2 receptors blocked the activation of caspase-3 pathway. These results demonstrated that high level of unbound sGαi2 protein can promote the cell death and engagement of this protein with D2 receptors can prevent this activity. Thus, it was proposed that balance between sGαi2 protein and D2 receptor plays a critical role in cell death. We have tested this theory in rat during brain development period, a model known for high rate of apoptosis.

We have used rats of postnatal age of 0 to 90 days of Wistar Han strain. In each age group, 10 rats were included. Whole brain obtained from these rats were homogenized and both nuclear and membrane fractions were treated with SDS sample buffer for further immunoblot studies. Statistical analysis of the physiologic variables was performed using a one way ANOVA followed by Tukey-Kramer post hoc tests. In our experiments, we found that the proportion of D2 receptor abundance was higher than sGαi2 protein even when the active caspase-3 level was higher. These observations suggest no relationship of caspase-3 activation with either sGαi2 protein or D2 receptor during rat brain development.

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