(S)-3,5-DHPG: A Review

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ABSTRACT

3,5-dihydroxyphenylglycine (3,5-DHPG) was the first agonist shown to be group I metabotropic glutamate receptor selective with its agonist effects residing exclusively in the S-isomer. Some results suggest that (S)-3,5-DHPG may be a partial agonist of mGluR$_{1a}$ and mGluR$_{5a}$ in neurons and astrocytes. It has been reported that (S)-3,5-DHPG can, under certain conditions, interact with NMDA receptors. (S)-3,5-DHPG exerts different effects on second messengers in adult and neonatal tissues. It stimulates phosphoinositide hydrolysis in a dose-dependent manner in both the adult and neonate hippocampus, inhibits stimulated cAMP levels in the adult and enhances the cAMP in the neonate. It is an effective antagonist of mGluRs linked to phospholipase D (PLD) in the adult and an agonist in the neonate brain or astrocyte cultures. (S)-3,5-DHPG induces elevation of [Ca$^{2+}$], and regulates multiple subtypes of Ca$^{2+}$ channels. This agonist of group I mGluRs may modulate neurotransmitters release, reflecting the diversity of mechanisms involved. Depending on the dose, (S)-3,5-DHPG enhances or decreases excitatory postsynaptic potentials (EPSPs) and under appropriate conditions it can induce long-term depression (LTD) and long-term potentiation (LTP). Some studies suggested a therapeutic role for (S)-3,5-DHPG in neuronal injury, regulation of intestinal motility and secretion, learning and memory processes and in cardiovascular system.

(S)-3,5-DHPG may be useful as a cognitive enhancing agent in memory impairment associated with ischemia or hypoxia. Recent investigations suggested possible beneficial effects of (S)-3,5-DHPG in Alzheimer’s disease.