Differentiated human midbrain-derived neural progenitor cells express excitatory strychnine-sensitive glycine receptors containing \( \alpha_2 \) subunits.

Abstract:

Human fetal midbrain-derived neural progenitor cells (NPCs) may deliver a tissue source for drug screening and regenerative cell therapy to treat Parkinson's disease. While glutamate and GABA(A) receptors play an important role in neurogenesis, the involvement of glycine receptors during human neurogenesis and dopaminergic differentiation as well as their molecular and functional characteristics in NPCs are largely unknown. Here we investigated NPCs in respect to their glycine receptor function and subunit expression using electrophysiology, calcium imaging, immunocytochemistry, and quantitative real-time PCR. Whole-cell recordings demonstrate the ability of NPCs to express functional strychnine-sensitive glycine receptors after differentiation for 3 weeks in vitro. Pharmacological and molecular analyses indicate a predominance of glycine receptor heteromers containing \( \alpha_2 \) subunits. Intracellular calcium measurements of differentiated NPCs suggest that glycine evokes depolarisations mediated by strychnine-sensitive glycine receptors and not by D-serine-sensitive excitatory glycine receptors. Culturing NPCs with additional glycine, the glycine-receptor antagonist strychnine, or the Na\(^{+}\)-K\(^{+}\)-Cl\(^{-}\) co-transporter 1 (NKCC1)-inhibitor bumetanide did not significantly influence cell proliferation and differentiation in vitro. These data
indicate that NPCs derived from human fetal midbrain tissue acquire essential glycine receptor properties during neuronal maturation. However, glycine receptors seem to have a limited functional impact on neurogenesis and dopaminergic differentiation of NPCs in vitro.