ABSTRACT

Promotion of neuronal differentiation through activation of N-methyl-D-aspartate receptors transiently expressed by undifferentiated neural progenitor cells in fetal rat neocortex

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Neural progenitor cell is a generic term for undifferentiated cell populations composed of neural stem, neuronal progenitor, and glial progenitor cells with abilities for self-renewal and multipotentiality. In this study, we have attempted to evaluate the possible functional expression of N-methyl-D-aspartate (NMDA) receptors by neural progenitor cells prepared from neocortex of 18-day-old embryonic rats. Cells were cultured in the presence of basic fibroblast growth factor (bFGF) for different periods up to 12 days under floating conditions. Reverse transcription-polymerase chain reaction and fluorescence imaging analyses revealed transient expression of functional NMDA receptors in neurospheres formed by clustered progenitors during the culture with bFGF. A similarly potent increase was seen in the fluorescence intensity after brief exposure to NMDA in cells differentiated after the removal of bFGF under adherent conditions, and an NMDA receptor antagonist invariably prevented these increases by NMDA. Moreover, sustained exposure to NMDA not only inhibited the formation of neurospheres when exposed for 10 days from day 2 to day 12 but also promoted spontaneous and induced differentiation of neurospheres to cells immunoreactive for a neuronal marker protein on immunocytochemistry and Western blotting analyses. These results suggest that functional NMDA receptors may be transiently expressed to play a role in mechanisms underlying the modulation of proliferation along with the determination of subsequent differentiation fate toward a neuronal lineage in neural progenitor cells of developing rat

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