

HUMAN ASTROCYTES CAN BE INDUCED BY IMIPRAMINE TO DIFFERENTIATE INTO CELLS WITH NEURONAL PHENOTYPE

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In mammals, neurogenesis continues throughout the life and multipotent stem cells can be isolated from the adult brain in two principal sites: the subventricular zone (SVZ) of the lateral ventricles, and the hippocampus. Several recent studies have expanded our conception of the role of astrocytes in neurogenesis and gliogenesis. In fact it has been proposed that astrocytes may contribute to this phenomenon not only as a source of trophic substances regulating neurogenesis, but also as the stem cells themselves. Moreover, we observed that human mature astrocytes in vitro treated with a cocktail of protein kinases activators and FGF-1 can differentiate into cells with a neuronal phenotype. Antidepressant drugs have been shown to increase neurogenesis in the adult rodent hippocampus. However mechanism that determine an increase of neurons after antidepressant treatment, has not been clarified. In order to better understand the role of astroglia in antidepressant induced neurogenesis, primary astrocyte cultures were established from human fetal brain. These cultures were extremely pure and 99% of cells were GFAP+. After 3-4 weeks in culture, cells were treated with the antidepressant imipramine. Cell morphology was rapidly modified by the treatment. In fact after 5 hours astrocytes changed their shape from a flat protoplasmic fibroblast-like morphology to cells with round body and long and thin processes. At different times from the treatment we analyzed the cultures for cells expressing neuronal and glial markers. Immunocytochemistry showed that cells were positive for nestin. On the other hand treatment induced the expression of neurofilaments (NF) and neuron specific enolase (NSE). GFAP was expressed in all untreated cells, but after 24 hours we observed some cells GFAP-/NF+ and GFAP+/NF+. These data were confirmed by western blot and RT-PCR.

These results confirm the neurogenic potential of astrocytes and suggest that antidepressant treatment induce astrocytes to differentiate into neurons.