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BDNF and FGF-2 in the development of human striatal primordium. An in vitro study

Erica Sarchielli[1], Mirca Marini[1], Ferdinando Paternostro[1], Emanuela Barletta[2], Pasquale Gallina[3], Gabriella B. Vannelli[1]

Depts [1]Anatomy Histology and Forensic Medicine, [2] Pathology, [3] Neurosurgery, University of Florence, Italy

Rebuilding brain structure and neural circuitries by transplantation of fetal tissue is a strategy to repair the damaged nervous system and is currently being investigated using striatal primordium in Huntington's disease (HD) patients (Lancet Neurol 2011;10:83-98).

We recently demonstrated that neuroblasts of a striatal primordium can develop within the diseased striatum of HD patients and move into the brain after neurotransplantation. Primordium development resulted in the building of a new structure with both morphological and functional imaging features of the corresponding mature structure, suggesting graft progression into striatal differentiation (Exp Neurol 2008; 213: 241-244; Exp Neurol 2010; 222: 20-41).

During development, striatal primordium originates in the ganglionic eminence which represents a conspicuous domain of the telencephalic proliferative zone and persists throughout fetal life. The striatal neuronal precursors divide, migrate, and differentiate establishing both intrinsic connections and afferent and efferent connections responsible for the basal ganglia circuits (Anat Rec 2002;267:191-195). The mechanisms underlying the striatal ontogenesis remains largely unknown.

Neurotrophic factors have pleiotropic effects on neuronal development and synaptic plasticity that underlie circuit formation and cognitive function. The demonstration of their reduced availability in diseased brain indicates that they play a role in various neurological disorders (Science 2001;293:493-498; PNAS 2005; 102;18189-18194).

To determine whether BDNF or FGF-2 can represent molecules that regulate neurogenesis and differentiation of striatal primordium, we used primary cell cultures from human ganglionic eminence isolated at the onset of striatum development in vivo. These primary cultures contained both stem cells as well as striatal precursors or members of maturing neuronal/non-neuronal cells. In addition, the cells express gene and protein of BDNF and FGF-2 and their cognate receptors. These neurotrophic factors promote specific environmental cues and distinct receptor-mediated signaling pathways for multiple aspects of the biology of striatal precursors, including survival, neurogenesis and migration.

Keywords: BDNF, FGF-2, striatal primordium, transplantation