Towards mobilizing the brain's own neural stem cells to restore striatal dysfunction in Parkinson patients.

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Research question and background

Neural stem cells (NSCs) shape the brain during development by differentiating into different specialized brain cell types including neurons, astrocytes and oligodendrocytes. It is now widely accepted that new neurons are born throughout life. The subventricular zone (SVZ) and the dentate gyrus of the hippocampus are considered to be the classical neurogenic regions in the adult human brain. It is this characteristic that holds a promise for future therapy for neurodegenerative disorders such as Parkinson's disease (PD). In PD, striatal depletion of dopamine is underlying the movement problems. Since the striatum is neighboring the SVZ, NSCs that are present in the SVZ are an attractive target to develop future PD therapies based on activating the brain's own repair capacity. Our group showed that NSCs are still present in the brains of PD patients and that these cells are still able to proliferate and differentiate *in vitro.* However, a prerequisite for therapy based on endogenous NSCs is to know more about the characteristics of these NSCs in the elderly and diseased brain.

Methods and tissues used

The hypothesis is that the SVZ NSCs express specific receptors that can be stimulated by growth factors in the CSF to increase neurogenesis leading to repair of the striatal dysfunction. To study this, we have established a technique to specifically isolate and culture adult human NSCs from the post-mortem human SVZ of elderly donors. These cells formed neurospheres and were able to differentiate into neurons, astrocytes and oligodendrocytes. We use this unique method to isolate NSCs from the SVZ of elderly control donors and PD patients and we will compare these cells based on proliferation and differentiation models and microarray and we will create cell-lines.

Results and conclusion

Mobilizing the endogenous SVZ NSCs to replenish striatal dopamine is an attractive approach to alleviate the motor symptoms in PD patients. Our novel technique to isolate and culture these cells from the patient's brain will allow, for the first time, extensive molecular and cellular analysis of these cells, which is essential to develop future therapies based on activating the brain's own repair capacity.