STEM CELL AND NEUROTROPHIC FACTORS IN ACUTE ISCHEMIC STROKE THERAPY

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Cerebral plasticity has capacity of repair itself and can therapeutically enhanced via rehabilitation or stimulation and administration of trophic factors (BDNF, FGF, VEGF), but also the exogenous administration of cellular material.
Neuropharmacological agents such as trophic factors and growth factors which might promote one or more repair mechanisms can improve the functional status following a stroke, alone or combined.
In our laboratory, in experimental stroke models in rats, exogenous i.p. administration of cerebrolysin in monotherapy shows efficacy in the neurological recovery, reduction in neuronal death, increase cell proliferation, increase VEGF and decrease inflammatory response in an experimental model in rats. We find similar results with citicoline.
On the other hand, several cell lines have been used: embryonic, hematopoietic and MSCs. Bone marrow derived MSCs seem to be the most widely used, being multipotent and capable of aiding the repair of tissues, easy to isolate and the beneficial effects of administration in experimental studies have been described with good results. In our laboratory, the allogenic administration of Bone marrow derived MSCs and adipose tissue (ASCs) by different hematic routes, intravenous (iv) and intracarotid (ic), in the acute phase, have demonstrated equal effectiveness on neurological recovery, brain protection and repair. Since iv administration was less hazardous, it is probably the best route to be used in translational applications. However, using the iv administration route there was neither migration to the lesion zone nor the formation of cell niches. Therefore, it might not be necessary that the stem cells migrate and graft onto the lesion site to obtain a good neurological improvement.
Moreover, we aimed to know if the combined treatment with trophic factors and MSCs in ischemic stroke could weight the previous benefit, but no synergic effect could be found.
After that, we hypothesised that the pre-treatment of MSCs with trophic factors before the iv administration in ischemic stroke animal models could weight the therapeutic effect. In this sense, preliminary *in vitro* data suggested that cerebrolysin pre-treatment of mesenchymal stem cells (MSCs) promotes transdiferentation toward neuronal progenitors at 24 h and continue up and increase at 72h.
In conclusion, all these treatments show efficacy in the neurological recovery, decrease neuronal death and increase cellular proliferation and probably act on the neurogenesis, angiogenesis, synaptogenesis. They could be a good therapeutic option in the stroke treatment, but it is necessary to develop news studies to can be used in translational applications in humans.