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EFFECT OF AMNIOTIC FLUID AND BONE MARROW STEM CELL THERAPY ON BLADDER DYSFUNCTION IN A PARKINSON'S DISEASE MODEL

Hypothesis / aims of study
Parkinson's disease (PD), a neurodegenerative disorder characterized by the loss of dopaminergic neurons, is one of the most common neurological diseases causing lower urinary tract dysfunction. Different cell types have been tested as an alternative therapy for PD, focusing on the motor function. We evaluated the effect of human amniotic fluid (hAFS) and bone marrow stem cells (hBMSC) on bladder dysfunction in a rat model where urodynamic changes were induced by unilateral injection of 6-hydroxydopamine (6-OHDA), a dopaminergic neurotoxin, into the medial forebrain bundle (MFB), mimicking the late phase of PD.

Study design, materials and methods
96 athymic nude female rats (150-200g) were injected with 8µg 6-OHDA into the right MFB. They were divided into 3 treatment groups (32 animals/group) and after 2 weeks they were injected into the same site with: 1. hAFS (10^5 cells/4µL); 2. hBMSC (10^5 cells/4µL); or 3.vehicle (4 µL) (sham). The human SC were transfected with GFP(+) lentivirus prior to the injections. After 3, 7, 14 and 28 days the bladder function of 8 animals from each group was analyzed by conscious cystometry. All the animals were euthanized after cystometry and their brains were extracted for further studies. Two groups of six age-matched healthy controls (non-lesioned) underwent cystometry in order to provide a baseline comparison data.

Results
Three days after the cell or vehicle injections, all 3 groups showed urodynamic changes compared to the first group of age-matched healthy controls, consisting of overactivity and high pressures. At 7 days, the same pattern was observed. Changes in bladder function were observed by 14 days after cell injection. AFS and BMSC groups exhibited significantly higher bladder capacity, and lower micturition frequency and threshold pressure compared to sham animals. Moreover, BMSC group showed significantly higher micturition volume and bladder compliance, and lower intermicturition pressure. At 28 days, these differences subsided and AFS and BMSC groups had similar cystometric parameters compared to sham animals. The GFP(+) cells were seen in the brain sections in the area of injection after 3 and 7 days. At 14 days only a few cells could be observed, in a more caudal position. At 28 days no cells were seen.

Interpretation of results
Unilateral injection of 6-OHDA into the MFB caused bladder dysfunction, which was consistent in sham animals throughout the study follow-up. AFS and BMSC injection into the site of lesion ameliorated the bladder dysfunction after 2 weeks. This effect was temporary, since after 4 weeks there were no differences in cystometric parameters among those groups and sham animals. The cells appeared to caudally migrate along the MFB in the direction of the substantia nigra, where the dopaminergic cell bodies are located. As opposed to integration, cells may act on the injured environment via cell signalling.

Concluding message
Cell therapy with AFS and BMSC temporarily ameliorated bladder dysfunction in a PD model induced by unilateral lesion of 6-OHDA. Identification of specific mechanisms of action and optimization of cell viability are subjects for further studies.

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