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Intranasal administration of mesenchymal stem cells ameliorates the abnormal dopamine transmission system and inflammatory reaction in the R6/2 mouse model of huntington disease [Abstract]

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Intravenous delivery of bone marrow mesenchymal stem cells in a transgenic mouse model of Alzheimer's disease

L. Danielyan, S. Steinbruecker, A. Lourhmati, M. Buadze, K. Arnold, C. Fabian, A. Stolzing, H.P. Nguyen, M. Schwab.

OBJECTIVES

Bone marrow mesenchymal stem cells (MSC) have been proven experimentally to be efficacious cell candidates for a variety of brain disorders including Alzheimer's disease (AD). Our previous study demonstrated that therapeutic efficacy of intranasally delivered MSC is superior to that of intracerebral MSC transplantation. Here we sought to evaluate the effects of intravenous (i.v.) MSC administration on the spatial memory, microglial activation and amyloid beta degrading enzyme neprilysin in a transgenic mouse model of AD.

METHODS

Mouse eGFP-MSCs vs. vehicle were administered intravenously to 6-month old 3xTg-AD mice. Memory deficit was monitored one week prior and 3 weeks after MSCs transplantation by forced choice alternation T-maze. Brain homogenates were analyzed for the expression of choline acetyltransferase (ChAT), synaptophysin, CD-68, CD206, Iba-1 and neprilysin.

Results

Spatial memory was improved by MSCs in the last week of testing. Western Blot analyses revealed an increase in ChAT and neprilysin in MSC-treated group, while synaptophysin, CD68, CD206 and Iba-1 remained unchanged. In contrast to our previous data on intranasal delivery of MSC showing a successful and efficacious delivery of MSC to the brain (especially to the hippocampus and cortex), eGFP-MSC could not be detected in the brains of 3xTg-AD after intravenous administration.

Conclusions

In a view of the invasiveness of surgical transplantation and consequently low survival of transplanted cells due to the strong inflammatory response to intracerebral injection, the successful establishment of non-invasive delivery methods allowing for repeated cell administration and avoiding inflammation provides an improved strategy for cell-based therapy of central nervous system disorders. Intravenous and intranasal administration of MSCs appear to have in common their influence on the expression of ChAT, neprilysin and markers of microglial activation and phagocytosis. However, the effect of intranasal MSC on the spatial memory and synaptogenesis is superior to that of MSC after i.v. administration. In addition the delivery of cells to the brain by intranasal administration is far more reliable and efficacious than after i.v.