Neuropathic pain correction method using mesenchymal stem cells and cannabinoid receptor CB_2 stimulation

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Introduction

Peripheral neuropathic pain is chronic pain due to damage or dysfunction of the peripheral nervous system. It significantly reduces the quality of life. This pathology affects up to 20% of the adult population, and the number of such patients is growing [1]. Mesenchymal stem cell (MSCs) transplantation is positioned as an effective treatment for neuropathic pain. MSCs can secrete a wide range of bioactive molecules and thus have anti-inflammatory, reparative, and analgesic effects without side effects. Cannabinoid receptors CB_1 and CB_2 may be involved in MSC's actions, and their stimulation will possibly improve the effects of MSCs [2].

Aim

- Selection of the optimal dose of adipose-derived mesenchymal stem cells (ADMSCs) transplantation in the area of peripheral nerve damage.
- Evaluation of the impact of cannabinoid receptors activation and deactivation in analgesic and protective effects of ADMSCs.

Methods

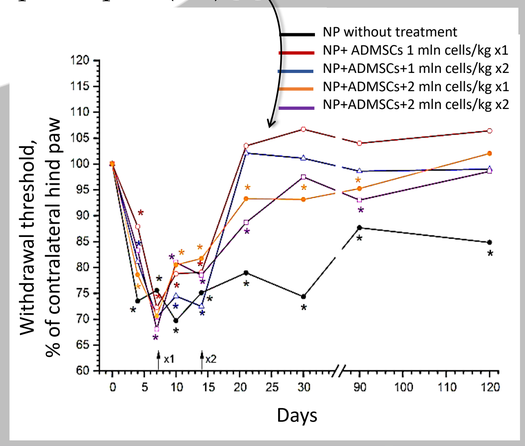
Neuropathic pain (NP) was induced in male Wistar rats by sciatic nerve transection of the left hind limb.

We determined how different doses of ADMSCs injected into the area of sciatic nerve transection on the 7th-day post-surgery will affect nociceptive responses to mechanical (Randall-Sellitto test) and thermal stimuli (Hot-plate test) [3].

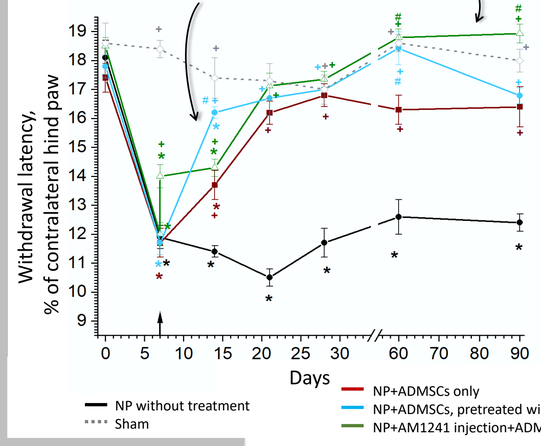
Then, we studied the impact of CB_2 receptors activation by an agonist AM1241 on ADMSCs or the area of sciatic nerve injury on analgesic effects developed after injection of an optimal dose of ADMSCs.

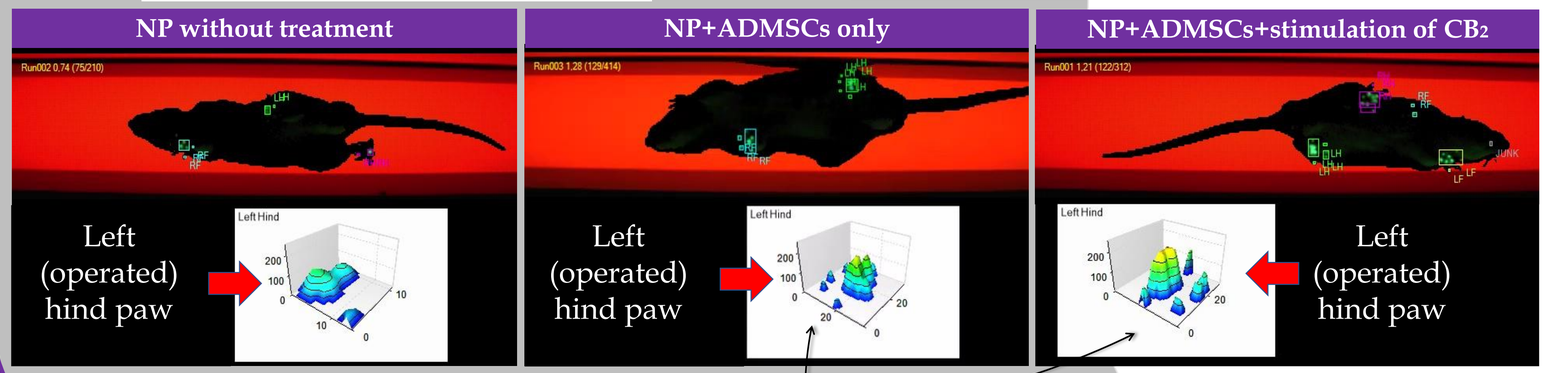
Results

In an in vivo experiment, we determined the mode of ADMSCs administration with the most pronounced and long-lasting analgesic effect in rats with neuropathic pain (NP) [3].



We have found an increase in the analgesic effect of ADMSCs through additional action on cannabinoid CB2 receptors, activated either on stem cells or in the area of sciatic nerve injury.





Using CatWalk XT setup (Noldus, Netherlands), we demonstrated that ADMSCs transplantation effectively abolished disturbances in pain-related gait parameters such as print area, max contact area, and max and mean print intensity of the hind paw with sciatic nerve transection. Stimulation of CB_2 receptors improved the effects of ADMSCs.

Conclusion

The results should be considered while developing protocols for cell therapy in patients with peripheral neuropathic pain of various origins, as well as for their combined use with substances that modulate cannabinoid receptors.

References

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