Frontiers in Pharmacology, 2018, vol.9, NMAR

Allogenic adipose derived stem cells transplantation improved sciatic nerve regeneration in rats: Autologous nerve graft model

Margarita Z., Gilazieva Z., Syromiatnikova V., Mullakhmetova A., Kadyrova G., Nigmetzyanova M., Mikhail S., Igor P., Yagudin R., Rizvanov A.

Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2018 Masgutov, Masgutova, Mukhametova, Garanina, Arkhipova, Zakirova, Mukhamedshina, Margarita, Gilazieva, Syromiatnikova, Mullakhmetova, Kadyrova, Nigmetzyanova, Mikhail, Igor, Yagudin and Rizvanov. We examined the effect of transplantation of allogenic adipose-derived stem cells (ADSCs) with properties of mesenchymal stem cells (MSCs) on posttraumatic sciatic nerve regeneration in rats. We suggested an approach to rat sciatic nerve reconstruction using the nerve from the other leg as a graft. The comparison was that of a critical 10 mm nerve defect repaired by means of autologous nerve grafting versus an identical lesion on the contralateral side. In this experimental model, the same animal acts simultaneously as a test model, and control. Regeneration of the left nerve was enhanced by the use of ADSCs, whereas the right nerve healed under natural conditions. Thus the effects of individual differences were excluded and a result closer to clinical practice obtained. We observed significant destructive changes in the sciatic nerve tissue after surgery which resulted in the formation of combined contractures in knee and ankle joints of both limbs and neurotrophic ulcers only on the right limb. The stimulation of regeneration by ADSCs increased the survival of spinal L5 ganglia neurons by 26.4%, improved sciatic nerve vascularization by 35.68% and increased the number of myelin fibers in the distal nerve by 41.87%. Moreover, we have demonstrated that S100, PMP2, and PMP22 gene expression levels are suppressed in response to trauma as compared to intact animals. We have shown that ADSC-based therapy contributes to significant improvement in the regeneration.

http://dx.doi.org/10.3389/fphar.2018.00086

Keywords

Autologous nerve graft, DRG, IVIS Spectrum, Myelin fibers, PCR, PNI

References

[1] Akbulut, H., Cüce, G., Aktan, T. M., and Duman, S. (2012). Expression of mesenchymal stem cell markers of human adipose tissue surrounding the vas deferens. Biomed. Res. 23, 166-169.

[2] Amici, S. A., Stephanie, A. A., Dunn, W. A., Murphy, A. J., Adams, N. C., Gale, N. W., et al. (2006). Peripheral myelin protein 22 is in complex with alpha6beta4 integrin, and its absence alters the Schwann cell basal lamina. J. Neurosci. 26, 1179-1189. doi: 10.1523/JNEUROSCI.2618-05.2006

[3] Angius, D., Wang, H., Spinner, R. J., Gutierrez-Cotto, Y., Yaszemski, M. J., and Windebank, A. J. (2012). A systematic review of animal models used to study nerve regeneration in tissue-engineered scaffolds. Biomaterials 33, 8034-8039. doi: 10.1016/j.biomaterials.2012.07.056

[4] Bolin, L. M., McNeil, T., Lucian, L. A., DeVaux, B., Franz-Bacon, K., Gorman, D. M., et al. (1997). HNMP-1: a novel hematopoietic and neural membrane protein differentially regulated in neural development and injury. J. Neurosci. 17, 5493-5502.

[5] Carlson, K. B., Singh, P., Feaster, M. M., Ramnarain, A., Pavlides, C., Chen, Z. L., et al. (2011). Mesenchymal stem cells facilitate axon sorting, myelination, and functional recovery in paralyzed mice deficient in Schwann cell-derived laminin. Glia 59, 267-277. doi: 10.1002/glia.21099

[6] Chen, Z., Pradhan, S., Liu, C., and Le, L. Q. (2012). Skin-derived precursors as a source of progenitors for cutaneous nerve regeneration. Stem Cells 30, 2261-2270. doi: 10.1002/stem.1186

[7] Clauser, L., Tieghi, R., Palmieri, A., and Carinci, F. (2013). Adipose-derived stem cells secrete neurotrophic factors. Ann. Oral Maxillofac. Surg. 1:12. doi: 10.13172/2052-7837-1-2-516

[8] Dai, R., Wang, Z., Samanipour, R., Koo, K. I., and Kim, K. (2016). Adipose-derived stem cells for tissue engineering and regenerative medicine applications. Stem Cells Int. 2016:6737345. doi: 10.1155/2016/6737345

[9] Dalamagkas, K., Tsintoua, M., and Seifaliana, A. (2016). Advances in peripheral nervous system regenerative therapeutic strategies: a biomaterials approach. Mater. Sci. Eng. 65, 425-432. doi: 10.1016/j.msec.2016.04.048

[10] D'Angelo, L., De Girolamo, P., Cellerino, A., Tozzini, E. T., Varricchio, E., Castaldo, L., et al. (2012). Immunolocalization of S100-like protein in the brain of an emerging model organism: Nothobranchius furzeri. Microsc. Res. Tech. 75, 441-447. doi: 10.1002/jemt.21075

[11] de Luca, A. C., Faroni, A., and Reid, A. J. (2015). Dorsal root ganglia neurons and differentiated adipose-derived stem cells: an in vitro Co-culture model to study peripheral nerve regeneration. J. Vis. Exp. 96:52543. doi: 10.3791/52543

[12] Donato, R. (2003). Intracellular and extracellular roles of S100 proteins. Microsc. Res. Tech. 60, 540-551. doi: 10.1002/jemt.10296

[13] Erba, P., Mantovani, C., Kalbermatten, D. F., Pierer, G., Terenghi, G., and Kingham, P. J. (2010). Regeneration potential and survival of transplanted undifferentiated adipose tissue-derived stem cells in peripheral nerve conduits. J. Plast. Reconstr. Aesthet. Surg. 63, e811-e817. doi: 10.1016/j.bjps.2010.08.013

[14] Fujiwara, S., Hoshikawa, S., Ueno, T., Hirata, M., Saito, T., Ikeda, T., et al. (2014). SOX10 Transactivates S100B to suppress schwann cell proliferation and to promote myelination. PLoS One 9:e115400. doi: 10.1371/journal.pone.0115400

[15] Furuhashi, M., and Hotamisligil, G. S. (2008). Fatty acid-binding proteins: role in metabolic diseases and potential as drug targets. Nat. Rev. Drug Discov. 6, 489-503. doi: 10.1038/nrd2589

[16] Heine, W., Conant, K., Griffin, J. W., and Höke, A. (2004). Transplanted neural stem cells promote axonal regeneration through chronically denervated peripheral nerves. Exp. Neurol. 189, 231-240. doi: 10.1016/j.expneurol.2004.06.014

[17] Hong, Y. B., Joo, J., Hyun, Y. S., Kwak, G., Choi, Y. R., Yeo, H. K., et al. (2016). A Mutation in PMP2 causes dominant demyelinating charcot-marie-tooth neuropathy. PLoS Genet. 12:e1005829. doi: 10.1371/journal.pgen.1005829

[18] Hoyng, S. A., de Winter, F., Tannemaat, M. R., Blits, B., Malessy, M. J. A., and Verhaagen, J. (2015). Gene therapy and peripheral nerve repair: a perspective. Front. Mol. Neurosci. 8:32. doi: 10.3389/fnmol.2015.00032

[19] Huang, E. J., and Reichardt, L. F. (2001). Neurotrophins: roles in neuronal development and function. Annu. Rev. Neurosci. 24, 677-736. doi: 10.1146/annurev.neuro.24.1.677

[20] Knoll, W., Natali, F., Peters, J., Nanekar, R., Wang, C., and Kursula, P. (2010). Dynamic properties of a reconstituted myelin sheath. Spectroscopy 24, 585-592. doi: 10.3233/SPE-2010-0479

[21] Lee, J. Y., Giusti, G., Friedrich, P. F., Bishop, A. T., and Shin, A. Y. (2016). Effect of vascular endothelial growth factor administration on nerve regeneration after autologous nerve grafting. J. Reconstr. Microsurg. 32, 183-188. doi: 10.1055/s-0035-1563709

[22] Li, J., Parker, B., Martyn, C., Natarajan, C., and Guo, L. (2013). The PMP22 gene and its related diseases. Mol. Neurobiol. 47, 673-698. doi: 10.1007/s12035-012-8370-x

[23] Liu, B., Liu, Y., Yang, G., Xu, Z., and Chen, J. (2013). Ursolic acid induces neural regeneration after sciatic nerve injury. Neural Regen. Res. 8, 2510-2519. doi: 10.3969/j.issn.1673-5374.2013.27.002

[24] Mantyh, P. W., Koltzenburg, M., Mendell, L. M., Tive, L., and Shelton, D. L. (2011). Antagonism of nerve growth factor-TrkA signaling and the relief of pain. Anesthesiology 115, 189-204. doi: 10.1097/ALN.0b013e31821b1ac5

[25] Masgutov, R. F., Masgutova, G. A., Zhuravleva, M. N., Salafutdinov, I. I., Mukhametshina, R. T., Mukhamedshina, Y. O., et al. (2016). Human adipose-derived stem cells stimulate neuroregeneration. Clin. Exp. Med. 16, 451-461. doi: 10.1007/s10238-015-0364-3

[26] Massing, M. W., Robinson, G. A., Marx, C. E., Alzate, O., and Madison, R. D. (2010). "Applications of proteomics to nerve regeneration research," in Neuroproteomics, ed. O. Alzate (Boca Raton, FL: CRC Press).

[27] Michetti, F., and Gazzolo, D. (2002). S100B protein in biological fluids: a tool for perinatal medicine. Clin. Chem. 48, 2097-2104.

[28] Odabas, S., Sayar, F., Güven, G., Yanikkaya-Demirel, G., and Piskin, E. (2008). Separation of mesenchymal stem cells with magnetic nanosorbents carrying CD105 and CD73 antibodies in flow-through and batch systems. J. Chromatogr. B Analyt. Technol. Biomed. Life Sci. 861, 74-80. doi: 10.1016/j.jchromb.2007.11.017

[29] Oh, S. H., Kim, J. R., Kwon, G. B., Namgung, U., Song, K. S., and Lee, J. H. (2013). Effect of surface pore structure of nerve guide conduit on peripheral nerve regeneration. Tissue Eng. Part C Methods 19, 233-243. doi: 10.1089/ten.TEC.2012.0221

[30] Ozdemir, M., Attar, A., Kuzu, I., Ayten, M., Ozgencil, E., Bozkurt, M., et al. (2012). Stem cell therapy in spinal cord injury: in vivo and postmortem tracking of bone marrow mononuclear or mesenchymal stem cells. Stem Cell Rev. 8, 953-962. doi: 10.1007/s12015-012-9376-5

[31] Pelletier, J., Roudier, E., Abraham, P., Fromy, B., Saumet, J. L., Birot, O., et al. (2015). VEGF-A promotes both pro-angiogenic and neurotrophic capacities for nerve recovery after compressive neuropathy in rats. Mol. Neurobiol. 51, 240-251. doi: 10.1007/s12035-014-8754-1

[32] Plewnia, C., Wallace, C., and Zochodne, D. (1999). Traumatic sciatic neuropathy: a novel cause, local experience and a review of the literature. Trauma 47, 986-991. doi: 10.1097/00005373-199911000-00036

[33] Quincozes-Santos, A., and Gottfried, C. (2011). Resveratrol modulates astroglial functions: neuroprotective hypothesis. Ann. N. Y. Acad. Sci. 1215, 72-78. doi: 10.1111/j.1749-6632.2010.05857.x

[34] Ron, M. G., Menorca, B. S., Theron, S., Fussell, B. A., and Elfar, J. C. (2013). Peripheral nerve trauma: mechanisms of injury and recovery. Hand Clin. 29, 317-330. doi: 10.1016/j.hcl.2013.04.002

[35] Ronchi, G., and Raimondo, S. (2017). Chronically denervated distal nerve stump inhibits peripheral nerve regeneration. Neural Regen. Res. 12, 739-740. doi: 10.4103/1673-5374.206638

[36] Salehi, H., Amirpour, N., Niapour, A., and Razavi, S. (2016). An overview of neural differentiation potential of human adipose derived stem cells. Stem Cell Rev. 12, 26-41. doi: 10.1007/s12015-015-9631-7

[37] Santamaria-Kisiel, L., Rintala-Dempsey, A. C., and Shaw, G. S. (2006). Calcium-dependent and -independent interactions of the S100 protein family. Biochem. J. 396, 201-214. doi: 10.1042/BJ20060195

[38] Schachtrup, C., Ryu, J. K., Helmrick, M., Vagena, E., Galanakis, D. K., Degen, J. L., et al. (2010). Fibrinogen triggers astrocyte scar formation by promoting the availability of active TGF-ß after vascular damage. J. Neurosci. 30, 5843-5854. doi: 10.1523/JNEUROSCI.0137-10.2010

[39] Snipes, G. J., Suter, U., Welcher, A. A., and Shooter, E. M. (1992). Characterization of a novel peripheral nervous system myelin protein (PMP-22/SR13). J. Cell Biol. 117, 225-238. doi: 10.1083/jcb.117.1.225

[40] Sullivan, R., Dailey, T., Duncan, K., Abel, N., and Borlongan, C. V. (2016). Peripheral nerve injury: stem cell therapy and peripheral nerve transfer. Int. J. Mol. Sci. 17:E2101. doi: 10.3390/ijms17122101

[41] Suresh, S., Wang, C., Nanekar, R., Kursula, P., and Edwardson, J. M. (2010). Myelin basic protein and myelin protein 2 act synergistically to cause stacking of lipid bilayers. Biochemistry 49, 3456-3463. doi: 10.1021/bi100128h

[42] Trehan, S. K., Model, Z., and Lee, S. K. (2016). Nerve repair and nerve grafting. Hand Clin. 32, 119-125. doi: 10.1016/j.hcl.2015.12.002

[43] Tse, K. H., Novikov, L. N., Wiberg, M., and Kingham, P. J. (2015). Intrinsic mechanisms underlying the neurotrophic activity of adipose derived stem cells. Exp. Cell Res. 331, 142-151. doi: 10.1016/j.yexcr.2014.08.034

[44] Voronina, T. A., Belopol'skaya, M. V., Kheyfets, I. A., Dugina, Y. L., Sergeeva, S. A., and Epshtein, O. I. (2009). Effect of ultralow doses of antibodies to S-100 protein in animals with impaired cognitive function and disturbed emotional and neurological status under conditions of experimental Alzheimer disease. Bull. Exp. Biol. Med. 148, 533-535. doi: 10.1007/s10517-010-0757-y

[45] Wakao, S., Kuroda, Y., Ogura, F., Shigemoto, T., and Dezawa, M. (2012). Regenerative effects of mesenchymal stem cells: contribution of muse cells, a novel pluripotent stem cell type that resides in mesenchymal cells. Cells 1, 1045-1060. doi: 10.3390/cells1041045

[46] Walsh, S. K., Kumar, R., Grochmal, J. K., Kemp, S. W., Forden, J., and Midha, R. (2012). Fate of stem cell transplants in peripheral nerves. Stem Cell Res. 2, 226-238. doi: 10.1016/j.scr.2011.11.004

[47] Woischneck, D., Schütze, M., Peters, B., Skalej, M., and Firsching, R. (2010). Cranial magnetic resonance imaging and serum marker S-100 for expert opinions in severe brain injuries. Versicherungsmedizin 62, 20-24.

[48] Zack-Williams, S. D., Butler, P. E., and Kalaskar, D. M. (2015). Current progress in use of adipose derived stem cells in peripheral nerve regeneration. World J. Stem Cells 7, 51-64. doi: 10.4252/wjsc.v7.i1.51

[49] Zakirova, E. Y., Azizova, D. A., Rizvanov, A. A., and Khafizov, R. G. (2015). Case of applying allogenic mesenchymal stem cells of adipogenic origin in veterinary dentistry. J. Anim. Vet. Adv. 14, 140-143. doi: 10.3923/javaa.2015.140.143

[50] Zenker, J., Stettner, M., Ruskamo, S., Domènech-Estévez, E., Baloui, H., Médard, J. J., et al. (2014). A role of peripheral myelin protein 2 in lipid homeostasis of myelinating schwann cells. Glia 62, 1502-1512. doi: 10.1002/glia.22696