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Transplantation of neural stem cells, Schwann cells and olfactory ensheathing cells for spinal cord injury

A Web of Science-based literature analysis☆

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Abstract

OBJECTIVE: To identify global research trends in transplantation of neural stem cells, Schwann cells and olfactory ensheathing cells for spinal cord injury.

DATA RETRIEVAL: We performed a bibliometric analysis of studies on transplantation of neural stem cells, Schwann cells and olfactory ensheathing cells for spinal cord injury published from 2002 to 2011 and retrieved from the Web of Science, using the key words spinal cord injury along with either neural stem cell, Schwann cell or olfactory ensheathing cell.

SELECTION CRITERIA: Inclusion criteria: (a) peer-reviewed published articles on neural stem cells, Schwann cells or olfactory ensheathing cells for spinal cord injury indexed in the Web of Science; (b) original research articles, reviews, meeting abstracts, proceedings papers, book chapters, editorial materials and news items; and (c) published between 2002 and 2011. Exclusion criteria: (a) articles that required manual searching or telephone access; (b) documents that were not published in the public domain; and (c) corrected papers.

MAIN OUTCOME MEASURES: (1) Annual publication output, distribution by journal, distribution by institution and top-cited articles on neural stem cells; (2) annual publication output, distribution by journal, distribution by institution and top-cited articles on Schwann cells; (3) annual publication output, distribution by journal, distribution by institution and top-cited articles on olfactory ensheathing cells.

RESULTS: This analysis, based on articles indexed in the Web of Science, identified several research trends among studies published over the past 10 years in transplantation of neural stem cells, Schwann cells and olfactory ensheathing cells for spinal cord injury. The number of publications increased over the 10-year period examined. Most papers appeared in journals with a focus on neurology, such as *Journal of Neurotrauma*, *Experimental Neurology* and *Glia*. Research institutes publishing on the use of neural stem cells to repair spinal cord injury were mostly in the USA and Canada. Those publishing on the use of Schwann cells were mostly in the USA and Canada as well. Those publishing on the use of olfactory ensheathing cells were mostly in the UK, the USA and Canada.

CONCLUSION: On the basis of the large number of studies around the world, cell transplantation has proven to be the most promising therapeutic approach for spinal cord injury.

Key Words

spinal cord; neuron; nerve fiber; neural stem cell; Schwann cell; olfactory ensheathing cell; transplantation; genetic engineering; tissue engineering; neural regeneration

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Research Highlights

(1) We performed a bibliometric analysis of published studies on neural stem cells, Schwann cells and olfactory ensheathing cells to repair spinal cord injury from 2002 to 2011 retrieved from the Web of Science.
(2) We analyzed the publication year, journals, institutions and highly cited papers.

INTRODUCTION

Spinal cord injury is severe trauma of the central nervous system. Over the years, various methods have been used to treat spinal cord injury, including surgical anastomosis, surgical decompression, omental transplantation, drug treatment, partial freeze, physical rehabilitation, and the application of enzyme preparations to reduce or eliminate connective tissue scarring. Although these methods can alleviate the pathological changes associated with spinal cord injury, they have been unable to provide satisfactory clinical improvement[1-2]. Recently, cell transplantation has become a hot therapeutic approach for the treatment of spinal cord injury.

Neural stem cells are pluripotent stem cells that have the potential to self-replicate and undergo multi-directional differentiation. Neural stem cells not only promote neuroregeneration, but can also be used in gene therapy for nervous system diseases by undergoing genetic modification to express exogenous neurotransmitters, neurotrophic factors and metabolic enzymes. These cells help demyelinated nerve fibers and newborn nerve fibers undergo myelination to maintain their integrity[3-4].

Schwann cells are glial cells in the peripheral nervous system. After spinal cord injury, Schwann cells can migrate to the site of injury. These cells can secrete a variety of neurotrophic factors to promote neuronal survival and encourage neurite outgrowth and functional synapse formation. Furthermore, Schwann cells can produce extracellular matrix components and cell adhesion molecules. These molecules promote neurite outgrowth and serve as a scaffold for migrating neurons. They can also fill necrotic voids and inhibit glial scar formation to improve the microenvironment[5-6].

Olfactory ensheathing cells are the only glial cells present in both the peripheral and central nervous system. They exhibit characteristics of both astrocytes and Schwann cells. Olfactory ensheathing cells can express many molecules related to cell adhesion and neurite outgrowth, and they secrete a multitude of neurotrophic factors to provide a good environment for nerve regeneration. Olfactory ensheathing cells can pass through the glial scar to provide the appropriate conditions for axonal regeneration[7-8].

In this study, we analyzed research trends among cell transplantation studies using these three different cell types for spinal cord injury based on a bibliometric analysis of publications indexed in the Web of Science and published from 2002 to 2011.

DATA SOURCES AND METHODOLOGY

Data retrieval

This study used bibliometric analyses to quantitatively and qualitatively investigate research trends in studies of transplantation of neural stem cells, Schwann cells and olfactory ensheathing cells for spinal cord injury. We searched the Web of Science, a database of research publications and citations, selected and evaluated by the Institute for Scientific Information in Philadelphia, PA, USA, using the key words spinal cord injury along with either neural stem cell, Schwann cell or olfactory ensheathing cell to find articles on the use of neural stem cells, Schwann cells or olfactory ensheathing cells, respectively, for the repair of spinal cord injury. We limited the period of publication from 2002 to 2011 and compiled a bibliography of all articles related to these cells. We downloaded the data on August 16, 2012.

Inclusion criteria

Inclusion criteria were as follows: (1) published peer-reviewed articles on any of the three types of cells, including original research articles, reviews, meeting abstracts, proceedings papers, book chapters, editorial material and news items, indexed in the Web of Science; (2) year of publication 2002–2011; and (3) citation database was Science Citation Index Expanded.

Exclusion criteria

We excluded articles that required manual searching or telephone access, documents that were not published in the public domain, and several corrected papers.

Outcomes for all articles referring to the three kinds of

cells for the repair of spinal cord injury were assessed using the following criteria: (1) annual publication output on neural stem cells; (2) distribution by journal on neural stem cells; (3) distribution by institution on neural stem cells; (4) most-cited articles from 2002 to 2011 on neural stem cells; (5) annual publication output on Schwann cells; (6) distribution by journal on Schwann cells; (7) distribution by institution on Schwann cells; (8) most-cited articles from 2002 to 2011 on Schwann cells; (9) annual publication output on olfactory ensheathing cells; (10) distribution by journal on olfactory ensheathing cells; (11) distribution by institution on olfactory ensheathing cells; and (12) most-cited articles from 2002 to 2011 on olfactory ensheathing cells.

RESULTS

Annual publication output relating to the use of neural stem cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011

A total of 537 publications from 2002 to 2011 on the use of neural stem cells to repair spinal cord injury were retrieved from the Web of Science. The number of relevant publications increased over the 10-year period. Only 14 papers were published and included in the Web of Science in 2002, but the number of published papers had increased to 101 in 2011. While the number of publications increased over this period, there was a slight decrease in 2010 (compared with 2009) (Figure 1).

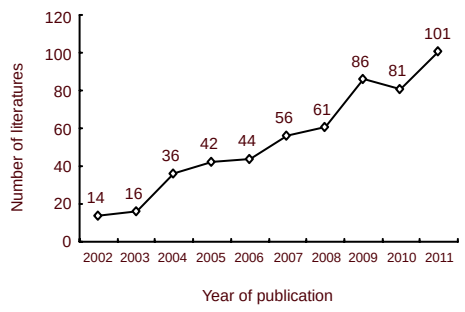

Figure 1 Annual number of publications on the use of neural stem cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011.

Distribution of output by journal for publications on the use of neural stem cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011

Journal of Neurotrauma published 23 papers, followed by *Journal of Neuroscience Research*, *Experimental Neurology* and *Cell Transplantation*, which published 21, 19 and 18 papers, respectively (Table 1).

Table 1 The top nine journals were selected based on the number of publications on the use of neural stem cells to repair spinal cord injury between 2002 and 2011

Journal	ISSN	No. of papers	% of total publications
Journal of Neurotrauma	0897-7151	23	4.283
Journal of Neuroscience Research	0360-4012	21	3.911
Experimental Neurology	0014-4886	19	3.538
Cell Transplantation	0963-6897	18	3.352
Stem Cells	1066-5099	17	3.166
Neural Regeneration Research	1673-5374	15	2.793
Journal of Neuroscience	0270-6474	12	2.235
Biomaterials	0142-9612	11	2.048
Brain Research	0006-8993	11	2.048

Distribution of output by institution for publications on the use of neural stem cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011

A total of 537 articles were analyzed according to institution. Keio University in Japan and Harvard University in the USA were the most prolific research institutes (Table 2). Four of the top 10 research institutes publishing in this field were in the USA, two were in Canada, and one institute each was in Japan, Sweden, China and Korea.

Table 2 The top 10 institutions publishing papers on the use of neural stem cells to repair spinal cord injury from 2002 to 2011

Institution	Coutry	No. of papers	% of total publications
Keio University	Japan	29	5.400
Harvard University	USA	27	5.028
University of California system	USA	25	4.655
University of British Columbia	Canada	22	4.097
University of Toronto	Canada	22	4.097
Karolinska Institute	Sweden	16	2.980
Sun Yat-sen University	China	15	2.793
Sanford-Burnham Medical Research Institute	USA	14	2.607
Drexel University	USA	12	2.235
Yonsei University	Korea	12	2.235

Highly cited papers on the use of neural stem cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011

A total of 537 papers on the use of neural stem cells to repair spinal cord injury were cited in the Web of Science from 2002 to 2011. “Functional recovery following traumatic spinal cord injury mediated by a unique polymer scaffold seeded with neural stem cells”, published in 2002 by the journal *Proceedings of the National Academy of Sciences of the United States of America*[9], was cited 418 times, which was more times than any other papers (Table 3).

Table 3 The top 10 cited papers on neural stem cells to repair spinal cord injury published from 2002 to 2011

Title	Author	Journal	Publication year	Total citations	Average per year
Functional recovery following traumatic spinal cord injury mediated by a unique polymer scaffold seeded with neural stem cells[9]	Teng YD, Lavik EB, Qu X, *et al*.	*Proceedings of the National Academy of Sciences of the United States of America*	2002	418	38.00
Neural stem cells constitutively secrete neurotrophic factors and promote extensive host axonal growth after spinal cord injury[10]	Lu P, Jones LL, Snyder EY, *et al*.	*Experimental Neurology*	2003	349	34.90
Doublecortin expression levels in adult brain reflect neurogenesis[11]	Couillard-Despres S, Winner B, Schaubeck S, *et al*.	*European Journal of Neuroscience*	2005	309	38.62
Neurogenesis in the adult brain: New strategies for central nervous system diseases[12]	Lie DC, Song H, Colamarino SA, *et al*.	*Annual Review of Pharmacology and Toxicology*	2004	306	34.00
Allodynia limits the usefulness of intraspinal neural stem cell grafts; directed differentiation improves outcome[13]	Hofstetter CP, Holmström NA, Lilja JA, *et al*.	*Nature Neuroscience*	2005	246	30.75
Transplantation of *in vitro*-expanded fetal neural progenitor cells results in neurogenesis and functional recovery after spinal cord contusion injury in adult rats[14]	Ogawa Y, Sawamoto K, Miyata T, *et al*.	*Journal of Neuroscience Research*	2002	236	21.45
Human neural stem cells differentiate and promote locomotor recovery in spinal cord-injured mice[15]	Cummings BJ, Uchida N, Tamaki SJ, *et al*.	*Proceedings of the National Academy of Sciences of the United States of America*	2005	224	28.00
The therapeutic potential of neural stem cells[16]	Martino G, Pluchino S	*Nature Reviews Neuroscience*	2006	219	31.29
Molecular dissection of reactive astrogliosis and glial scar formation[17]	Sofroniew MV	*Trends in Neurosciences*	2009	193	64.33
Stem and progenitor cell-based therapy of the human central nervous system[18]	Goldman S	*Nature Biotechnology*	2005	171	21.38

Of the 10 most-cited papers, two were published in *Proceedings of the National Academy of Sciences of the United States of America*, and the remaining eight papers were published in eight different journals. Of these 10 most-cited papers, four were published in 2005, two in 2002, and one each in 2003, 2004, 2006 and 2009.

Annual publication output relating to the use of Schwann cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011 (Figure 2)

Figure 2 Annual number of publications on the use of Schwann cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011.

A total of 541 papers on the use of Schwann cells to repair spinal cord injury, published from 2002 to 2011, were retrieved from the Web of Science. The number of relevant publications increased over the 10-year period; 31 papers were published and included in the Web of Science in 2002, and the number of published papers increased to 104 in 2011. However, the number of papers published decreased slightly in 2003, 2005, 2007, 2008 and 2010.

Distribution of output by journal for publications on the use of Schwann cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011 (Table 4)

Table 4 The top 10 journals were selected based on the number of publications on the use of Schwann cells to repair spinal cord injury between 2002 and 2011

Journal	ISSN	No. of papers	% of total publications
Experimental Neurology	0014-4886	47	8.688
Journal of Neurotrauma	0897-7151	40	7.394
Glia	0894-1491	25	4.621
Journal of Neuroscience	0270-6474	24	4.436
Biomaterials	0142-9612	20	3.697
Journal of Neuroscience Research	0360-4012	15	2.773
Brain Research	0006-8993	13	2.403
Journal of Comparative Neurology	0021-9967	11	2.033
Brain	0006-8950	10	1.848
Cell Transplantation	0963-6897	10	1.848

Experimental Neurology published 47 papers, followed

by *Journal of Neurotrauma*, *Glia* and *Journal of Neuroscience*, which published 40, 25 and 24 papers, respectively (Table 4).

Distribution of output by institution for publications on the use of Schwann cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011

A total of 541 articles were analyzed by institution. University of California system and University of Miami in the USA were the most prolific research institutes (Table 5). Five of the top 10 research institutes publishing in this field were in the USA, three were in Canada, and one institute each was in Germany and China.

Table 5 The top 10 institutions for publications on the use of Schwann cells to repair spinal cord injury from 2002 to 2011

Institution	Coutry	No. of papers	% of total publications
University of California system	USA	45	8.318
University of Miami	USA	42	7.763
University of British Columbia	Canada	18	3.327
Yale University	USA	18	3.327
Hannover Medical School	Germany	17	3.142
University of Toronto	Canada	16	2.957
University of Alberta	Canada	15	2.773
University of Louisville	USA	15	2.773
Sun Yat-sen University	China	14	2.588
Johns Hopkins University	USA	12	2.218

Highly cited papers on the use of Schwann cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011

A total of 541 papers on the use of Schwann cells to repair spinal cord injury, published from 2002 to 2011 were cited in the Web of Science. “cAMP and Schwann cells promote axonal growth and functional recovery after spinal cord injury”, published in 2004 by the journal *Nature Medicine* [19], was cited 323 times, which was more than any other paper. Of the 10 most-cited papers, four were published in *Journal of Neuroscience*, and the remaining six papers were published in six different journals. Of these 10 most-cited papers, four were published in 2005, three in 2002, and one each in 2003, 2004 and 2007 (Table 6).

Annual publication output relating to the use of olfactory ensheathing cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011

A total of 351 publications on the use of olfactory ensheathing cells to repair spinal cord injury, published from 2002 to 2011, were retrieved from the Web of Science. The number of relevant publications increased over the 10-year period; 10 papers were published and included in the Web of Science in 2002, but the number of published papers increased to 63 in 2011. However, the number of papers published slightly decreased in 2008 and 2009 (Figure 3).

Table 6 The top 10 cited papers on the use of Schwann cells to repair spinal cord injury published from 2002 to 2011

Title	Author	Journal	Publication year	Total citations	Average per year
cAMP and Schwann cells promote axonal growth and functional recovery after spinal cord injury[19]	Pearse DD, Pereira FC, Marcillo AE, *et al*.	*Nature Medicine*	2004	323	35.89
Schwann cell but not olfactory ensheathing glia transplants improve hindlimb locomotor performance in the moderately contused adult rat thoracic spinal cord[20]	Takami T, Oudega M, Bates ML, *et al*.	*Journal of Neuroscience*	2002	248	22.55
Allodynia limits the usefulness of intraspinal neural stem cell grafts; directed differentiation improves outcome[13]	Hofstetter CP, Holmström NA, Lilja JA, *et al*.	*Nature Neuroscience*	2005	246	30.75
Combining Schwann cell bridges and olfactory-ensheathing glia grafts with chondroitinase promotes locomotor recovery after complete transection of the spinal cord[21]	Fouad K, Schnell L, Bunge MB, *et al*.	*Journal of Neuroscience*	2005	213	26.62
Guidance of glial cell migration and axonal growth on electrospun nanofibers of poly-epsilon-caprolactone and a collagen/poly-epsilon-caprolactone blend[22]	Schnell E, Klinkhammer K, Balzer S, *et al*.	*Biomaterials*	2007	190	31.67
Olfactory ensheathing cells promote locomotor recovery after delayed transplantation into transected spinal cord[23]	Lu J, Féron F, Mackay-Sim A, *et al*.	*Brain*	2002	187	17.00
Remyelination of the spinal cord following intravenous delivery of bone marrow cells[24]	Akiyama Y, Radtke C, Honmou O, *et al*.	*Glia*	2002	154	14.00
BDNF-expressing marrow stromal cells support extensive axonal growth at sites of spinal cord injury[25]	Lu P, Jones LL, Tuszynski MH.	*Experimental Neurology*	2005	149	18.62
Functional recovery in traumatic spinal cord injury after transplantation of multineurotrophin-expressing glial-restricted precursor cells[26]	Cao Q, Xu XM, Devries WH, *et al*.	*Journal of Neuroscience*	2005	139	17.38
Axonal regeneration through regions of chondroitin sulfate proteoglycan deposition after spinal cord injury: A balance of permissiveness and inhibition[27]	Jones LL, Sajed D, Tuszynski MH	*Journal of Neuroscience*	2003	139	13.90

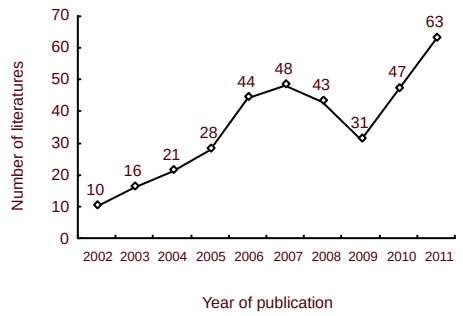

Figure 3 Annual number of publications on olfactory ensheathing cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011.

Distribution of output by journal for publications on the use of olfactory ensheathing cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011

Experimental Neurology published 26 papers, followed by *Glia*, *Journal of Neurotrauma* and *Neural Regeneration Research*, which published 16, 16 and 12 papers, respectively (Table 7).

Table 7 The top 11 journals were selected based on the number of publications on the use of olfactory ensheathing cells to repair spinal cord injury between 2002 and 2011

Journal	ISSN	No. of papers	% of total publications
Experimental Neurology	0014-4886	26	7.407
Glia	0894-1491	16	4.558
Journal of Neurotrauma	0897-7151	16	4.558
Neural Regeneration Research	1673-5374	12	3.419
Brain Research	0006-8993	10	2.849
Brain	0006-8950	9	2.564
Journal of Neuroscience	0270-6474	9	2.564
Neuroscience Letters	0304-3940	9	2.564
Journal of Comparative Neurology	0021-9967	8	2.279
Cell Transplantation	0963-6897	7	1.994
Journal of Neuroscience Research	0360-4012	7	1.994

Distribution of output by institution for publications on the use of olfactory ensheathing cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011

A total of 351 articles were analyzed by institution. University of British Columbia in Canada and Yale University in the USA were the most prolific research institutes (Table 8).

Three of the top 11 research institutes publishing in this field were in the UK, two each were in the USA and Canada, and one institute each was in Germany, Australia, China and France.

Table 8 The top 11 institutions for publications on the use of olfactory ensheathing cells to repair spinal cord injury from 2002 to 2011

Institution	Coutry	No. of papers	% of total publications
University of British Columbia	Canada	20	5.698
Yale University	USA	20	5.698
University of California system	USA	17	4.843
Hannover Medical School	Germany	15	4.274
University of Glasgow	UK	14	3.989
University of Cambridge	UK	13	3.704
Griffith University	Australia	10	2.849
Second Military Medical University	China	10	2.849
University College London	UK	10	2.849
Aix-Marseille University	France	9	2.564
University of Toronto	Canada	9	2.564

Highly cited papers on the use of olfactory ensheathing cells to repair spinal cord injury indexed in the Web of Science and published from 2002 to 2011 (Table 9)

A total of 351 papers on the use of olfactory ensheathing cells to repair spinal cord injury, published from 2002 to 2011, were cited in the Web of Science. “Functional recovery following traumatic spinal cord injury mediated by a unique polymer scaffold seeded with neural stem cells”, published in 2002 by the journal *Proceedings of the National Academy of Sciences of the United States of America*[9], was cited 418 times, which was more than any other paper. Of the 10 most-cited papers, two were published in *Brain*, and the remaining eight papers were published in eight different journals. Of these 10 most-cited papers, three each were published in 2002 and 2006, and one each in 2003, 2004, 2005 and 2007.

DISCUSSION

A bibliometric analysis, based on Web of Science publications, identified several research trends over the past 10 years in studies on the use of neural stem cells, Schwann cells and olfactory ensheathing cells to repair spinal cord injury. The number of publications increased over the 10-year period, which indicates that these three types of cells became increasingly important for treating spinal cord injury. Most papers appeared in journals with a focus on neurology, such as *Journal of Neurotrauma, Experimental Neurology* and *Glia*. Research institutes publishing on the use of neural stem cells to repair spinal cord injury are mostly in the USA and Canada. Those publishing on the use of Schwann cells to repair spinal cord injury were mostly in the USA and Canada too.

Table 9 The top 10 cited papers on the use of olfactory ensheathing cells to repair spinal cord injury published from 2002 to 2011

Title	Author	Journal	Publication year	Total citations	Average per year
Functional recovery following traumatic spinal cord injury mediated by a unique polymer scaffold seeded with neural stem cells[9]	Teng YD, Lavik EB, Qu X, *et al*.	*Proceedings of the National Academy of Sciences of the United States of America*	2002	418	38.00
Neural tissue engineering: Strategies for repair and regeneration[28]	Schmidt CE, Leach JB	*Annual Review of Biomedical Engineering*	2003	355	35.50
Therapeutic interventions after spinal cord injury[29]	Thuret S, Moon LD, Gage FH	*Nature Reviews Neuroscience*	2006	198	28.29
Guidance of glial cell. migration and axonal growth on electrospun nanofibers of poly-epsilon-caprolactone and a collagen/poly-epsilon-caprolactone blend[22]	Schnell E, Klinkhammer K, Balzer S, *et al*.	*Biomaterials*	2007	190	31.67
Olfactory ensheathing cells promote locomotor recovery after delayed transplantation into transected spinal cord[23]	Lu J, Féron F, Mackay-Sim A, *et al*.	*Brain*	2002	187	17.00
Autologous olfactory ensheathing cell transplantation in human spinal cord injury[30]	Féron F, Perry C, Cochrane J, *et al*.	*Brain*	2005	172	21.50
Remyelination of the spinal cord following intravenous delivery of bone marrow cells[24]	Akiyama Y, Radtke C, Honmou O, *et al*.	*Glia*	2002	154	14.00
Peripheral olfactory ensheathing cells reduce scar and cavity formation and promote regeneration after spinal cord injury[31]	Ramer LM, Au E, Richter MW, *et al*.	*Journal of Comparative Neurology*	2004	132	14.67
Olfactory mucosa autografts in human spinal cord injury: a pilot clinical study[32]	Lima C, Pratas-Vital J, Escada P, *et al*.	*Journal of Spinal Cord Medicine*	2006	119	17.00
Cellular transplants in China: Observational study from the largest human experiment in chronic spinal cord injury[33]	Dobkin BH, Curt A, Guest J	*Neurorehabilitation and Neural Repair*	2006	102	14.57

Those publishing on the use of olfactory ensheathing cells to repair spinal cord injury were mostly in the UK, the USA and Canada.

From our analysis, we believe that spinal cord regeneration is a complex process limited by multiple factors. Future research may focus on the following aspects: (1) Cell transplantation combined with genetic engineering techniques to eliminate the disadvantage of cell transplantation for spinal cord injury; (2) Cell transplantation combined with tissue engineering to replace spinal cord defects with carrier or scaffolding material to provide sites for transplanted cells to grow and differentiate; (3) Multiple types of cells jointly transplanted to create a suitable microenvironment for spinal cord repair; (4) Identification of a suitable source of seed cells to overcome problems related to cell differentiation, immunogenicity and regulation in transplantation. Researchers have obtained promising results in animal experiments[34]. We believe that with further investigation, researchers will make substantial breakthroughs in the treatment of spinal cord injury.

Author contributions: Xing Zhang wrote the manuscript. Xing Zhang, Fei Yin, Li Guo, Dongxu Zhao, Gu Gong and Lei Gao retrieved the references, extracted the data, and conceived and designed the study. Qingsan Zhu contributed to the review, conception and design, paper revision, and study instruction. All authors approved the final version of the manuscript.

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