

Restoration and protection of brachial plexus injury: hot topics in the last decade

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Abstract

Brachial plexus injury is frequently induced by injuries, accidents or birth trauma. Upper limb function may be partially or totally lost after injury, or left permanently disabled. With the development of various medical technologies, different types of interventions are used, but their effectiveness is wide ranging. Many repair methods have phasic characteristics, *i.e.*, repairs are done in different phases. This study explored research progress and hot topic methods for protection after brachial plexus injury, by analyzing 1,797 articles concerning the repair of brachial plexus injuries, published between 2004 and 2013 and indexed by the Science Citation Index database. Results revealed that there are many methods used to repair brachial plexus injury, and their effects are varied. Intervention methods include nerve transfer surgery, electrical stimulation, cell transplantation, neurotrophic factor therapy and drug treatment. Therapeutic methods in this field change according to the hot topic of research.

Key Words: nerve regeneration; brachial plexus injury; repair; neuroprotection; nerve transfer; cell transplantation; electroacupuncture; neurotrophic factor; drugs; bibliometrics; neural regeneration

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Introduction

Brachial plexus injury is a disabling condition. In particular, total brachial plexus root avulsion is a most severe disability in the upper extremity, and the prognosis is poor. Therefore, the accurate diagnosis and effective treatment of brachial plexus injuries is an ongoing issue (Lao, 2010). Methods of rehabilitation for conserving and restoring function after brachial plexus injuries are still being standardized. In active exploration whether independent movement can be effectively restored after injury, whether brain plasticity is accelerated and reforms to regulate the injured nerves, and whether rehabilitation involving human brain plasticity is effective are yet to be explored (Xu et al., 2010).

With the progress of medical technology and the attention of professional rehabilitation personnel to brachial plexus injury research, neural function can be restored to a certain degree in patients with brachial plexus injuries. Various intervention methods are often simultaneously and effectively used in clinic settings. Based on information from the Science Citation Index (SCI) database, this study summarized international developments in addressing brachial plexus injury and analyzed the hot topics in treating brachial plexus injury.

Data and methods

Data source

1,797 articles published between January 2004 and June 2013 were retrieved from the SCI database. The key words used were brachial plexus injury, repair, surgery, protection, nerve trans-

fer, cell, acupuncture, neurotrophic factors, and medicine.

Inclusion criteria

(1) Peer reviewed articles related to brachial plexus injury; (2) methodological studies of brachial plexus injury.

Exclusion criteria

(1) Articles unrelated to the study aim; (2) unpublished articles; (3) news articles unrelated to the study aim; (4) articles that needed to be traced by telephone or manual search.

Analysis index

(1) Different intervention methods for repairing brachial plexus injury, (2) highly published authors, (3) publication date, (4) institutes producing many articles, (5) countries of origin, (6) journals, and (7) citation rates.

Results

Bibliometric analysis of articles published in the SCI database between 2004 and 2013, and addressing the repair of brachial plexus injury

Publication rates by country

Countries that had a number of articles published in the SCI database between 2004 and 2013 are listed in **Table 1**: 654 articles concerning brachial plexus injury were published in the USA, followed by 135 in China, 115 in the UK, 101 in France, 88 in Brazil, 75 in Germany, 74 in Canada, 66 in Turkey, 58 in Japan, and 53 in Italy.

Table 1 The first 10 countries with articles on brachial plexus injury
indexed by Science Citation Index database from 2004 to 2013

Country	Number of literatures (%)	Proportion (%)
USA	654	36.394
China	135	7.513
UK	115	6.399
France	101	5.620
Brazil	88	4.897
Germany	75	4.174
Canada	74	4.118
Turkey	66	3.672
Japan	58	3.228
Italy	53	2.949

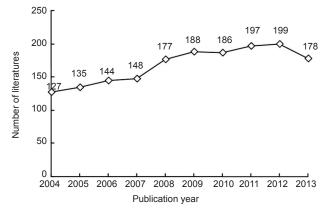


Figure 1 Econometric analysis of years from 2004 to 2013 in articles on brachial plexus injury indexed by Science Citation Index database.

No.	Title	First author	Source journal	Publication date	Total citations
1	Physical and psychological factors predict outcome following whiplash injury	Sterling M	Pain	March 2005	149
2	Ultrasound guidance improves success rate of axillary brachial plexus block	Chan VW	Canadian Journal of Snaesthesia-Journal Canadien D Anesthesie	March 2007	124
3	Nerve puncture and apparent intraneural injection during ultrasound-guided axillary block does not invariably result in neurologic injury	Bigeleisen PE	Anesthesiology	October 2006	124
4	Efficacy of two cannabis based medicinal extracts for relief of central neuropathic pain from brachial plexus avulsion: results of a randomised controlled trial	Berman JS	Pain	December 2004	111
5	Axillary artery cannulation: Routine use in ascending aorta and aortic arch replacement	Strauch JT	Annals of Thoracic Surgery	July 2004	111
6	Physical and psychological factors maintain long- term predictive capacity post-whiplash injury	Sterling M	Pain	May 2006	103
7	Ultrasound guidance compared with electrical neurostimulation for peripheral nerve block: a systematic review and meta-analysis of randomized controlled trials	Abrahams MS	British Journal of Anaesthesia	March 2009	97

Analysis of when articles on brachial plexus injury were published during the period from 2004 to 2013

Between 2004 and 2013, 1,797 articles addressing brachial plexus injury were indexed by SCI, as shown in **Figure 1**. The highest annual number of published articles was more than 180. The number of articles showed a stable increasing trend, but the increase was not apparent. From 2008, the number of articles about brachial plexus injury exceeded 160 annually and was gradually increasing, until a decline in 2013.

Citations of a paper

In bibliometrics, one of the main criteria to measure the quality of a publication is its citation rate. This is a key index to assess the academic value of the literature to fellow scholars. 1,797 articles addressing brachial plexus injury were indexed by SCI in 2004–2013. In both 2004 and 2006 two "classic" articles were found, with one "classic" article found in each of the years 2005, 2007 and 2009. This indicates that the repair and protection of brachial plexus injuries was a

hot topic in the field of hand surgery in these years (Table 2).

Publication distribution for articles addressing brachial plexus injury

Most of the articles on brachial plexus injury were published in neurosurgery journals. A total of 80 articles were published in the *Journal of Hand Surgery (American Volume)*, accounting for 4.452%, 73 by *Journal of Neurosurgery*, 71 by *Neurosurgery*, and less than 50 by other journals (**Table 3**).

Number of articles on brachial plexus injury treatment by intervention method

As illustrated in **Figure 2**, nerve transfer was the most frequently reported choice for the repair of brachial plexus injury. Cell transplantation, electroacupuncture combined with exercise therapy, nerve growth factor therapy, and other nutritional medicine approaches have become therapies in the repair of brachial plexus injury in recent years, and have been increasing selected since 2011.

Journal	Number of literatures	Proportion (%)
Journal of Hand Surgery American Volume	80	4.452
Journal of Neurosurgery	73	4.062
Neurosurgery	71	3.951
Plastic and Reconstructive Surgery	48	2.671
Microsurgery	48	2.617
Journal of Reconstructive Microsurgery	35	1.948
Journal of Bone and Joint Surgery American Volume	34	1.892
Journal of Hand Durgery European Volume	30	1.669
American Journal of Obstetrics And Gynecology	30	1.669
Journal of Bone and Joint Surgery British Volume	29	1.614

Table 3 Journals with many articles on brachial plexus injury published from 2004 to 2013 indexed by Science Citation Index database

Table 4 Citations of articles on brachial plexus injury treated by nerve transfer published from 2004 to 2013 indexed by Science Citation Index database

No.	Title	First author	Source jounal	Publication date	Total citations
1	Reconstruction of C_5 and C_6 brachial plexus avulsion injury by multiple nerve transfers: Spinal accessory to suprascapular, ulnar fascicles to biceps branch, and triceps long or lateral head branch to axillary nerve	Bertelli JA	Journal of Hand Surgery- Smerican Volume	January 2004	149
2	Results of reinnervation of the biceps and brachialis muscles with a double fascicular transfer for elbow flexion	Mackinnon SE	Journal of Hand Surgery- American Volume	September 2005	72
3	Transfer of fascicles from the ulnar nerve to the nerve to the biceps in the treatment of upper brachial plexus palsy	Teboul F	Journal of Bone and Joint Surgery-American Volume	July 2004	62
4	Continuous Peripheral Nerve Blocks: A Review of the Published Evidence	Ilfeld BM	Anesthesia and analgesia	October 2011	55
5	Combined nerve transfers for C5 and C6 brachial plexus avulsion injury	LeechavengvongsS	Journal of Hand Surgery- American Volume	February 2006	55
6	Surgical repair of brachial plexus injury: a multinational survey of experienced peripheral nerve surgeons	Belzberg AJ	Journal of Neurosurgey	September 2004	60

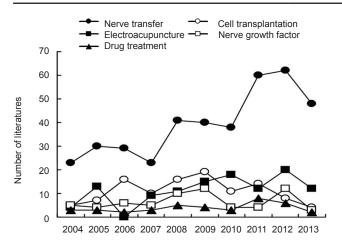


Figure 2 Number of articles on brachial plexus injury treated by five intervention methods published from 2004 to 2013 indexed by Science Citation Index database.

Citations of articles concerning the surgical treatment of brachial plexus injuries

Table 4 shows the most highly cited articles about nerve transfer for brachial plexus injury between 2004 and 2013. The most frequently cited article was written by Bertelli et al.

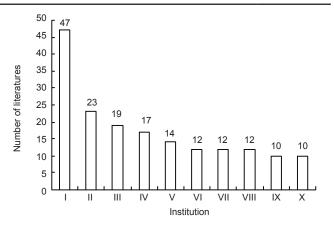


Figure 3 Institutions where the articles on surgery for brachial plexus injury come from indexed by Science Citation Index database published from 2004 to 2013.

I: Fudan University; II: Mayo Clinic; III: Governador Celso Ramos Hosp; IV: Washington University; V: Eastern Virginia Med Sch; VI: Second Mili tary Medical University; VII: Harvard University; VIII: Chang Gung Memorial Hospital; IX: Ogori Daiichi Gen Hosp; X: Leiden University.

and published in the *Journal of Hand Surgery (American Volume)*, having been cited 74 times at the time of this study. The article title is *"Reconstruction of* C_5 and C_6 brachial plexus

No.	Title	First author	Source jounal	Publication date	Total citations
1	Differential expression of the capsaicin receptor TRPV1 and related novel receptors TRPV3, TRPV4 and TRPM8 in normal human tissues and changes in traumatic and diabetic neuropathy	Facer P	BMC Neurology	May 2007	89
2	End-to-side nerve repair in the upper extremity of rat	Bontioti E	Journal of the Peripheral Nervous system	March 2005	54
3	Artificial nerve tubes and their application for repair of peripheral nerve injury: an update of current concepts	Ichihara S	Injury-international Journal of the Care of theInjured	October 2008	41
4	Laser phototherapy (780 nm), a new modality in treatment of long-term incomplete peripheral nerve injury: A randomized double-blind placebo- controlled study	Rochkind S	Photomedicine and Laser Surgery	October 2007	41
5	Co-treatment with riluzole and GDNF is necessary for functional recovery after ventral root avulsion injury	Bergerot A	Experimental Neurology	June 2004	36

Table 5 The first five articles with high citations on cell transplantation for treating brachial plexus injury indexed by Science Citation Index database from 2004 to 2013

Table 6 The first five articles with high citations on electroacupuncture for treating brachial plexus injury indexed by Science Citation Index database from 2004 to 2013

No.	Title	Author	Source jounal	Publication date	Total citations
1	Ultrasound guidance improves success rate of axillary brachial plexus block	Chan VW	Canadian Journal of Anaesthesia-Journal Canadien D Anesthesie	May 2007	124
2	Ultrasound guidance compared with electrical neurostimulation for peripheral nerve block: a systematic review and meta-analysis of randomized controlled trials	Abrahams MS	British Journal of Anaesthesia	March 2009	97
3	Evaluation and management of peripheral nerve injury	Campbell WW	Clinical Neurophysiology	September 2008	92
4	ASRA Practice Advisory on Neurologic Complications in Regional Anesthesia and Pain Medicine	Neal JM	Regional Anesthesia And Pain Medicine	September– October 2008	77
5	Extraneural versus Intraneural Stimulation Thresholds during Ultrasound-guided Supraclavicular Block	Bigeleisen PE	Anesthesiology	June 2009	58

Table 7 The first three articles with high citations on neurotrophic factor for treating brachial plexus injury indexed by Science Citation Index database from 2004 to 2013

No.	Title	Author	Source jounal	Publication date	Total citations
1	Rho-kinase inhibition enhances axonal plasticity and attenuates cold hyperalgesia after dorsal rhizotomy	Ramer LM	Journal of Neuroscience	December 2004	58
2	Co-treatment with riluzole and GDNF is necessary for functional recovery after ventral root avulsion injury	Bergerot A	Experimental Neurology	June 2004	36
3	End-to-side nerve repair in peripheral nerve injury	Beris A	Journal of Neurotrauma	May 2007	28

Table 8 The first four articles with high citations on drug treatment for treating brachial plexus injury indexed by Science Citation Index database from 2004 to 2013

No.	Title	First author	Source jounal	Publication date	Total citations
1	Efficacy of two cannabis based medicinal extracts for relief of central neuropathic pain from brachial plexus avulsion: results of a randomised controlled trial		Pain	December 2004	111
2	ASRA Practice Advisory on Neurologic Complications in Regional Anesthesia and Pain Medicine	Neal JM	Regional anesthesia and pain medicine	September– October 2008	77
3	Phototherapy for enhancing peripheral nerve repair: A review of the literature	Gigo-Benato D	Muscle & nerve	June 2005	61
4	Regional anesthesia in anesthetized or heavily sedated patients	Bernards CM	Regional Anesthesia and Pain Medicine	September– October 2008	40

avulsion injury by multiple nerve transfers: Spinal accessory to suprascapular, ulnar fascicles to biceps branch, and triceps long or lateral head branch to axillary nerve.

The second was written by Mackinnon et al. and also published in the *Journal of Hand Surgery (American Volume)* in 2005 entitled *Results of reinnervation of the biceps and brachialis muscles with a double fascicular transfer for elbow flexion.* This article verified and described nerve transfer for the recovery of bicep function, and proposed that motor tracts transplanted in ulnar and median nerves could successfully restore the innervation for elbow flexion.

The third was written by Teboul et al., and published in the *Journal of Bone and Joint Surgery (American Volume)* in 2004 and entitled *Transfer of fascicles from the ulnar nerve to the nerve to the biceps in the treatment of upper brachial plexus palsy.* This article retrospectively summarized the effectiveness of transplanting one or more ulnar nerve bundles into biceps to restore elbow flexion in the upper extremity of paralyzed patients. It also discussed the usefulness of performing secondary flexor-plasty 12 months after fascicular nerve graft, in patients with persistent grade 3 or less elbow flexion strength.

The fourth was written by Ilfeld and published in *Anesthesia And Analgesia* in 2011, entitled *Continuous peripheral nerve blocks: a review of the published evidence.* This article mainly discussed the application of a continuous peripheral nerve block during nerve transfer, concluding that avoiding intraoperative complications by using continuous peripheral nerve block was an area that anesthesiologists should focus on.

The fifth most highly cited article was by Leechavengvongs et al and published in *Journal of Hand Surgery (American Volume)* in 2006, entitled *Combined nerve transfers for* C_5 and C_6 brachial news avulsion injury. This study explored combined nerve transfer in the treatment of C_5 and C_6 root avulsion.

The sixth was written by Belzberg et al in 2004 and published in the *Journal of Neurosurgery*, entitled *Surgical repair of brachial plexus injury: a multinational survey of experienced peripheral nerve surgeons*. Belzberg et al suggested that the identification of which patients with brachial plexus injury had a better prognosis after surgery was well defined, but that the practical repair methods of specific lesions required standardization. They stated that among experienced hand surgeons, different methods for the repair of brachial plexus injury were used. Areas of difference included diagnostic methods, the definition of the injury, surgical intervention time and indications, position of nerve transfer at the elbow and shoulder abduction sites, and neuroma treatment.

In these six articles, we found that the most highly cited manuscripts mainly focused on nerve transfer for brachial plexus injury. Most of these were published in 2004, with the most recent highly cited paper published in 2011.

Institutions publishing articles on surgery for brachial plexus injury

Among the articles addressing surgery for brachial plexus injury published between 2004 and 2013 (**Figure 3**), there were 47 articles from Fudan University in China, 23 articles from the Mayo Clinic in the USA, 19 articles from the Governador Celso Ramos Hospital in Brazil, 17 articles from Washington University in the USA, amongst others. Two of the 10 institutions were from China: Fudan University (first) and the Second Military Medical Hospital (sixth).

Citations of articles using cell transplantation for brachial plexus injury

Two of the five highly cited articles were published in 2007. The repair method described in these was not cell transplantation alone, but a combination of materials and cells. The highest cited article was written by Facer et al. in 2007 and published in *BMC Neurology*, entitled *Differential expression* of the capsaicin receptor *TRPV1* and related novel receptors *TRPV3*, *TRPV4* and *TRPM8* in normal human tissues and changes in traumatic and diabetic neuropathy. At the time of this study, it had been cited 89 times (**Table 5**).

Citations of articles using electroacupuncture for brachial plexus

The most highly cited articles about electroacupuncture for brachial plexus injury were published between 2007 and 2009. The highest ranking of these had been cited 124 times at the time of this study, and is entitled *Ultrasound guidance improves success rate of axillary brachial plexus block*, written by Chan, Vincent W. S. et al. in 2007, and published in *Canadian Journal of Anaesthesia-Journal Canadien D Anesthesie*. Each of the other four articles on this topic has also been cited more than 58 times (**Table 6**).

Citations of articles investigating neurotrophic factor for brachial plexus injury treatment

The most highly cited articles using neurotrophic factor therapy for brachial plexus injury were mainly published in neurology journals and involved basic research. The repair method described mainly involves remodeling nerves. These publications suggest that neurotrophic factor for the treatment of brachial plexus injury has been gradually gaining attention (**Table 7**).

Citations of articles concerning drug treatment for brachial plexus injury

When sorted by citation rates, drug treatment for brachial plexus injury was ranked in third place, behind surgery (first), and electroacupuncture (second). As shown in **Table 8**, the highest cited article discussing drug treatment was written by Berman et al and published in *Pain* in 2004, entitled *Efficacy of two cannabis based medicinal extracts for relief of central neuropathic pain from brachial plexus avulsion: results of a randomised controlled trial.* This article demonstrated the effect of marijuana on chronic pain related to brachial plexus avulsion, using a clinical randomized, double-blind, and placebo-controlled crossover methodology. The results showed that marijuana was generally well tolerated with the most adverse indications being mild to moderate intoxication-type reactions, which quickly resolved.

Discussion

After a long period of basic and clinical investigation, the

study of brachial plexus injury repair has undergone a long and difficult development process characterized by several stages of 'hot topics' in the area.

Using bibliometrics to investigate the literature on this topic, this study explored various intervention methods in the treatment of brachial plexus injury, and concludes as follows:

(1) Nerve transfer is always the first choice for the treatment of brachial plexus injury. Studies mainly focus on transfer after C_{5-6} brachial plexus avulsion. Recently, the number of articles on nerve transfer for brachial plexus injury has plateaued. However, this remains a hot topic. In regards to the institutions publishing in this area, organizations in China ranked first.

(2) The number of articles on cell transplantation and the use of neurotrophic factor for brachial plexus injury is low, but these articles were published more recently, and the number is gradually increasing. Although these articles were basic research, rather than surgery, the aims and results of cell transplantation and neurotrophic factor therapies are more focused on restorative and remodeling functions. Also, the combination of these and other therapies has recently become an area of focus for hand surgeons.

(3) The major new trend in the use of electroacupuncture for brachial plexus injury concerns the inhibitory effects of electroacupuncture on pain, according to the number of highly cited articles on this topic published between 2004 and 2013. In recent years, drug intervention has also obtained satisfactory outcomes and entered Phase III clinical trials.

(4) The analysis of countries showed that articles on repairing and protecting brachial plexus injuries were mainly from the USA. The number of papers far exceeded those from other countries, and lead the way in the study of this field.

(5) Articles concerning the repair and protection of brachial plexus injuries in China focused on surgical treatment, and are high in number and academic quality. Nevertheless, a few articles addressing electroacupuncture, drug treatment, cell transplantation and neurotrophic factor therapy were from China, so the number and quality of these could be improved.

It is hoped that this bibliometric and qualitative content analysis provides valuable information for hand surgery experts and researchers in the study of the repair and protection of brachial plexus injuries.

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