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## Usage of acupuncture in neurosurgical conditions

**Maria Gołębiowska<sup>1,\*</sup>, Beata Gołębiowska<sup>2</sup>**

<sup>1</sup> I Faculty of Medicine, Medical University of Lublin,  
1 Al. Raclawickie Str, 20-059 Lublin, Poland

<sup>2</sup> Pediatric Neurology Department, III Chair of Pediatrics,  
Medical University of Lublin, 6 Prof. A. Gebali Str., 20-093 Lublin, Poland

\*E-mail address: [golebiowska.maria8@gmail.com](mailto:golebiowska.maria8@gmail.com)

### ABSTRACT

As the “innervated universe” of our body, the brain, holds the secrets determining humanity, over centuries there was a huge necessity to understand its complexity and ongoing processes. Surgical interventions for neurological diseases entered their Enlightenment Era with Modern Neurosurgery principles, works of Harvey Cushing and Ernest Sachs. Despite over two centuries of extensive research in various neuroscientific aspects, neurological conditions still await for innovative treatment options. Modern medical world complements Western medicine with traditional therapeutic options known and passed from generations to generations, with one of the most broad and oldest traditions - Traditional Chinese Medicine. The aim of this study is to present the use and effectiveness of acupuncture in treatment and rehabilitation of neurosurgical conditions. Therefore substantial articles on use of acupuncture in neurosurgery have been analyzed. Among 184 articles in PubMed Medline database from years 2008-2018, 9 articles were selected for further analysis. Most of the studies focused on reduction of need of general anesthesia in neurosurgical cases and also on influence on anti-inflammatory and immunological reactions. Another group of research investigated acupuncture as supportive therapy for thalamic hemorrhage and cerebral vasospasm post-SAH. Studies complemented and compared treatment of specific symptoms in neurosurgical conditions, such as post operative nausea and vomiting, anxiety. Reviewed research presents improvements in usage of acupuncture for neurosurgical conditions. Hopefully with introduction of quality standards of acupuncture research, as well as increased interest of medical and patient environments in supportive therapies, the scientific based proofs of acupuncture effectiveness will provide assistance in treatment of neurosurgical conditions.

**Keywords:** acupuncture, traditional chinese medicine, TCM, neurosurgery

## **1. INTRODUCTION**

### **1. 1. Beginnings of neurosurgery**

“The brain is the organ of destiny. It holds within its humming mechanism secrets that will determine the future of the human race.” It is then no surprise that many medical daredevils from the beginning of human civilizations decided to explore and understand the complexity of this innervated universe of human body. Starting from Cro-Magnon first trepanated skulls of 40 000 years, later Surgical Papyrus of Ancient Egypt and first observations of battlefield wounds of the brain and consequent impairment of the bodies of the patients, researchers starting from ancient times were determined to prove its functions. [1] From surgical point of view, trepanation had been used in Ancient Times as experimental method of treatment of epilepsy - previously considered as symptom of madness and possession by demons. In some cultures, trepanation was a fashionable procedure, in which possession of a piece of their own skull fulfilled function of the amulet and protection against evil. The first doctor in history, who developed the methods of skull trepanation and recommendations for its use in the case of medical conditions, was Hippocrates. [2] Drifting through the dark medical centuries, the enlightenment of neuroscience and neurosurgery started in 19<sup>th</sup> century with Galvani’s animal experiments of nerves electricity, Richard Caton human hemispheres electricity, which along with histological achievements of Golgi and Cajal mark as the beginning of modern brain studies. [3,4] Modern neurosurgery began with achievements of Harvey Cushing and Ernest Sachs, Fathers of Neurosurgery. Harvey Cushing was responsible for introduction of X-ray in brain tumors diagnostics, development of surgical equipment such as Cushing forceps, Cushing ventricular cannula and significant improvement of neurosurgical patients survival. [5] Ernest Sachs, founding member of Society of Neurological Surgeons, wrote several first neurosurgical textbooks on treatment of brain tumors, perioperative care of neurosurgical patients, development of neurosurgery. [6] Nowadays, despite two centuries of extensive studies on functions of the brain, preventions and treatment of its abnormalities, the curiosity of the scientists about this unique organ is never truly satisfied.

### **1. 2. Principles of Traditional Chinese Medicine**

Traditional Chinese Medicine (TCM) founded more than 2,500 years ago, is a medical practice originated from the Yingyangism philosophy, dated back to Chinese Shang dynasty. TCM includes the wisdom of three mythological rulers of China, belonging to Cultural Heroes - Three Sovereigns and Five Emperors. According to the Sovereign series, Three Sovereigns - Fu Xi, Shennong and Yellow Emperor, begun the human race and taught people how to utilize earth resources. Fu Xi is considered the creator of humanity, Shennong acted as master of plants, and is regarded as the attributed author of The Classic of Herbal Medicine. Thirdly, the Yellow Emperor created Yellow Emperor’s Inner Cannon - the fundamental doctrinal source of TCM, where philosophy of Yin and Yang, Qi flow and Five Elements is explained in medical aspect.

Nowadays we consider TCM as the set of treatment methods, including most importantly acupuncture and herbal medicine, but also preventive measures with dietary therapy, tai chi and qigong exercises and tui na massage techniques. [7-9]

The primary philosophy of acupuncture, the flow of life force energy - Qi - through meridians; channel network, which can be stimulated by inserting needles in specific areas, known as acupoints, has no known scientific explanation. Acupoints are located all over the body and act as landmarks for acupuncture treatment. Acupoints can be stimulated in different ways - manual needling (traditional acupuncture), delivering heat to the needle or electroacupuncture. [10] As in all of the alternative treatment therapies, acupuncture is a subject to many controversies and fronts. Some systematic reviews find little evidence on acupuncture treating certain conditions and being effective pain treatment, claiming it serves more as a placebo. [11] On the other hand, some of the published research claims effectiveness of acupuncture in eliminating lower back pain, arthritis pain, headache and migraine, also nausea associated with post-operative and cancer treatment. [12] Delivered in a correct method and manner, acupuncture has a low rate of minor adverse events, with main group of infections and iatrogenic pneumothorax. [13]

Data of World Health Organization on utilization of acupuncture among member states in 2012 showed acknowledged usage of acupuncture in 103 countries, 29 countries regulated the provision of the treatment (including eg. United States, United Kingdom, Australia, New Zealand, Canada, France and Germany) and in 18 states, acupuncture is covered within health insurance. [14] NHIS data revealed that over 6,5% of Americans have been using acupuncture as in 2007. [15]

## **2. AIM OF THE STUDY**

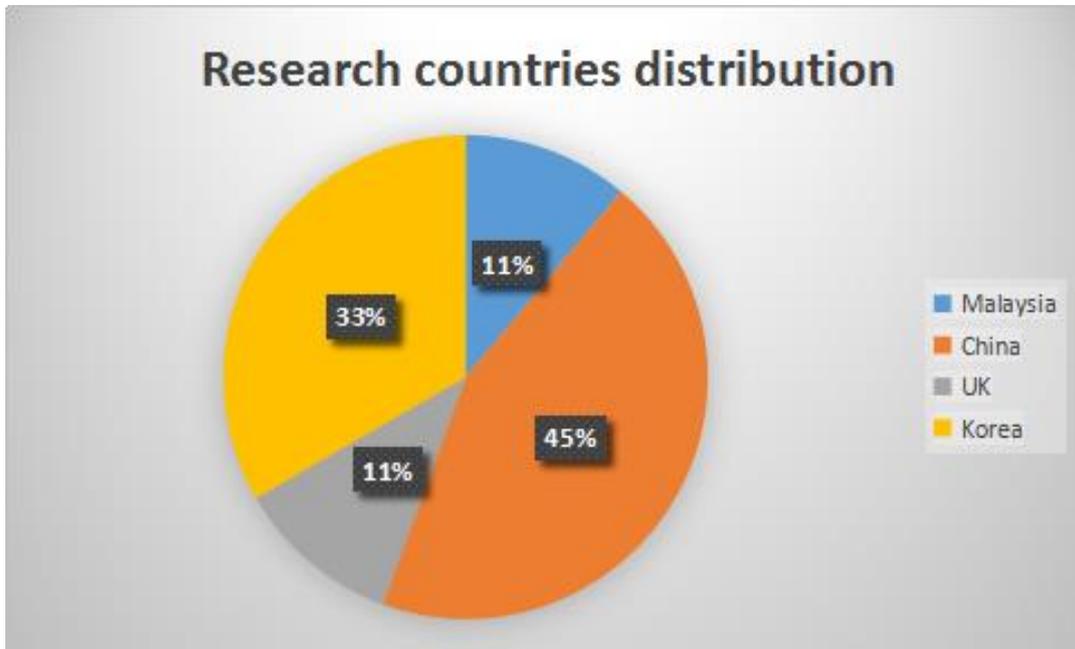
The aim of this study is to present the use and effectiveness of acupuncture in treatment and rehabilitation of neurosurgical conditions.

## **3. METHODS**

Substantial articles on use of acupuncture in neurosurgery have been analyzed. Among articles in PubMed Medline database from years 2008-2018, 9 articles were selected for analysis.

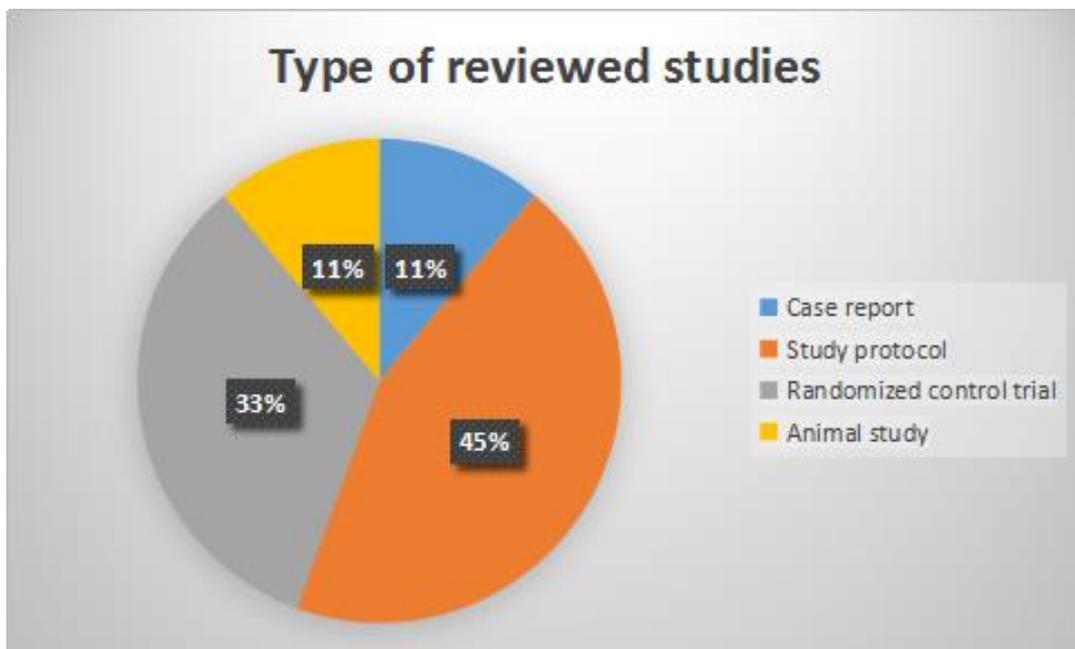
## **4. RESULTS**

Majority of the countries were from Asian region (89%), with 11% of research performed in European region (UK).



**Chart 1.** Countries distribution. Prepared by authors.

Reviewed studies comprised of study protocols (45%), randomized control trials (33%), case reports (11%) and animal studies (11%).



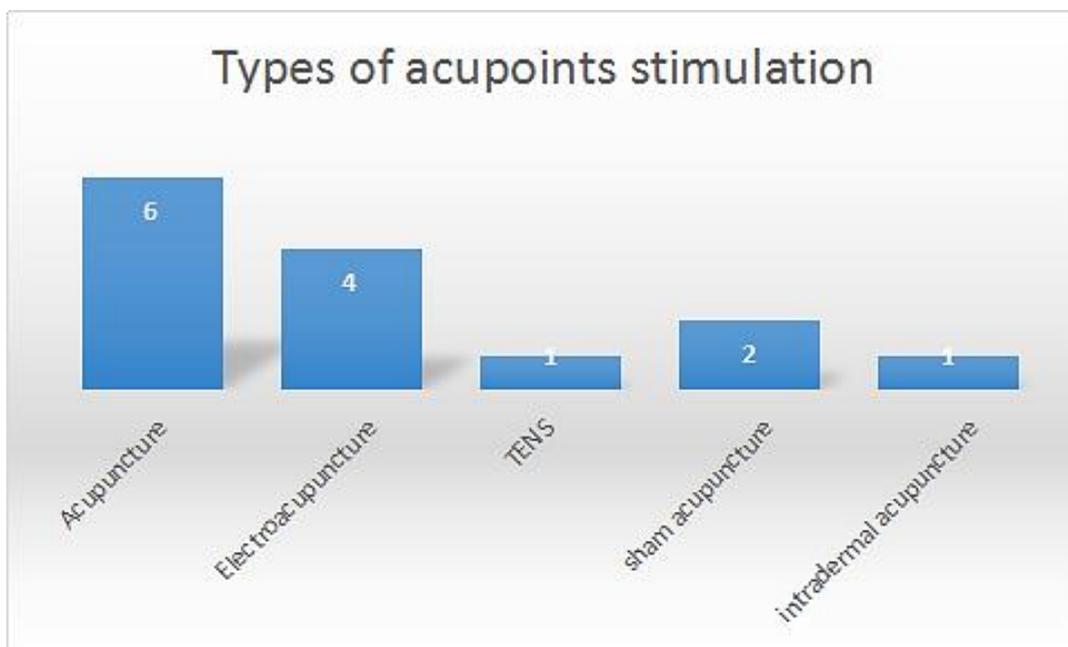
**Chart 2.** Type of reviewed studies. Prepared by authors.

Below we present the acupoints used in the studies with their study and primary, TCM considerations.

**Table 1.** Most common acupoints used in studies regarding treatment of neurosurgical conditions, and their primary considerations. Prepared by authors.

<b>Acupoints</b>	<b>Study</b>	<b>Primary consideration</b>	<b>Study consideration</b>
ST36 (Zusanli)	Cho et al., Cho et al.	Low immunity, chronic illnesses management Stomach and the Spleen symptoms Important point for maintainance of overall health	Anti-inflammatory and immunoregulative effects, cerebral vasospasm in subarachnoid hemorrhage
PC6 (Neiguan)	Lv et al., Cho et al., Cho et al.	Qi stagnation, chronic heart symptoms Chest disorders (asthma, angina) Spirit disorders - insomnia, stress, nervousness Nausea	Postoperative nausea and vomiting, Anti-inflammatory and immunoregulative effects, cerebral vasospasm in subarachnoid hemorrhage
Baihui (GV20), DU 20	Wang et al.	Stroke, headache, depression	thalamic hemorrhage
Ex-Hn3 (Yintang)	Wiles et al.	Calms the spirit, frontal headache, eyes and sinus disorders	Anxiety
GB3, GB 14, GB 19, GB 20	Sidhu et al.	Insomnia, fears, dizziness, eye diseases	anesthesia

Among acupoints stimulation, the majority of studies chose the traditional acupuncture method (6 studies), however some of the studies decided to use variations, like electroacupuncture (4 studies), TENS (1 study) and intradermal acupuncture (1 study). 2 studies decided to compare real acupuncture with sham acupuncture.



**Chart 3.** Types of acupoints stimulation. Prepared by authors.

Below we present the types of acupuncture stimulation with the description of the method.

**Table 2.** Explanation of types of acupoint stimulation. Prepared by authors.

Type of acupuncture stimulation	Description of method
Acupuncture	Insertion of acupuncture needles to specific acupoints, manipulated manually
Electroacupuncture	Insertion of acupuncture needles to specific acupoints, manipulated with small electric current between the needles
Sham acupuncture	Insertion of needles at wrong points, not indicated for specific treatment - used as a control group
Intradermal acupuncture	Acupuncture with intradermal needles, taped to the body, which can be left to maximum 48h
TENS	Transcutaneous electrical nerve stimulation - electrodes attached to implanted receiver, receiving power from antenna attached to skin surface

#### **4. 1. Awake surgery and electroacupuncture**

Awake surgery is one of the neurosurgical innovations assisting in most accurate and precise tumor resections with minimalization of iatrogenic complications. Awake craniotomy, team effort of neurosurgeon, anesthesiologist and neuropsychologist, is most widely used in surgery of motor and language brain areas, during which patient is conscious and can meet the commands while neurosurgeon is directly mapping the cortical areas responsible for those functions. [16, 17] Anesthesiologically, variety of techniques can be included, with most common “asleep, awake, asleep” (general anesthesia (propofol / dexmedetomidine + remifentanyl) at the beginning and end of the operation - including resection, the patient is awakened with simultaneous local anesthesia only during mapping), or most controversial, “awake, awake, awake” - where patient is conscious throughout the process. During surgery, patient can perform certain activities commanded by neuropsychologist, including limb movements, words repetition, and even- in case of outstanding musicians - playing the instrument, while the cortex areas responsible for those skills are carefully mapped by the neurosurgeon. [18, 19] In case report presented by Sidhu et al., the primary indication for electroacupuncture assisted awake craniotomy was not the necessity of cortex mapping, but the contraindications regarding general anesthesia in 65 year old patient with subdural hematoma. Patient suffered from uncontrolled OSA, DM, hypertension, additionally use of anesthesia and following treatment could potentially affect intracranial pressure and cerebral vasodilatation. 1 hour hematoma evacuation was performed under electroacupuncture treatment of points GB-3, GB-14, GB-19, and GB-20, known for analgesia effect. Patient recovered without any complications, and tolerated the procedure well. The case report showcased the alternative possibilities of analgesia treatment in life-saving procedures, when use of anesthesia is contraindicated. [20]

#### **4. 2. Antiinflammatory and immunoregulation effects of acupuncture**

Perioperative infections are one of the most common, and one of the most fearful complications in any surgical field, especially in neurosurgery, possibly resulting in meningitis or brain abscess. Antibiotic prophylaxis has been proven effective, however not without adverse events. Recent studies proved the downregulation effect of acupuncture on TNF-alfa (in rats after electroacupuncture of ST36, Zusanli point) IF-6, IL-10 and IL-1beta, which are known for proinflammatory response, also in rheumatological (lower ESR and CRP levels in rheumatoid arthritis patients), and gastroenterological cases (lower CRP and higher IL-10 in patients with acute pancreatitis). [21-23] In 2015 study by Li et al, effectiveness of several acupoints electroacupuncture was compared to sham acupuncture and control group in total 29 patients undergoing supratentorial craniotomy. Levels of TNF, IL-8, IL-10, IgM, IgA, IgG were measured before induction of anesthesia, 4h after induction of anesthesia, 1 day and 2 days after surgery. In acupuncture group and sham acupuncture groups, IL-10 as well as IL-8 levels in peripheral blood increased significantly compared with in 1 and 2 days after surgery. IL-10 increased 4 h after anesthesia induction and 1 day post-operatively in control group. Within IgA levels, in control group significant decrease was observed 4h after anesthesia induction, 1 and 2 days after surgery. Within comparison between the groups, level of IL-8 increased significantly 1 and 2 days after surgery in both acupuncture groups comparing to control group, and IgA levels decreased in control group 4h after anesthesia induction and 1 day after surgery comparing to the both acupuncture groups (p=0.05). No

statistically significant difference was found between both electroacupuncture and sham acupuncture groups. The combination of acupuncture and general anesthesia reduces the suppression of immune system in patients following craniotomy. [24] Next trial study protocol from Cho et al. will focus on the regulatory functions of acupuncture in immune system with measurement of CRP, ESR, TNF- $\alpha$ , IL- $\beta$  and IL-6 protein in patients undergoing craniotomy due to brain tumor, unruptured aneurysm or facial spasm causes. Forty patients will be allocated to group one acupuncture, electroacupuncture, intradermal acupuncture who will receive six acupuncture sessions for 8 days and lastly control group two with conventional management. The acupoints chosen for the study are LI4, LI11, PC6, ST36, GB39 and LR3, and GV20 (GV20 only if is not close to the surgical site). The inflammatory markers will be assessed 48h before the surgery, 2, 4 and 7 days after surgery. Primary outcome measurement will include changes in CRP levels, whereas secondary outcome measurement will assess changes in other markers, number of days when patient had a fever, antibiotic use in addition to regular antibioticotherapy, pneumonia and urinary tract infection incidents as well as other infection symptoms noted in the course of perioperative care. [25]

#### **4. 3. Role of acupuncture in treatment of spontaneous intracerebral hemorrhage**

Spontaneous intracerebral hemorrhage is a neurological condition with second poorest prognosis, with 15% of cases occurring in thalamus. Thalamic hemorrhage (TH) conservative and surgical treatment, due to its location is still controversial and highly depends on surgical skills and the size of the hematoma. [26] In patients with hematoma bigger than 30cc, regardless of the chosen treatment, the mortality is still up to 80%. While in minor hematoma up to 10cc conservative treatment is preferable and associated with lower mortality rates, then in the moderate TH of volume between 10-30cc, decision on the treatment is still in question. Based on animal studies outcomes with acupuncture of DU20 point and neuroprotective effects in basal ganglia following cerebral hemorrhage, Baihui (GV20) acupuncture improving neurologic symptoms with inhibition of neuronal apoptosis, reduction of cerebral edema, regulation of the inflammatory response to a hematoma; Wang et al. decided to determine the effectiveness of acupuncture in treatment of thalamic hemorrhage.

The study will involve 488 patients throughout 6 years, who will be randomly assigned to 8 groups depending on the size of the hematoma and treated with conventional treatment (pharmacological treatment for ICP management and surgical intervention if necessary) with acupuncture (study group) and without acupuncture (corresponding control group). Hypothesis of neurological improvements after 36 sessions acupuncture treatment will be evaluated with National Institutes of Health Stroke Scale (NIHSS) -test of 11 neurological symptoms scored between 0 and 42. Scores below 5 indicate mild impairment, 5-24 moderately severe-severe impairment, above 25 - severe neurological impairment. NIHSS will be evaluated in the end of the initial treatment, 30 days and 90 days after hemorrhage incident. The study is supposed to end in year 2021. [27]

#### **4. 4. Electroacupuncture in post-hypertensive putaminal hematoma (HPH) motor recovery**

Zhang et al. in 2015 focused on hypertensive putaminal hematoma cases, and possibility of better motor recovery with simultaneous application of neuronavigation-assisted aspiration (NA) and electroacupuncture (EA). It was proved before that neuronavigated aspiration

decreased brain injury, ischemia and edema, while electroacupuncture improved motor recovery in stroke patients. [28, 29] In 10 years span (2003-2013) 240 patients with HPH were randomly assigned to 4 groups (neuronavigation - minimally invasive surgery and electroacupuncture, neuronavigation - minimally invasive surgery only, electroacupuncture only, conservative treatment, respectively). Effectiveness of treatment was assessed with Fugl-Meyer Assessment of Physical Performance, Modified Ashworth Scale for gastrocnemius muscular tension and Barthel index, used for measuring independence of daily activities, were measured after 8 weeks. Study resulted in significant improvement in motor recovery in group 1 (NA+EA) compared to conservative treatment ( $p < 0.01$ ), as well as decreased edema and ischemia comparing to conservative treatment and EA only ( $p < 0.05$ ). NA-only and EA-only groups had also not as effective as combined, but still significant motor recovery comparing to conservative treatment ( $p < 0.05$ ). MAS score improved comparing groups NA+EA, NA only, EA only and conservative treatment group ( $p < 0.05$ ). Barthel index, indicating activities of daily living improved in NA+EA group. [30]

#### **4. 5. Acupuncture for cerebral vasospasm in subarachnoid hemorrhage**

Zusanli (ST36) acupuncture point has been known for centuries to lower blood pressure, which was associated recently with increase of endothelial NO, and as a result reduction of the damages to endothelial cells of the vessels. [31;32] Vasospasm, result of NO reduction in cerebral vessels, is associated with 23% SAH-related death and disability. Also, Neiguan (PC6) increases myocardial oxygen and results in reduction of heart ischemia. Therefore, study protocol by Cho et al. decided to include acupuncture of ST36-PC6 points in SAH treatment protocol in 80 participants of the study. The acupuncture treatment will commence 96 hours after diagnosis and successful clipping or coiling, 12 sessions within 2 weeks time. Effectiveness will be measured with occurrence of delayed ischemic neurological deficit (DIND) - unaccountable new focal neurological deficit lasting more than 2h, assessed every day by the investigators (primary outcome); also incidences of angiographic vasospasm, TCD vasospasm, vasospasm-related infarct, changes of NO and endothelin-1 in plasma, mortality at the end of treatment and 14 days after as well as modified Rankin Score will be investigated (secondary outcome). [33]

#### **4. 6. Treatment of anxiety in neurosurgical patients - Yintang acupuncture**

Among all surgical patients, in 24-73% pre-operative anxiety occurs, with highest rate in neurosurgical cases - around 87%. Treatment of anxiety with sedative medication in these cases is unfavourable due to complications in post-operative outcomes assessments. Wiles et al. In 2017 decided to elaborate on effectiveness of acupuncture of Ex-Hn3 (Yintang) point in lowering anxiety level in neurosurgical patients awaiting surgical procedures. 128 patients were selected randomly to intervention (acupuncture) group and to control group, where no intervention was made. Before and after treatment (in control group - within 30 minutes time frame), patients were asked to assess the anxiety level with State-Trait Anxiety Inventory (STAI-S6) questionnaire and Amsterdam Pre-operative Anxiety and Information Scale (APAIS). Study confirmed reduction of anxiety levels in acupuncture group - median anxiety STAI score reduced significantly from 46.7 to 40.0 ( $p < 0.001$ ). No change was observed in the control group (41.7 first questionnaire to 43.3 second questionnaire,  $p = 0.829$ ). No adverse events were reported in both groups. [34]

#### **4. 7. Postoperative nausea and vomiting treatment**

Postoperative nausea and vomiting (PONV), is an incident of nausea and/or vomiting in ICU within 24 hours post-surgery, symptom often described as worse than postoperative pain. In neurosurgical settings it occurs from 50 to 79% of cases, with no differences depending on location of craniotomy. Common prophylaxis method in high-risk adults of PONV is antiemetic treatment - Scopolamine patch two hours before surgery, Dexamethasone after induction, ondansetron at the end of surgery; postoperative pain control and rescue antiemetics - prochlorperazine or droperidol if incident occurs. However, there is no therapy fully effective for PONV treatment. [35] Therefore non-pharmacological options have been introduced in perioperative settings, among many transcutaneous electrical nerve stimulation (TENS), acupuncture, electroacupuncture, hand acupressure. The acupoint used for this purposes is Neiguan, P6. Study protocol of Lv et al. aims to prove the effectiveness of different P6 stimulation methods for prevention of PONV. Study group of 300 patients will be divided to five intervention groups: 1) P6 acupuncture bilaterally for 30 minutes, with maintenance of de qi sensation with additional stimulation every 10 minutes, 2) sham acupuncture- acupuncture of wrong point, bilaterally for 30 minutes without additional stimulation; 3) P6 stimulation via active TENS electrodes bilaterally for 30 minutes, with stimulation frequency and intensity depending on feeling of de qi sensation; 4) P6 sham stimulation with inactive TENS bilaterally for 30 minutes; and 5) conventional antiemetic treatment . Outcomes will be measured with PONV incident occurrence in 24h postoperatively (primary outcome) and complete response rate, incidents of PONV 2h, 6h, 24h after surgery, severity of the incidents, total rescue antiemetic - metoclopramide - used and patient satisfaction from treatment. The study will potentially confirm P6 effectiveness in PONV management as well as indicate, which method of stimulation is more effective (acupuncture vs. TENS). [36]

#### **4. 8. Peripheral nerve injury management with electroacupuncture stimulation**

Animal study by Cha et al. focused on management of peripheral nerve injury with electroacupuncture. Researchers previously found an activation pattern of optical signals after electrical stimulation of hind paw in neuropathic rats in primary somatosensory cortex, which supports better understanding of nerve plasticity. In this research, in study group of neuropathic rats, sham injury rats and control group, changes in S1 cortex after electrical stimulation was assessed, and as a secondary aim, rats underwent electroacupuncture treatment on ST36 and SP9 (Yinlingquan) points to confirm analgesic properties of those acupoints in neuropathic pain. In the first phase, inflamed and amplified neural activity in S1 cortex in nerve-injured group occurred and no significant signal changes were observed in sham and control groups. After electroacupuncture, reduction of optical signals and activation of S1 cortex regions and time-dependent recovery was noted, with peak fluorescence intensity reduction until 90 minutes after stimulation, and fading of the maximum activated area 60 minutes after EA. This confirms the hypothesis that electroacupuncture lowers the neuropathic pain due to inhibition of excitatory neuronal signaling in S1 cortex, and may be used as future adjuvant treatment solution. As neuropathic pain is a condition greatly affecting quality of life of the patients, as well as the available treatment, such as surgical interventions, pharmacological treatment with anticonvulsants, botulinum or neuromodulators is still

imperfect, there is a constant need for new therapeutic options in pain relief of the patients. [37]

## 5. CONCLUSIONS

As modern medicine still did not answer all medical questions and solved the problems of many severe conditions, shift towards alternative therapies is observed. Neurosurgery is one of the disciplines with highest rate of most severe and fatal cases, often leading to disabilities and significant decrease of the quality of life. Within presented review authors observe growing interest in use of acupuncture in supporting surgical treatment of neurosurgical conditions in last 10 years. Most of the presented research is still in conduction of study protocol or animal research, however the group of randomized control trials and case reports bring promising results in treatment of anxiety in neurosurgical patients, improvement of inflammatory response and utilization of acupuncture in awake craniotomies.

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