REVIEW
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Efficacy of acupuncture to regain consciousness in patients with traumatic brain injury: a systematic review and meta-analysis

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Competing interests

The authors declare no conflicts of interest.

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Peer review information

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Abbreviations

TBI, traumatic brain injury; GCS, Glasgow coma score; GOS, Glasgow outcome score; RCT, randomized controlled trial; CRS-R, Coma Recovery Score-Revised; BI, Barthel Index; RR, relative risk; MD, mean difference; CI, confidence interval; SD, standard deviation.

Citation

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Abstract

Background: Traumatic brain injury (TBI) is a leading cause of death and disability worldwide, and consciousness disorder is a common problem in TBI patients. Acupuncture has been used to improve neurological deficits in patients with TBI. This meta-analysis aims to evaluate the effects and safety of acupuncture in improving consciousness in patients with TBI when compared with other therapies. **Methods:** A systematic search was conducted in electronic databases PubMed, EMBASE, Web of Science, the Cochrane Central Register of Controlled Trials, Allied and Complementary Medicine Database, WHO International Clinical Trials Registry Platform, ClinicalTrials.gov, and Google Scholar for randomized controlled trials that investigated the effect of acupuncture on patients with TBI. From the inception of databases to March 2023. **Results:** A total of 653 participants were included in nine trials. We found that acupuncture adjunct to routine treatment significantly improved the wakeup rate of patients in TBI when compared with routine treatment alone (relative risk = 1.36, 95% confidence interval: 1.16 to 1.59, I^2 = 4.78%, P = 0). Additionally, we found that acupuncture is significantly associated with reduced impaired consciousness after TBI when adjunct to medicine therapy. As a safe intervention, acupuncture can also improve the activities of daily living for people with TBI (mean difference = 15.71, 95% confidence interval: 9.19 to 22.22, I^2 = 0%, P = 0). **Conclusion:** Acupuncture can improve consciousness and braise wakeup of patients with TBI when adjunct to conventional treatment compared with routine treatment alone. Further high-quality studies are needed to confirm these findings and to determine the optimal acupuncture treatment parameter for TBI.

Keywords: acupuncture; consciousness; traumatic brain injury; systematic review; meta-analysis

Introduction

Traumatic brain injury (TBI) is a global health problem that is becoming one of the primary reasons for mortality [1]. More than 611 people are hospitalized and 176 deaths are related to TBI per day [2]. Around 11,920 euros per patient for an average of 8–13 days is paid as hospital costs, which can be escalated with the patient's condition [3]. TBI is classified as mild, moderate, and severe according to an assessment of the Glasgow coma score (GCS), and a GCS having less than 8 scores is classified as having severe injury [4]. Patients who fail to recover get conditions of disorders of consciousness like coma, vegetative state, and minimal consciousness. Approximately 15% of peoples with severe brain injury remains in a vegetative state or coma without recovery [5].

Hypoxia, insufficient glucose supply, cerebral ischemia, and abnormal enzyme metabolism can cause a disorder of metabolism in the brain, leading to impairment of reticular structure function and low brain functioning [6] TBI-induced coma is a significant factor in poor clinical prognoses, including death [7]. Numerous trials aimed at enhancing consciousness in patients have explored interventions including drugs (amantadine, methylphenidate, bromocriptine) and non-drug methods (deep brain stimulation, transcranial magnetic stimulation, vagal nerve stimulation, sensory stimulation, music therapy, and traditional practices) across various regions. However, only amantadine has demonstrated positive outcomes in aiding functional recovery for traumatic brain injury patients [8]. Deep brain stimulation can be costly and time-intensive, and transcranial magnetic stimulation might not be universally accessible in healthcare settings [9]. Traditional non-pharmacological therapies bring new ideas to the treatment of TBI.

Acupuncture, as one of traditional Chinese medicine, involves inserting needles into specific acupoints to balance Qi (Qi refers to the basic substance that constitutes the human body and maintains life activities, and is the unity of substance and function) flow through meridians. It is safe and effective for various conditions. By impacting the central nervous system, acupuncture triggers the release of natural pain-relievers and neurotransmitters, potentially lowering inflammation, boosting neuroprotection, and enhancing neurological function [10]. Acupuncture stimulates neural growth, nerve fiber regeneration, and synaptic enhancement, improving neural connections and function in targeted areas [11]. A case study published in 2011 suggests that acupuncture can speed up the recovery of unconsciousness when combined with medicine [12]. Acupuncture at Shuigou (GV26) boosts cerebrum blood flow and enhances consciousness, likewise, Neiguan (PC6) stimulation elevates orexin neurons for rapid patient arousal [13, 14]. Additionally, it showed that the wakeup rate has been improved after acupuncture for patients with delayed wakeup with anesthesia [15]. Existing systematic study shows that acupuncture can increase GCS and Glasgow outcome score (GOS) scores in unconscious patients after TBI [16, 17]. However, none of the research conducted so far has assessed the wake-up rate after TBI. The wake-up rate after a coma is a critical measure of a patient's neurological recovery and overall prognosis [18]. It is uncertain how acupuncture therapy impacts the awakening of patients with TBI. So, it is essential to conduct a systematic review to evaluate the effect of acupuncture on the wakeup rate after TBI. Thus, the primary objective of this meta-analysis is to investigate the efficacy of acupuncture in improving the wake-up rate in patients with TBI while also assessing its safety as a therapeutic intervention.

Methods

This protocol of study has been registered in the International Prospective Register of Systematic Reviews (Identification number: CRD42022381044) on the 13th of December, 2022. This protocol follows the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol [19].

Eligibility criteria

Types of studies
All the articles selected for the study were randomized controlled trials (RCT) in humans. Studies including reviews, review protocols, pilot studies, cross-sectional studies, observational studies, case studies, meta-analyses, and animal studies were excluded.

Type of participants
Patients diagnosed with TBI using different diagnostic tools such as computerized tomography of the head and magnetic resonance imaging, regardless of age, gender, sex, race, and nationality.

Type of intervention and comparators
The intervention group consists of patients receiving acupuncture as the principal treatment which includes manual acupuncture or electro-acupuncture. Acupuncture means needling in specific meridian acupoints [20].

The control group consists of patients receiving treatment other than acupuncture like placebo acupuncture (interventions that mimic acupuncture/real treatment in some aspects but differ in others, such as skin penetration) [21], Western medicine, basic treatment, rehabilitation, oxygen therapy, or combined treatment.

Types of outcome measures
We assessed primary outcomes as wake-up rate: the percentage of patients waking up after the final treatment. Secondary outcomes include GCS [22], which is objectively used to measure the neurological status of the patient; GOS [23], which is broadly used to assess the outcomes in the patient with TBI; Coma Recovery Scale-Revised (CRS-R) score [24], which is the standardized neurobehavioral assessment measure designed for use in the patients of disorder of consciousness. Other outcomes including Montreal Cognitive Function Assessment [25] score, mini-mental state examination [26] score, or Barthel Index (BI) [27] would be analyzed if eligible. Additionally, the safety of acupuncture would also be reported [28]. Subgroup analysis including various protocols or timing of outcome measurement would be conducted if eligible. The primary and secondary outcomes were reported after the completion of the treatment.

Search strategy for the selection of studies

Search strategy
Different English databases such as PubMed, EMBASE, Web of Science, the Cochrane Central Register of Controlled Trials, Allied and Complementary Medicine Database, World Health Organization International Clinical Trials Registry Platform, ClinicalTrials.gov, and Google Scholar were searched to find the potential articles. We considered the articles published from the inception of databases to 2023 March. Further, we checked the reference list of relevant trials and reviews. The search strategy used in PubMed is depicted in Supplementary Table S1.

Language
Articles published in English and Chinese were included in the study.

Study selection
We independently searched the available articles. The involved articles were then imported to Endnote X9 to access the duplication of articles. Then, all the articles were accessed for the title and abstract whereas the articles missing the title and abstract were excluded. After that, the reviewer screened the full text of the articles for further selection. The process of study selection was reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Data extraction and management
All the available data was gathered including the first author, published year, basic characteristics of patients, degree of TBI, GCS

before treatment, duration of coma, characteristics of control and intervention, parameters of the intervention such as acupoints used, type of acupuncture, frequency of acupoints stimulation, retention time, treatment duration, follow up duration, primary outcomes, secondary outcomes, adverse events and so on. In the case of missing data, we tried to contact the original authors through phone or email and when data was not available, we excluded the article mentioning the clear reason for exclusion. Any dispute between the two authors was concluded with a discussion with the corresponding author MZ.

Assessment of bias risk

The risk of bias was evaluated according to the Cochrane Collaboration's tool for assessing the risk of bias in randomized trials. This comprised five different categories such as selection bias, performance bias, detection bias, attrition bias, and reporting bias [29]. We reported the article as high, low, and unclear risk according to the following mentioned domains.

Data synthesis and analysis

We used STATA V.17.0 for the analysis of data. We used risk ratio (RR) for dichotomous data and mean differences (MD) for continuous data with a 95% confidence interval (CI). In the case of incomplete data, we contacted the authors to request it.

Assessment of heterogeneity

We used the I^2 test to access the heterogeneity. If $I^2 > 50$ or $P < 0.1$, we referred to it as significant heterogeneity, and subgroup analyses were performed to evaluate the potential reason. We used a random effect model for the continuous data and a fixed effect model for the dichotomous outcomes. Owing to various methods being applied, a random-effects model was utilized to evaluate the effect sizes.

Subgroup analyses, sensitivity analyses and meta-regression analysis

If the result was high heterogeneity, we would do further analysis to find the potential reason. For subgroup analyses, we would analyze the effects with different treatment methods or controls. Besides, we also hope to evaluate the effect of different interventions on the outcomes, so we performed subgroup analysis based on the intervention used, course of diseases, degree of TBI, duration of intervention, and its frequency. For sensitivity analyses, we would exclude each included study one by one and then conduct the effect size combination for analysis. For meta-regression analysis, we would evaluate the relationship between the frequency of acupoint stimulation, the total number of acupuncture, the number of acupuncture points used, the follow-up duration of acupuncture, and the effect size of consciousness in TBI.

Evidence quality assessment

We used the method of Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) [30] to examine the quality of studies and Grading of Recommendations Assessment, development, and Evaluation (GRADE) to examine the evaluation quality of major outcomes. We graded the evidence quality as high, moderate, low, and critically low [31].

Publication bias assessment

If we have sufficient articles, we will assess publication bias. Otherwise, we will perform the egger test with STATA V.17.0.

Results

Study selection

Initially, we identified 307 articles, of which 80 articles were excluded due to duplication. Further, the remaining 227 articles were screened according to the abstract, the relevant topics, and article types, 24 articles were included. Eventually, 9 articles met the eligibility criteria after reading the full text. The detailed flow chart is illustrated in Figure 1.

Basic characteristics of the included studies

Nine trials were included in the meta-analysis in which all the studies were published in Chinese and carried out in China from the year 2004 to 2021.

Basic characteristics of the participants

A total of 653 participants were included in the seven trials, with 320 (49%) in the treatment group and 333 (51%) in the control group. Study sample sizes ranged from 29 to 102 participants. In the treatment group, the mean age of patients was 43.84 (standard deviation (SD) 11.02) years, while in the control group, it was 42.91 (SD) 12.57) years. The average duration of the disease course for the treatment group was 16.16 (SD 6.8) days. All included articles documented coma scores before treatment, but none of them provided specific details on the degree and severity of TBI. Refer to Table 1 for a comprehensive summary of the baseline characteristics.

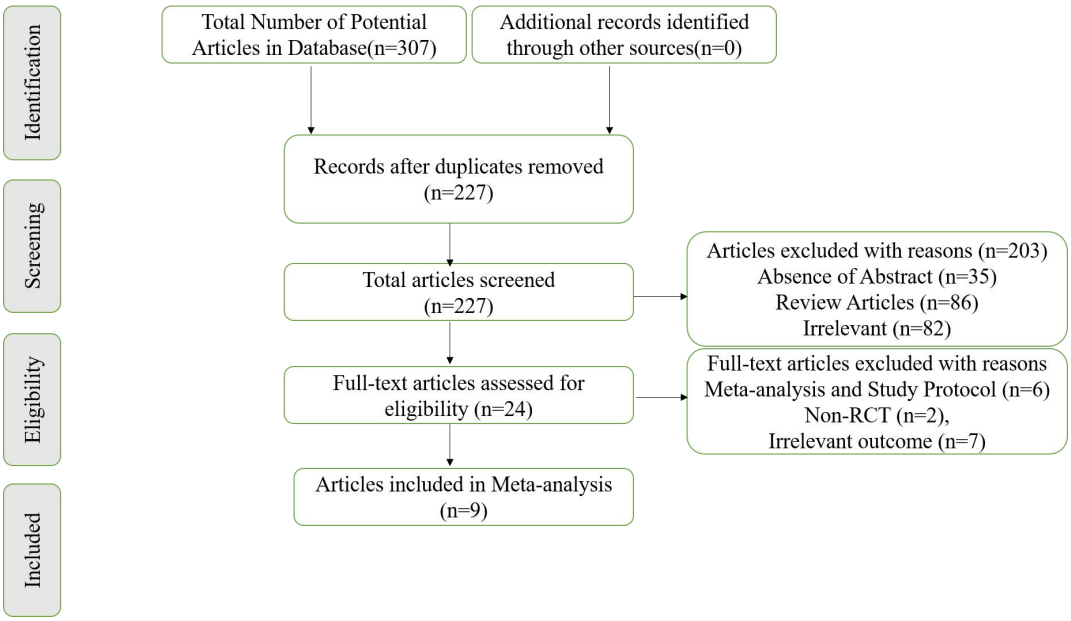

Figure 1 Flowchart according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses. RCT, randomized controlled trial.

Table 1 Basic characteristics of included studies

First Author	Year	Country	Sample size (T/C)	Mean age (T/C) (years)	Duration of diseases (days)	GCS before treatment (T/C)	Intervention (T/C)	Outcomes
Zhang YM [32]	2013	China	90 (30/30/30)	T = 37.1 ± 9.1 C = 37.2 ± 10.1	T = 9.1 ± 4.0 C = 9.3 ± 3.7	3–8 point	EA/WM	GCS↑, GOS↑, Wakeup rate↑
Bao YC [33]	2021	China	98 (48/50)	T = 44 ± 12 C = 45 ± 15	T = 30.3 ± 10.2 C = 30.6 ± 16.8	T = 5.92 ± 1.31 C = 5.86 ± 1.39	A + R + HBO/R + HBO	GCS↑, CRS-R↑, Wakeup rate↑
Bao YC [34]	2020	China	100 (50/50)	T = 43 ± 16 C = 45 ± 15	T = 24.3 ± 11.8 C = 30.6 ± 16.8	T = 5.96 ± 1.41 C = 5.86 ± 1.39	A + R + HBO/R + HBO	GCS↑, CRS-R↑, Wakeup rate↑
Liu J [35]	2020	China	100 (50/50)	T = 46 ± 14 C = 45 ± 16	T = 27.1 ± 15.1 C = 25.4 ± 17.1	T = 5.44 ± 1.72 C = 5.74 ± 2.03	EA + WM/WM	GCS↑, GOS↑, BI↑
Peng F [36]	2010	China	56 (29/27)	T = 39.1 ± 12.2 C = 40.2 ± 9.8	T = 8.3 ± 3.7 C = 7.9 ± 4.1	T = 5.08 ± 1.47 C = 5.10 ± 2.11	EA + WM/WM	GCS↑, GOS↑, Wakeup rate↑, wakeup time↓
FU YY [37]	2009	China	32 (16/16)	T = 41.8± 18.5 C = 36.8± 18.5	T = 10.4 ± 6.7 C = 12.9 ± 7.0	T = 4.06 ± 1.06 C = 3.87 ± 1.02	EA + WM/WM	GCS↑, Wakeup rate↑
Xiang ZX [38]	2004	China	42 (14/14/14)	48.12	28.26	T = 5.22 ± 1.63 C = 5.23 ± 1.53	EA + WM + HBO/WM + HBO	GCS↑, GOS↑
Guo ZQ [39]	2018	China	64 (32/32)	T = 53 ± 6 C = 53 ± 5	T = 7.7 ± 2.9 C = 8.6 ± 3.8	T = 8.5 ± 2.5 C = 8.6 ± 2.4	A + WM/WM	GCS↑, GOS↑, BI↑
Tu XH [40]	2010	China	102 (51/51)	T = 42.5 ± 11.4 C = 41.1 ± 11.2	NA	GCS: T = 6.2 ± 1.2 C = 6.1 ± 1.1	A + WM/WM	GCS↑, Wakeup rate↑, Wakeup time↓

↑, upregulated by intervention; ↓, downregulated by intervention; T, Treatment; C, Control; GCS, Glasgow coma score; GOS, Glasgow Outcome Score; CRS-R, Coma Recovery Score-Revised; BI, Barthel Index; A, Acupuncture; EA, Electroacupuncture; R, Rehabilitation; HBO, Hyperbaric Oxygen; WM, Western Medicine.

Basic characteristics of the intervention

We found no articles that compared acupuncture with a sham or placebo. All of the trials compared acupuncture combined with pharmacological interventions or oxygen therapy. Five studies compared acupuncture stimulation combined with routine medicine and routine medicine alone [35–37, 39, 40]. Likewise, two studies compared manual acupuncture adjunct to rehabilitation, oxygen therapy, and routine medicine with rehabilitation, oxygen therapy, and routine medicine [33, 34]. Two studies compared three design trials, one as naloxone injection, routine medicine, and electroacupuncture, the next as routine medicine with oxygen therapy, routine medicine with electroacupuncture, and routine medicine with oxygen therapy combined with electroacupuncture respectively [32, 38]. Five studies mentioned the depth of acupuncture insertion which ranged from 5 mm–25 mm. The most commonly used acupoints were Neiguan (PC6) and Shuigou (GV26), used in eight trials. DU meridian is the most used meridian for acupuncture. The treatment duration of the observational group was from 14 days to 90 days. However, one study doesn't mention it. Needle retention time varied from 30 minutes per day to 120 minutes per day. One article carried out manual acupuncture and electroacupuncture for 60 minutes per day and the next carried out for 90 minutes per day. All nine articles mentioned the GCS before treatment. The detail of the frequency of acupoints is illustrated in Table 2, further duration of treatment, retention time, depth of insertion, and acupuncture sessions were illustrated in Supplementary Table S2.

Risk of bias of included studies

For assessing the risk of bias, the Cochrane collaboration risk of bias was used. All nine articles were randomized and described the process of randomization, but the allocation concealment was unclear in some studies. All of the articles did not implement blinding for patients, personnel as well as outcome assessment in the studies. As a result, we rated it as a relatively high risk of bias for all the studies. Additionally, one article reported dropout [32], and the other two articles were also reported as reporting bias [33, 37] since they have incomplete results. The risk of bias was summarized in Figure 2.

Primary outcomes

Wakeup rate. Six studies assessed the wakeup rate of the patients after the final treatment [32–34, 36, 37, 40], and the pooled data showed that the rate of wakeup of patients in the observation group was significantly higher than that in the control group (RR = 1.36, 95% CI: 1.16 to 1.59, I^2 = 4.78%, P = 0) as per Figure 3.

Secondary outcome

GCS. We found all nine trials assessed GCS for the measurement of coma score. Seven articles reported the data for GCS after treatment [33–35, 37–40]. Two articles compared routine treatment and oxygen therapy with the same combined acupuncture. Another six studies compared routine treatment alone with routine treatment and acupuncture. Oxygen therapy and routine medicine in the control group are compared with acupuncture added to the treatment group in one article. These seven studies revealed that the acupuncture group has significantly improved GCS than the control group (MD = 1.82, 95% CI: 1.25 to 2.4, I^2 = 59.83%, P = 0), Figure 4.

GOS. With regards to GOS outcome, five articles assessed the score after the final treatment. Among them, three articles [32, 35, 39] assessed scores as dichotomous data, and we found that the acupuncture was significantly associated with a reduction in the occurrence of impaired consciousness after TBI when adjunct to medicine therapy compared to medicine therapy alone (RR = 1.54, 95% CI: 1.17 to 2.04, I^2 = 0%, P = 0), as per Figure 5. Furthermore, one study [38] reported continuous data, we found that acupuncture

did not improve GOS score when adjunct to drug plus oxygen therapy compared to oxygen with medicine therapy (MD = 0.34, 95% CI: –0.22 to 0.9, P = 0.24), Supplementary Figure S1. One study didn't report clear data after the treatment; however, it showed GOS notably increased in the experimental group than in the control group [36].

Wakeup time. Pooled data from two study [36, 40] compared the wake-up time of the patients in terms of days in intervention and control group. The analysis showed that acupuncture significantly reduced wake-up time in acupuncture adjunct with medicine group compared with control group (MD = –9.18, 95% CI: –11.08 to –7.28, I^2 = 0%, P = 0), as per Figure 6.

Other outcome

CRS-R. Two articles evaluated the outcome as CRS-R Score [33, 34] which compared the effect of routine treatment, oxygen therapy, and acupuncture in the experimental group with routine treatment and oxygen therapy in the control group. It showed a dramatically improvement in CRS-R score in the treatment group compared to control group (MD = 1.61, 95% CI: 0.73 to 2.49) with moderate heterogeneity I^2 = 50.41%, P = 0), as per Figure 7. These results indicate acupuncture can improve the CRS-R score in patients with a disorder of consciousness.

BI. Two RCT from two studies [35, 39] reported BI and the analyzed result showed that BI is significantly improved in the intervention group comparing with the control group (MD = 15.71, 95% CI: 9.19 to 22.22, I^2 = 0%, P = 0), as per Figure 8. It suggests that acupuncture can significantly improve activities of daily living.

Table 2 Frequency of the most used acupoint stimulation

Name of acupoint	Number of times used	Name of acupoint	Number of times used
Shuigou (GV26)	8	Jinjin (EX-HN12)	1
Neiguan (PC6)	8	Yuye (EX-HN12)	1
Sanyinjiao (SP6)	5	Xuehai (SP10)	1
Hegu (LI4)	4	Taixi (KI3)	1
Baihui (GV20)	3	Fenglong (ST40)	1
Taichong (LR3)	2	Yinlingquan (SP9)	1
Yintang (EX-HN3)	2	Zusanli (ST36)	1
Weizhong (BL40)	2	Shuifen (RN9)	1
Chize (LU5)	2	Qihai (RN6)	1
Yongquan (KI1)	1	Fengfu (GV16)	1
Renying (ST9)	1	Jiquan (HT1)	1
Quze (PC3)	1	Yifeng (SJ17)	1
Yamen (GV15)	1	Wangu (GB12)	1
Houxi (SI3)	1	Lianquan (RN10)	1

PC, pericardium; GV, governor vessel; SP, spleen; LI, large intestine; LR, liver; EX-HN, extra points-head and neck; KI, kidney; BL, bladder; ST, stomach; LU, lungs; SI, small intestine.

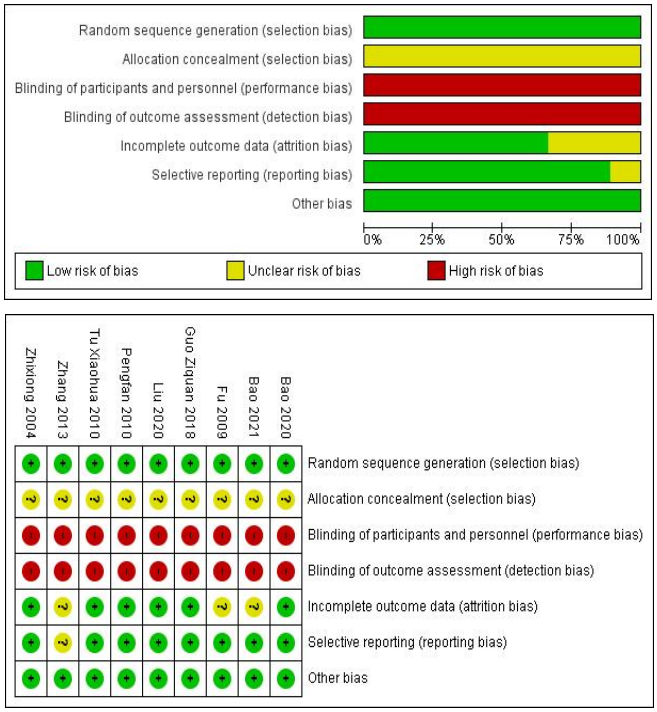

Figure 2 Risk of bias of included studies according to Cochrane collaboration risk of bias

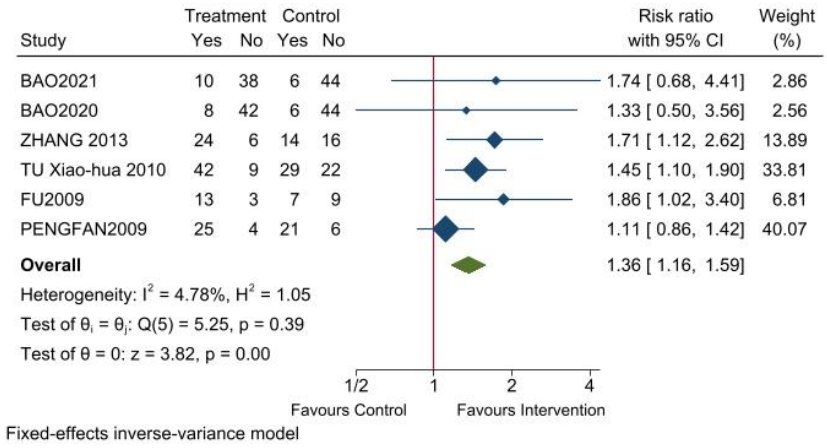

Figure 3 Forest plot of Wakeup rate. CI, confidence interval.

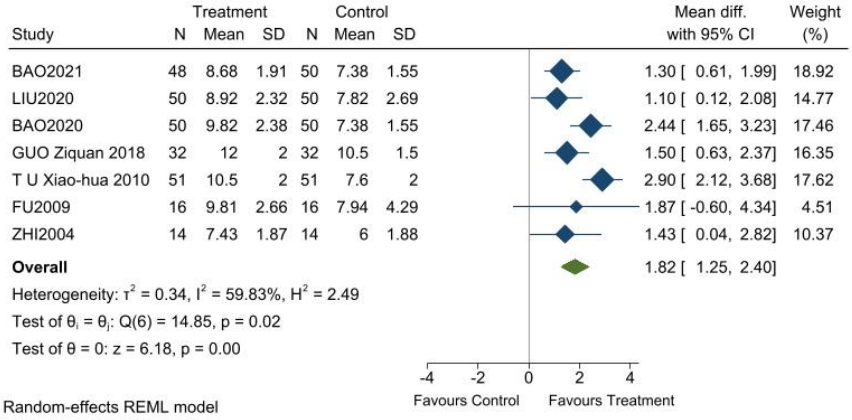

Figure 4 Forest plot of GCS. CI, confidence interval; GCS, Glasgow coma score; SD, standard deviation; REML, restricted maximum likelihood.

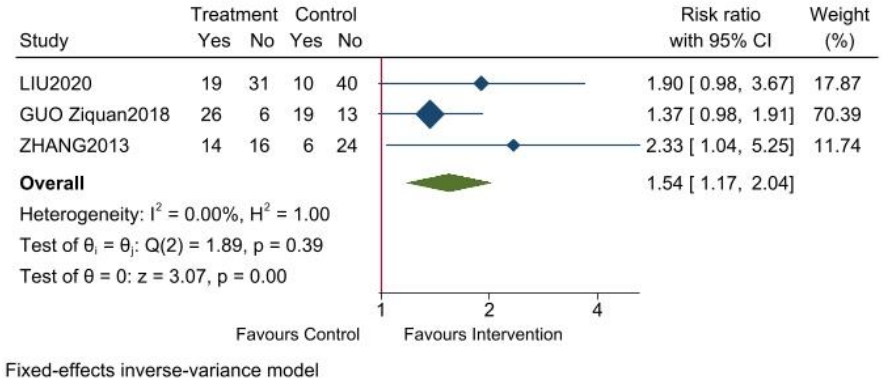

Figure 5 Forest plot of GOS. GOS, Glasgow outcome score; CI, confidence interval.

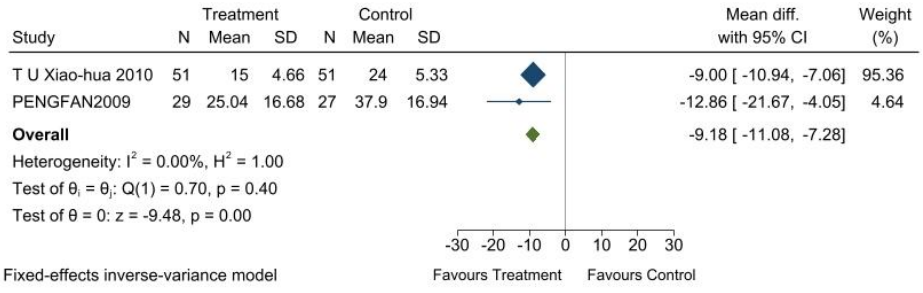

Figure 6 Forest plot of wakeup time. CI, confidence interval; SD, standard deviation.

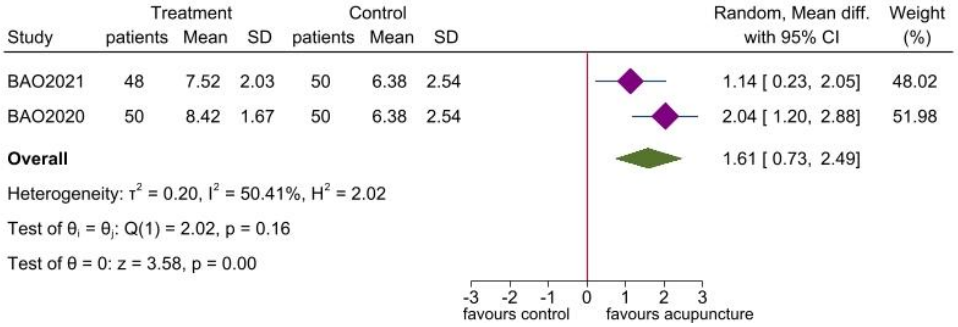

Figure 7 Forest plot of CRS-R. CRS-R, Coma Recovery Score-Revised; CI, confidence interval; SD, standard deviation.

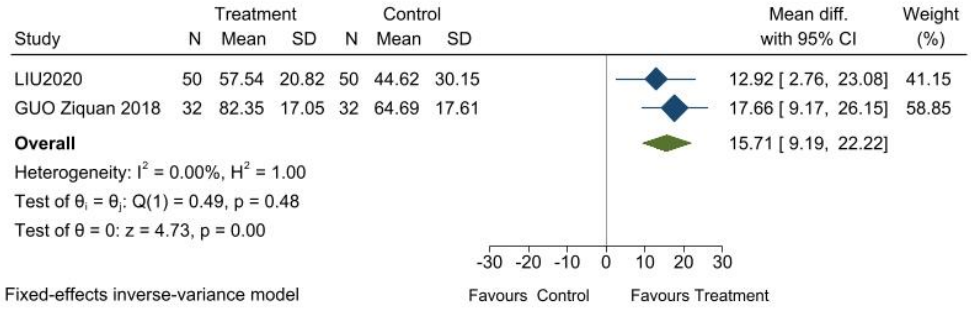

Figure 8 Forest plot of Barthel Index. CI, confidence interval; SD, standard deviation.

Adverse event

Only one study reported an adverse event during the intervention in the treatment group [38]. Some patients receiving acupuncture treatment felt pain and fever, but all of them were tolerated, and no patients fell off.

Subgroup analysis. To evaluate the effect of different intervention on wakeup rate of consciousness after TBI, we conducted subgroup analysis according to the intervention used in control and treatment group. The findings indicate that combining acupuncture with standard medical treatment is more advantageous for enhancing the wake-up rate in TBI patients when compared with medicine alone (RR = 1.35, 95% CI: 1.15, 1.59, I^2 = 39.72%, P = 0.17). However, when rehabilitation, oxygen therapy, and acupuncture were used together, acupuncture therapy did not show a significant improvement in wakeup rate (RR = 1.53, 95% CI: 0.78, 3.01, I^2 = 0%, P = 0.7), as per Figure 9.

Further analysis was done according to the duration and frequency of intervention after final treatment. Acupuncture performed for 30 days (RR = 1.56, 95% CI: 1.27, 1.91, I^2 = 0%, P = 0.92) showed better result than acupuncture carried out for 90 days (RR = 1.11, 95% CI: 0.86, 1.42, I^2 = 100%, P = not applicable) as per Figure 10. This result shows that acupuncture may have better effect in wakeup rate within 30 days of treatment. Secondly, frequency of acupuncture per day was analyzed which illustrates that acupuncture for 30 minutes per day (RR = 1.56, 95% CI: 1.27, 1.91, I^2 = 0%, P = 0.92) may be significantly better than acupuncture for 120 minutes per day (RR = 1.11, 95% CI: 0.86, 1.42, I^2 = 100%, P = not applicable) as per Figure 11. Additionally, subgroup analysis based on the course of diseases revealed that patients with a disease duration of less than 15 days had a significant improvement (RR = 1.3, 95% CI: 1.06, 1.59, I^2 = 56.23%, P = 0.1). Conversely, for patients with a disease duration more than 15 days, the observed association was not statistically significant (RR = 1.53, 95% CI: 0.78, 3.01, I^2 = 0%, P = 0.7), as per Figure 12.

Due to low heterogeneity of included studies, sensitivity analyses and meta-regression analysis were not carried out.

Publication bias. Egger test using STATA 17.0 was used for the publication bias and the result showed that there was no publication bias (β1 = 1.13, standard error of β1 = 0.891, Z = 1.27, P = 0.2035 > 0.1), as per Figure 13.

Quality of evidence. We used the method of Standards for Reporting Interventions in Clinical Trials of Acupuncture to examine the quality of studies and Grading of Recommendations Assessment, development, and Evaluation to examine the evaluation quality of major outcomes. Results were mentioned in Supplementary Table S3 and Supplementary Table S4.

Discussion

All prospective randomized controlled studies that are currently available have been included in the meta-analysis. The application of acupuncture demonstrated notable enhancements in the wakeup rate, consciousness function, and reduction in awakening time for patients with TBI. The overall meta-analysis results indicated the beneficial impact of acupuncture on improving the wakeup rate, GCS, GOS, CRS-R, wakeup time, and BI for patients with consciousness disorders following TBI, with minimal occurrences of adverse events. Notably, the frequently utilized acupoints included Shuigou (GV26) and Neiguan (PC6), with the Governing Vessel (DU) meridian being the most commonly employed treatment meridian. Additionally, the subgroup analysis emphasized the significance of a 30-day treatment duration, administered at a frequency of 30 minutes per day, in optimizing the efficacy of acupuncture. These findings underscore the critical role of timing and treatment duration, highlighting the potential benefits of early intervention within 15 days of disease onset.

Our research is consistent with previous studies, which also concluded that acupuncture can enhance various aspects of outcomes in individuals with a disorder of consciousness, such as improving GCS, GOS, enhancing activities of daily living, increasing efficacy rate, and reducing mortality [16]. Additionally, our study focally concluded that acupuncture can dramatically increase the wakeup rate of patients with unconsciousness which can be related with improved neurological impairments. Research discovered that Hand Twelve Well Points acupuncture can stimulate dopaminergic neurons in the

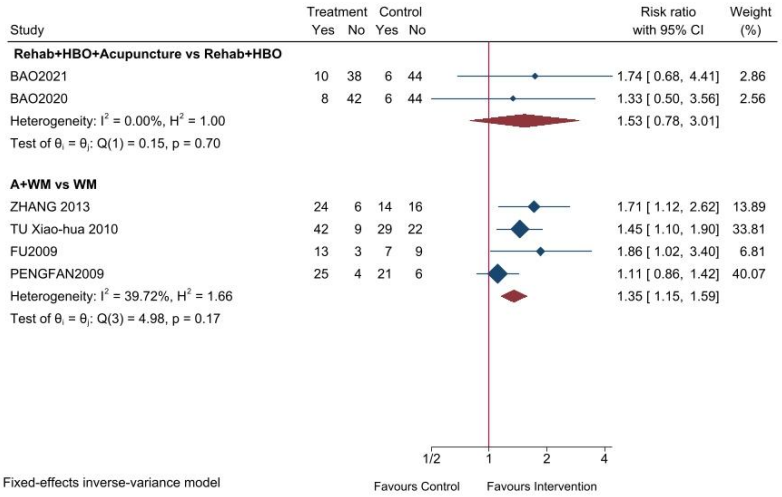

Figure 9 Forest plot of subgroup analysis of wakeup rate according to the intervention. CI, confidence interval; HBO, Hyperbaric Oxygen.

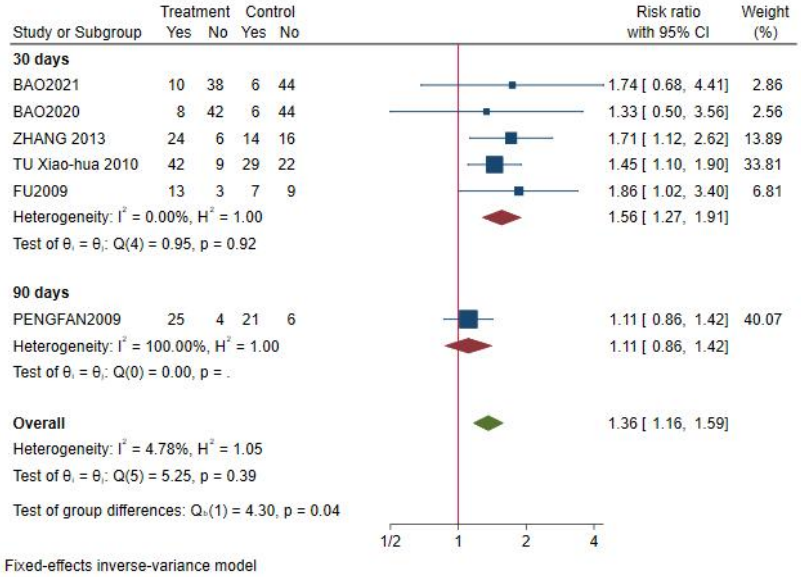

Figure 10 Forest plot of subgroup analysis of wakeup rate according to the duration of treatment. CI, confidence interval.

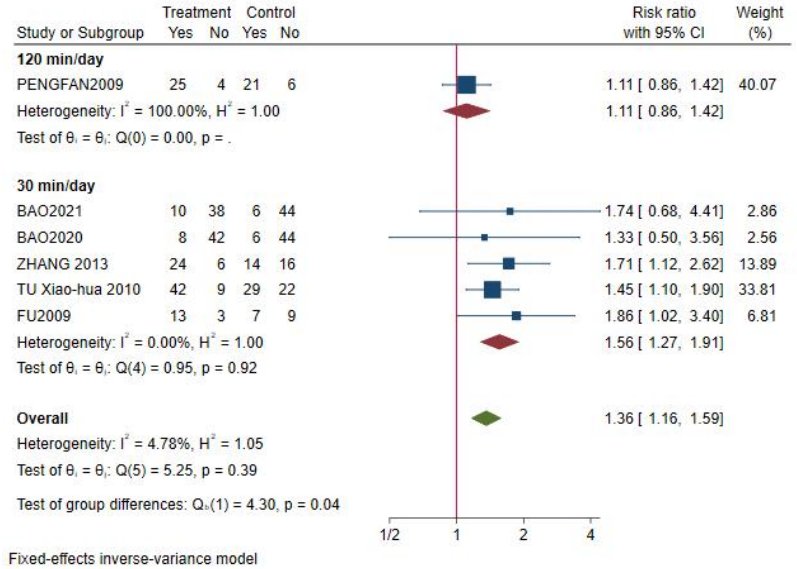

Figure 11 Forest plot of subgroup analysis of wakeup rate according to the frequency of treatment per day. CI, confidence interval.

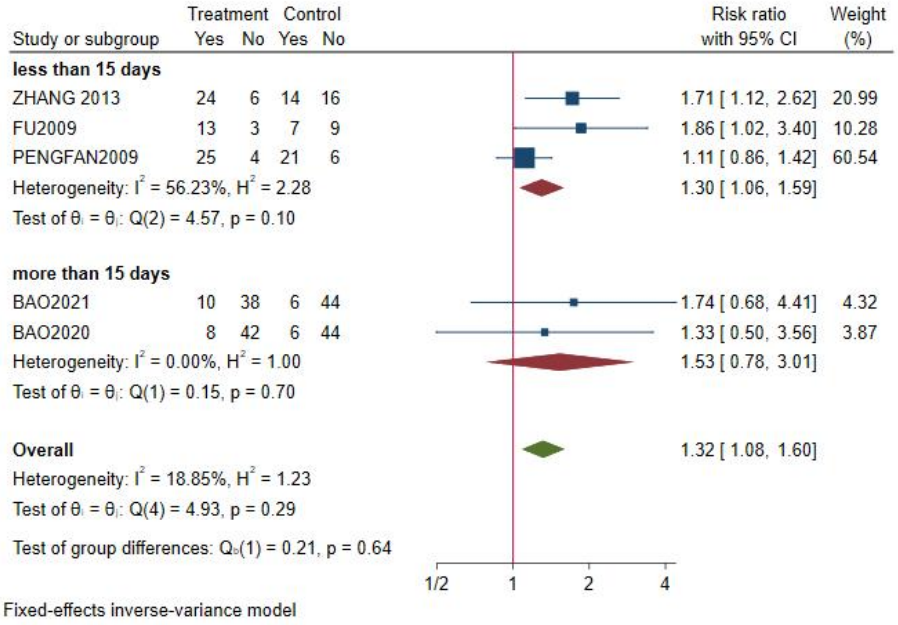

Figure 12 Forest plot of subgroup analysis of wakeup rate according to the duration of diseases. CI, confidence interval.

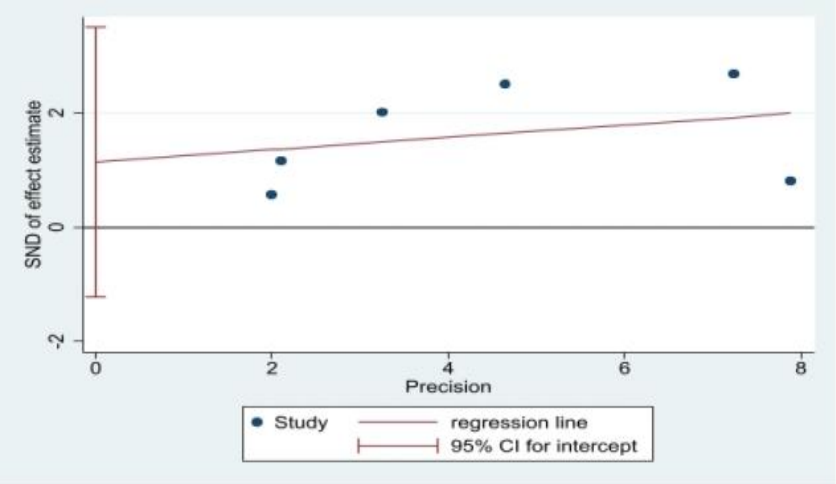

Figure 13 Egger graph for publication bias. CI, confidence interval; SND, standard normal deviate.

ventral periaqueductal gray leading to the generation and release of additional dopamine. This process can improve ascending reticular activating system neural projection and may aid the recovery of comatose rats with brain injuries [41]. According to an animal experiment using rats with TBI, it was observed that administrating electroacupuncture at Shuigou (GV26) could lead to an improvement in their neurological functions. This improvement could be attributed to a potential decrease in the level of BKCa, which helps in regulate both the firing of neurons and neurotransmitters, release channel protein and mRNA expression [42]. Additionally, acupuncture at Neiguan (PC6) has the potential to enhance behavioral functions, decrease brain cell apoptosis in the affected regions and facilitate the recovery process following TBI [43]. Furthermore, we found that acupuncture is a safe intervention, since only one study reported limited tolerable pain or other feelings, no adverse events were reported in other research. Compared with existing treatments for TBI related consciousness impairment, which may pose various adverse events such as irritation, discomfort and seizures, acupuncture may be a potentially safe and adjunct effective method. Although one study concluded that the effect after the addition of acupuncture to drug plus oxygen treatment was not significant in GOS score [42], this may be related to high risk of bias due to lack of baseline data, unclear blinding, not-approved random method. In addition, considering that there was only one study with the issue, we assess the efficacy of acupuncture in terms of the GOS which shows better result in intervention group.

Based on our findings, there are several implications for practice. Acupuncture therapy could be considered an effective adjunct treatment option for the patient with TBI. The result suggests that combining acupuncture therapy with pharmacological intervention or oxygen therapy may lead to improvement of wakeup rate, as well as GCs, GOS, and CRS-R scores with minimal adverse effects. Physicians working with TBI patients could consider including acupuncture therapy in their treatment plans, especially for patients who may not respond to the pharmacological interventions or who have adverse reactions to the medication. Acupuncture can positively influence the wake-up rate of coma patients with traumatic brain injuries and it appears to mitigate the progression of secondary brain injury [44]. Acupuncture contributes to an improved wake-up rate by stimulating brain activity, enhancing arousal, and potentially aiding in recovery from a comatose state in patients with TBI. It can enhance the activity of daily living which is associated with improving the quality of life of the patient that can be related to their families and society. We find that acupuncture therapy combined with routine treatment may have the better improvement in consciousness disorder so the integrative treatment plan combining acupuncture may be preferred.

The study has some limitations such as the small sample size of the included studies, lack of blinding in the acupuncture group, most of the articles haven't described the sham control of the acupuncture, and the fact that all the studies were conducted in China. Therefore, conducting more RCTs with larger sample sizes, sham control to the patients in different countries is necessary. Further studies could be conducted as following. Initially, the use of standardized tools to evaluate the outcomes of acupuncture therapy for TBI patients is also important for more consistent and accurate comparisons between studies and ensure that the outcomes are clinically meaningful. In addition, investigate the optimal timing and frequency of acupuncture treatment for TBI patients which would involve whether acupuncture therapy is most effective when administered immediately after the injury or whether it can be effective in the rehabilitation process. Finally, exploring the potential mechanism underlying the efficacy of acupuncture therapy for TBI patients which involves conducting mechanistic studies such as magnetic resonance imaging and electroencephalogram examination to better understand how acupuncture may be affecting the brain and promoting recovery after TBI. Overall, the study suggests that acupuncture therapy combined with pharmacological intervention or oxygen therapy may be an effective treatment for patients with TBI. Furthermore, although other outcome measures, such as mini-mental state examination, Montreal Cognitive Function Assessment, Loewenstein Occupational Therapy Cognitive Assessment, Galveston Orientation and Amnesia Test are crucial for cognitive disorders of patients with TBI, due to the lack of studies reporting the above outcomes based on the inclusion criteria, we did not conduct a meta-analysis for them. Hopefully, future studies will be performed to comprehensively assess the effects of acupuncture on coma, activities of daily livings, and quality of life in patients with TBI, so as to provide more evidence for TBI management in the clinic.

Conclusion

Our research found that adjunct acupuncture may increase the wakeup rate, consciousness function and shorten awakening time for patients with TBI, further higher-quality studies are needed to validate these findings and select the optimal acupuncture treatment for traumatic brain injury.

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