Meta Analysis

**Efficacy of median nerve electrical stimulation on the recovery of patients with consciousness disorders: a systematic review and meta-analysis**

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**Abstract**

**Objective:** To identify whether median nerve stimulation (MNS) may be a potential candidate for the treatment of consciousness disorders via a systematic review and meta-analysis.

**Methods:** PubMed, Cochrane Library, China National Knowledge Infrastructure, Chinese VIP Information, Wanfang, and SinoMed databases were searched. Risk of bias was assessed using the Cochrane Collaboration’s tool. The Glasgow Coma Scale (GCS), Disability Rating Scale (DRS), electroencephalogram (EEG), days in the Intensive Care Unit (ICU), and cerebral blood flow measures were compared between the median nerve stimulation and control groups. The meta-analysis was conducted using Review Manager software.

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Results: We identified 2244 studies, of which 23 (with data from 1856 patients) qualified for the analysis. MNS improved GCS scores (mean difference [MD] = 2.15), EEG scores (MD = 1.61), cerebral mean blood flow velocity (MD = 4.23), and cerebral systolic blood flow velocity (MD = 10.51). Furthermore, it decreased DRS scores (MD = −1.77) and days in the ICU (MD = −2.02). The effects of MNS on GCS scores increased with longer treatments (1 week, MD = 1.03; 1 month, MD = 2.35) and were better with right MNS (right, MD = 2.36; bilateral, MD = 1.72).

Conclusions: MNS may promote recovery from consciousness disorders.

Keywords
Median nerve stimulation, consciousness disorder, intensive care, vegetative state, meta-analysis, systematic review, treatment

Introduction
Consciousness disorders are conditions in which patients lose their ability to correctly recognize and perceive the surrounding environment and their state. Severe consciousness disorders include vegetative states, comas, and minimally conscious states. Consciousness disorders are among the most severe outcomes of central nervous system diseases. They are mainly caused by damage to the brainstem’s reticular structure and its extensive projection system, causing dysfunction of the reticular activating system and influencing the transformation and integration of the cortex.

With continuously improving medical practices, fewer patients now die from brain diseases; however, survivors are susceptible to consciousness disorders. Because of the severe inhibition of brain function that occurs in consciousness disorders, patients have difficulty taking care of themselves; this burdens their families and society and causes many social and ethical problems. As a result, medical practitioners need to promote such patients’ recoveries and help them return to the social world.

The current mainstream view is that, if they are in a coma for an extended period or a vegetative state after craniocerebral disease should receive treatment to promote their return to consciousness as soon as possible. Clinical studies have demonstrated that injured neurons can regain biological activity and function through suitable treatment and rehabilitation. Furthermore, patients with severe brain damage usually have a relatively long coma duration and a high incidence of complications. Therefore, early and effective wake-up treatment—rather than salvage treatment after the coma has lasted for a long time—is critical for treating brain damage.

Commonly used wake-up methods include early treatment of the primary disease, prevention and treatment of complications, reduction of intracranial pressure, withdrawal of drugs that hinder the recovery of consciousness, timely application of wake-up drugs, hyperbaric oxygen therapy, and electrical nerve stimulation. However, none of these methods are entirely effective for patients with consciousness disorders.

In recent years, some studies have reported that median nerve electrical stimulation (MNS) is a promising treatment. Unfortunately, their sample sizes were
relatively small and their results were not entirely consistent with one another. As a result, the findings of a single study may not be representative of the research as a whole. We therefore conducted a systematic review and meta-analysis of the published studies on the effects of MNS in patients with consciousness disorders, to identify whether MNS may be a potential candidate for the treatment of consciousness disorders.

**Methods**

We registered this research at the International Prospective Register of Systematic Reviews (registration number CRD42021260031) and have reported it according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement 2020 (PRISMA 2020).7

**Search strategy**

We searched for relevant clinical studies published in English and Chinese as of July 2021. The following databases were searched: PubMed, the Cochrane Library, the China National Knowledge Infrastructure, Chinese VIP Information, the Wanfang database, and the SinoMed database. Combined text and Medical Subject Heading (MeSH) terms were used for searching. All potentially eligible studies were considered for review, no matter the primary outcome. Furthermore, we manually used the reference lists of specific articles to search for other relevant studies.

**Inclusion and exclusion criteria**

The inclusion criteria were interpreted under the patients, interventions, controls, outcomes, and studies (PICOS) framework. Studies were included if they fulfilled the following: 1) P: patients had consciousness disorders regardless of the cause (GCS score \( \leq 12 \)); 2) I: MNS was used to improve the consciousness state; 3) C: basic therapy, a sham procedure, or a blank control was used as a control group; 4) O: at least one quantitative consciousness evaluation was able to be extracted; and 5) S: randomized controlled clinical trials were included. Studies were excluded if they were conducted in patients with severe diseases of other vital organs; or if the studies lacked a clear description of the study design, specific interventions, or necessary participant information.

**Study selection, data extraction, and quality assessment**

Three authors independently conducted the study selection process. In cases of disagreement, a group discussion or consultation with another author was used to resolve the issue. Titles and abstracts of all searched articles were first screened using pre-established inclusion and exclusion criteria. For the final determination of inclusion, full texts of candidate studies were read in detail. Once all conditions were satisfied, data extraction and detailed analysis were performed.

Three authors extracted the data and assessed the quality of the included studies independently, followed by a comparison between single evaluations. We extracted the following data into a prespecified table: 1) demographic data (disease, total number of participants, age, sex); 2) treatment protocols (methods, treated side, basic treatment); 3) related time points (follow-up time, treatment time, evaluation time); and 4) main outcomes including Glasgow Coma Scale (GCS) scores, electroencephalogram (EEG) scores, Disability Rating Scale (DRS) scores, cerebral blood flow, and days in the Intensive Care Unit (ICU).

For quality assessment, the Cochrane Collaboration’s tool 1.0 was used to assess the risk of bias in seven aspects: random sequence generation, allocation concealment, blinding of patients and personnel,
blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other sources of bias. Bias was expressed as “high risk,” “low risk,” or “unclear risk” using RevMan5.3 (The Nordic Cochrane Centre for The Cochrane Collaboration, Copenhagen, Denmark).

**Statistical analysis**

We assessed the effects of MNS on recovery from consciousness disorders in terms of five outcomes: GCS, ECG, DRS, cerebral blood flow, and days in the ICU. All outcomes were analyzed as continuous variables, and GCS scores were the primary outcome. We reported absolute differences between patients receiving different interventions and calculated pooled estimates of mean differences (MD) in all outcomes between MNS and control groups. The Cochrane I² test was used to assess heterogeneity among the studies. If heterogeneity was low (I² < 50%), we used the fixed-effects model for pooled analysis. If heterogeneity was high (I² values > 50%), we used a random-effects model to adequately account for the additional uncertainty associated with the use of data from different studies.

We categorized heterogeneity as low (I² values < 25%), moderate (I² values < 50%), or high (I² values > 50%). If heterogeneity was high, a sensitivity analysis was performed to explore the cause. The funnel plot and Egger test were used to assess small-study effects. Review Manager (RevMan 5.3) and Stata 14.0 were used for all statistical analyses. p < 0.05 was considered significant.

**Results**

As shown in Figure 1, we searched for relevant articles and identified 2244 studies from the aforementioned databases. After screening, 23 studies with data from 1856 patients were deemed eligible for the final analysis.

**Study characteristics**

The characteristics of the 23 included studies, published between 1999 and 2020, are shown in Table 1. Of these studies, 13 focused on traumatic brain injury (TBI); four focused on hypertensive intracerebral hemorrhage (HICH); two focused on various causes; and one each focused on intracranial aneurysm (IA), persistent vegetative state (PVS), acute cerebral infarction (ACI), and diffuse axonal injury (DAI).

**Quality of included studies**

The quality of included studies was assessed using the Cochrane Collaboration’s tool 1.0 for assessing the risk of bias. Figures 2a and 2b show detailed information about this assessment. All studies had complete outcome data and reported all anticipated outcomes. Thirteen studies reported how the random sequence was generated, whereas 10 stated that patients were randomly allocated into two groups without mentioning how randomization was performed. Nineteen of the included studies did not declare the blinding of assessment, leading to a high risk of assessment bias. To assess whether this bias affected our final results, we performed a pooled analysis of studies that used blinding or did not. The total effects remained consistent (Figures S1, S2).

No studies described the blinding of outcome assessments. No studies had any other biases. Figure 2c shows the funnel plot of included studies. We use the Egger test to evaluate the symmetry of the funnel plot; the result was not significant, indicating that there were no small-study effects.

**GCS scores before treatment.** The GCS score was our primary outcome, and was
reported by all included studies. We first compared GCS scores before treatment to assess the comparability among the included studies. As shown in Figure 3a, although one study did not report GCS scores before treatment,23 there were no differences between the MNS and control groups before treatment, and heterogeneity was very low ($I^2 = 0\%$).

**GCS scores after treatment and sensitivity analysis.** Figure 3b shows the comparison of GCS scores after treatment regardless of treatment time; the overall effect size (MD) was 1.49 (95% confidence interval [CI]: 1.05, 1.92) with a $Z$ value of 6.75 ($p < 0.00001$). However, there was also high heterogeneity ($p < 0.00001$, $I^2 = 94\%$). To identify the reason for such high heterogeneity, we performed a sensitivity analysis (see Figure 3c). After removing seven studies,13,14,16,20,23,24,30 the $I^2$ decreased to 35%, but the overall outcome remained the same. This finding indicates that although heterogeneity was high, it was unlikely to influence the outcome.

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**Figure 1.** Flow chart of study selection.
VIP, Chinese VIP Information Database; CNKI, the China National Knowledge Infrastructure; RCT, randomized controlled trial.
| Study ID | Included patients | Age (years) | Sex (male/female) | Treatment of MNS group (sample size; therapy) | Treatment of control group (sample size; therapy) | Follow-up time | Treatment time | Evaluation time point | Main outcome |
|----------|------------------|-------------|-------------------|---------------------------------------------|-----------------------------------------------|----------------|----------------|---------------------|--------------|
| Wang 2019 | Various reasons | C:40.9 ± 7.1; T:39.11 ± 6.85 | | 31; normal therapy + bilateral MNS | 31; normal therapy | 4 w | 4 w | 4 w | GCS, DRS, brain blood flow |
| Xue 2021 | TBI | C:39.7 ± 13.1; T:42.3 ± 14.45 | | 42; normal therapy + bilateral MNS | 41; normal therapy | 1 m | 2 w | 2 w | GCS |
| Yan 2020 | HICH | C:47.1 ± 14.3; T:48.5 ± 13.7 | | 28; normal therapy + right MNS | 27; normal therapy | 1 m | 1 m | 1 m | GCS, GOS |
| Cheng Xiaowu 2021 | TBI | C:52.03 ± 8.93; T:52.11 ± 8.56 | | 30; normal therapy + right MNS | 30; normal therapy | 3 w | 2 w | 2,3 w | GCS |
| Wei 2017 | TBI | C:45.3 ± 6.1; T:44.5 ± 5.7 | | 41; normal therapy + right MNS | 41; normal therapy | 2 w | 2 w | 2 w | GCS, brain blood flow |
| Liang 2012 | PVS | C:57.4 ± 6.7; T:54.9 ± 7.3 | | 20; normal therapy + left MNS | 20; normal therapy | 2 m | 2 m | 2 m | GCS |
| Liang 2016 | TBI | C:47.95 ± 8.03; T:48.43 ± 8.28 | | 46; normal therapy + right MNS | 43; normal therapy | 3 m | 1 m | 1 m | GCS |
| Wen 2017 | TBI | C:36.48 ± 11.0; T:36.67 ± 10.78 | | 63; normal therapy + right MNS | 63; normal therapy | 6 m | 1 m | 1 m | GCS, EEG |
| Chen 2014 | HICH | C:60.9 ± 4.72; T:61.73 ± 5.07 | | 30; normal therapy + right MNS | 30; normal therapy | 4 w | 4 w | 1,2,3,4 w | GCS, days in ICU |
| Xu 2004 | TBI | C:37.8 ± 4.6; T:37.1 ± 4.36 | | 15; normal therapy + bilateral MNS | 15; normal therapy | 1 w | 1 w | 1 w | GCS, brain blood flow |
| Nekkanti 2016 | DAI | – | – | 10; normal therapy + right MNS | 10; normal therapy | 1 m | 1 m | 1 m | GCS |
| Tao 2019 | ACI | C:59.3 ± 2.8; T:58.1 ± 2.3 | | 41; normal therapy + right MNS | 41; normal therapy | 1 m | 1 m | 1 m | GCS |
| Ruan 2019 | Various reasons | – | – | 35; normal therapy + right MNS | 35; normal therapy | 6 m | 2 w | 6 m | GCS, GOS, DRS |

(continued)
| Study ID | Included patients | Age (years) | Sex (male/female) | Treatment of MNS group (sample size; therapy) | Treatment of control group (sample size; therapy) | Follow-up time | Treatment time | Evaluation time point | Main outcome |
|----------|-------------------|------------|------------------|---------------------------------------------|-------------------------------------------------|----------------|---------------|---------------------|--------------|
| Lei 2015 | TBI               | C:41.3±10; T:43.2±9.2 | C:154/6; T:145/71 | 221; normal therapy + right MNS | 216; normal therapy | 6 m | 2 w | 1 w, 2 w | GCS |
| Lan 2018 | IA                | C:55.5±9.2; T:53.5±10.2 | C:15/9; T:13/11 | 24; normal therapy + bilateral MNS | 24; normal therapy | 3 m | 3 m | 3 m | GCS, brain blood flow |
| Zhao 2020 | TBI              | C:38.19±6.32; T:37.68±7.54 | C:26/20; T:22/24 | 46; normal therapy + right MNS | 46; normal therapy | 1 m | 1 m | 1 m | GCS, EEG, brain blood flow |
| Yin 2015 | TBI              | – – | – – | 40; normal therapy + bilateral MNS | 40; normal therapy | 1 m | 1 m | 1 m | GCS, brain blood flow |
| Yin 2015 | HICH             | – – | – – | 18; normal therapy + bilateral MNS | 18; normal therapy | 1 m | 1 m | 1 m | GCS, EEG, brain blood flow |
| Chen 2018 | HICH           | C:58.75±8.6; T:58.57±8.44 | C:9/11; T:10/11 | 21; normal therapy + right MNS | 20; normal therapy | 6 m | 2 w | 1,2,4 w | EEG, GCS, DRS, days in ICU |
| Yang 2017 | TBI             | C:36.7±14; T:35.8±12.9 | C:38/18; T:34/22 | 56; normal therapy + right MNS | 56; normal therapy | 2 m | 1 w | 1 w, 2 m | GCS, DRS, brain blood flow |
| Cooper 1999 | TBI       | C:23.5±12.5; T:24±15.5 | C:1/5; T:1/5 | 6; normal therapy + right MNS | 3; normal therapy | 1 m | 2 w | 1 w, 2 w | GCS, EEG, days in ICU |
| Yang 2016 | TBI             | C:35.34±11.1; T:36.72±12.53 | C:18/12; T:16/14 | 30; normal therapy + right MNS | 30; normal therapy | 1 m | 1 m | 1 m | GCS, EEG |
| Li 2014   | TBI             | C:43.8±11.2; T:44.6±10.6 | C:19/12; T:20/11 | 31; normal therapy + right MNS | 31; normal therapy | 4 w | 1 m | 1 m | GCS, DRS, EEG |

Data are presented as the mean ± standard deviation. Items that were unable to be extracted from the original articles are described as “—.”

ACI, acute cerebral infarction; C, control group; DAI, diffuse axonal injury; DRS, Disability Rating Scale scores; EEG, electroencephalogram scores; GCS, Glasgow Coma Scale scores; HICH, hypertensive intracerebral hemorrhage; IA, intracranial aneurysm; ICU, intensive care unit; m, month; MNS, median nerve stimulation; PVS, persistent vegetative state; T: treatment group; TBI, traumatic brain injury; w, week.
GCS scores at different time points after treatment. As previously mentioned, the included studies had different treatment and follow-up times, so we performed a pooled analysis of different time points. Figure 3d shows the GCS scores after 1 week of treatment. Five studies were included,\textsuperscript{17,18,27–29} and the overall effect size (MD) was 1.03 (95% CI: 0.24, 1.81) with a Z value of 2.57 (p = 0.01) and acceptable heterogeneity (p = 0.02, $I^2 = 64\%$).

Figure 3e shows the GCS scores after 2 weeks of treatment. Seven studies were included,\textsuperscript{10,12,13,17,22,27,29} and the overall effect size (MD) was 1.86 (95% CI: 0.48, 3.23) with a Z value of 2.64 (p = 0.008) and high heterogeneity (p < 0.00001, $I^2 = 95\%$).

Figure 3f shows the GCS scores after 1 month of treatment. Fourteen studies were included,\textsuperscript{9–11,14–17,19,20,24–26,30,31} and the overall effect size (MD) was 2.35 (95% CI: 1.84, 2.87) with a Z value of 8.99 (p < 0.00001) and high heterogeneity (p < 0.00001, $I^2 = 92\%$). Together, these findings indicate that MNS increases the GCS scores of patients with consciousness disorders regardless of treatment time, and that the extent of improvement increases with the duration of treatment.

GCS scores for different causes of consciousness disorders. The included studies focused on many different causes of loss of consciousness, such as TBI, HICH, IA, and PVS. To measure the effects of MNS on different kinds of patients, we performed a subgroup analysis, shown in Figure 3g. Twelve studies focused on TBI;\textsuperscript{10–13,15,16,18,22,24,25,29,31} the MD was 2.33 (95% CI: 1.65, 3.02) with a Z value of 6.66 (p < 0.00001) and high heterogeneity (p < 0.00001, $I^2 = 87\%$).

Four studies focused on HICH;\textsuperscript{11,17,26,27} the MD was 2.25 (95% CI: 1.07, 3.43) with a Z value of 3.75 (p = 0.0002) and high heterogeneity (p = 0.0002, $I^2 = 85\%$).

Two studies focused on various causes;\textsuperscript{9,21} the MD was 1.22 (95% CI: 0.58, 1.86) with a Z value of 3.75 (p = 0.0002) and no
Figure 3. GCS scores. (a) GCS scores before treatment. A random-effects model was used to assess whether there were differences in GCS baseline scores between different studies. (b) GCS scores after treatment. (c) Sensitivity analysis of GCS scores after treatment. (d) GCS scores after 1 week of treatment. (e) GCS scores after 2 weeks of treatment. (f) GCS scores after 1 month of treatment. (g) GCS scores for different causes of consciousness disorders and (h) GCS scores for different sides of MNS.

CI, confidence interval; GCS, Glasgow Coma Scale; MNS, median nerve stimulation; SD, standard deviation.
heterogeneity ($I^2 = 0\%$). One study focused on ACI$^{20}$ with an MD of 3.06 (95% CI: 2.74, 3.38), one study focused on DAI$^{19}$ with an MD of 2.50 (95% CI: 0.48, 4.52), one study focused on IA$^{23}$ with an MD of 3.50 (95% CI: 2.16, 4.48), and one study focused on PVS$^{14}$ with an MD of 1.85 (95% CI: 1.70, 2.00).

**GCS scores for different sides of MNS.** Among the included studies, MNS was performed either on the right side or bilaterally. We therefore performed a pooled analysis for the different sides (Figure 3h). In six studies,$^{9,10,18,23,25,26}$ MNS was performed bilaterally, and the MD was 1.72 (95% CI: 1.02, 2.41) with a Z value of 4.86 ($p < 0.0001$) and high heterogeneity ($p = 0.03$, $I^2 = 72\%$). In the other included studies,$^{11–13,15–17,19–22,24,27–31}$ MNS was performed in the right arm of patients; the MD was 2.36 (95% CI: 1.75, 2.98) with a Z value of 7.52 ($p < 0.00001$) and high heterogeneity ($p < 0.00001$, $I^2 = 91\%$).

**DRS scores**

The DRS was used to assess the extent to which TBI patients went from coma to community, to rate the influence of injury and estimate how long recovery might take.$^{32}$ Five included studies reported this score$^{9,20,27,28,31}$ (Figure 4). The MD was $-1.77$ (95% CI: $-2.31$, $-1.22$) with a Z value of 6.38 ($p < 0.00001$) and no heterogeneity ($I^2 = 0\%$). This finding indicates that MNS lowers DRS scores in patients with consciousness disorders caused by TBI.

**EEG scores**

The EEGs were acquired through 10 to 20 international leads; patients were stimulated with pain and sound, and then passively opened or closed their eyes. Finally, the EEGs were comprehensively analyzed and scored using a dichotomous variable scale$^{33}$ to get the EEG score; a higher EEG score indicated better prognosis. As shown in Figure 5, three included studies described this outcome: the MD was 1.61 (95% CI: 1.20, 2.02) with a Z value of 7.72 ($p < 0.00001$) and low heterogeneity ($I^2 = 35\%$).$^{24,27,31}$ This finding indicates that MNS improves the prognosis of patients with consciousness disorders.

**Days in the ICU**

The analysis of days in the ICU is displayed in Figure 6. Three studies were included$^{17,26,27}$; the MD was $-2.02$ (95% CI: $-2.69$, $-1.34$) with a Z value of 5.86 ($p < 0.00001$) and no heterogeneity ($I^2 = 0\%$).

**Cerebral blood flow**

As shown in Figure 7a, three studies reported cerebral mean blood flow velocity (VM);$^{9,24,28}$ the MD was 4.23 (95% CI: 2.56, 5.90) with a Z value of 4.97 ($p < 0.00001$) and low heterogeneity ($I^2 = 24\%$). The results of the cerebral
systolic blood flow velocity (VS) from five studies \( ^{11,23-25,28} \) are displayed in Figure 7b. The MD was 10.51 (95% CI: 5.79, 15.23) with a Z value of 4.36 (\( p < 0.00001 \)) and high heterogeneity (\( p < 0.00001, \Gamma^2 = 91\% \)). Together, these findings suggest that MNS increases cerebral blood flow, and especially the VS.
Discussion

Electrical stimulation—including cervical spinal cord electrical stimulation, thalamic nucleus electrical stimulation, and peripheral nerve electrical stimulation—is a globally used rehabilitation treatment method. In 1999, Cooper et al. proposed that the application of MNS can hasten awaking in coma patients. Many studies have since confirmed this proposition. MNS is advantageous in that it involves a simple operation, no trauma, relatively few complications, and a low cost. Moreover, its effects have been confirmed by neuroelectrophysiology (EEG evoked potential), neuroimaging, cerebral blood flow velocity, and neurotransmitters, meaning that it is widely used in clinical applications. Our analysis revealed that MNS can improve the GCS scores of patients with consciousness disorders regardless of their cause. It can also improve EEG scores and cerebral blood flow and decrease DRS scores and the number of days spent in the ICU.

The mechanisms for the effects of MNS may be as follows: 1) it increases bilateral cerebral blood flow, thus improving blood supply in the penumbra area of the cerebral ischemia, reducing the number of necrotic nerves, and promoting the repair and regeneration of neurons; (2) it enhances electrical activity in the brain, thus improving neuroelectrophysiological manifestations because persistent peripheral electrical stimulation excites the brainstem reticular system and the cerebral cortex; (3) it directly stimulates the brainstem reticular structure and cerebral cortex; and (4) it affects the secretion of neurotransmitters. Moreover, Manganoti et al. reported that electrical nerve stimulation can improve local blood flow in lesions, improve the oxygen and blood supply capacity of brain cells, and effectively reduce edema symptoms in necrotic areas, thus saving dysfunctional neurons and promoting resuscitation.

Consciousness disorders may persist for a long period; it is therefore important to examine the optimal length of MNS treatment. To address this issue, we conducted a subgroup analysis according to different treatment times. Our results indicated that even a week of MNS improves GCS scores, and that the extent of GCS improvements increases with prolonged treatment times.

Regarding the side on which MNS should be performed, our analysis indicated that either right or bilateral MNS promotes the recovery of consciousness disorders, and that the effect size of right MNS is larger than that of bilateral MNS. However, no studies have focused on left MNS. We ascribe this phenomenon to the following mechanism: when performing MNS, ideally one should take advantage of the feature that the functional location of the hand occupies the largest proportion of the projection in the cerebral cortex. Thus, electrical stimulation signals acting on the median nerve can attain the largest projection range in the cerebral cortex and more effectively promote wake-up. Because most human brains are left-hemisphere dominant, electrical stimulation of the right median nerve is usually more effective.

Our study has some limitations. First, some outcomes had high heterogeneity and there was selection bias in some studies. We tried to resolve the high heterogeneity using sensitivity analysis. After excluding several studies, heterogeneity was decreased without altering the outcome; this finding suggests that heterogeneity did not influence the outcome of our analysis. The selection bias was mainly caused by a lack of blinding in many included clinical studies. Although our sensitivity analysis revealed that this played a minor role in our results, it remains a significant bias in the present study. Second, the 23 included studies involved patients whose consciousness...
disorders were due to seven different causes, five of which were addressed in only one or two studies; thus, additional research should be performed to validate our conclusions. Third, most of the clinical trials included in this study were conducted in China and published in Chinese; this restricts our ability to generalize our conclusions. Moreover, we only analyzed the effects of right and bilateral MNS on consciousness disorders. More studies should be performed to explore the effects of left MNS. Finally, most included outcome indices were not true measures of consciousness, but were rather measures of physiological processes related to consciousness; improvements in such measures cannot be fully recognized as improvements in consciousness. In future studies of consciousness, more convincing indices (such as the Coma Recovery Scale-Revised) should be used to reflect the state of consciousness.

Conclusions

In our quantitative analysis, right or bilateral MNS promoted the recovery of consciousness disorders regardless of their cause. It also improved GCS scores, EEG scores, and cerebral blood flow while decreasing DRS scores and days spent in the ICU. Improvements in GCS scores were greater when MNS treatment times were longer. Furthermore, right MNS was more effective than bilateral MNS for improving GCS scores. Nonetheless, further high-quality clinical trials that examine the use of left MNS in consciousness disorders and are conducted in countries other than China are needed to confirm our results.

Author contributions

PW designed the study and modified the format; HZ wrote the paper; LL, YS, and ZZ searched and selected the relevant studies; XY, HXZ, and LZ extracted and analyzed the data; and WC and FY created the tables and figures.

Declaration of conflicting interests

The authors declare that there are no conflicts of interest.

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Supplemental material

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