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# Acupuncture-related techniques for postoperative cognitive complications: a systemic review and meta-analysis

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## Abstract

**Background** Postoperative cognitive complications are major challenges for postoperative recovery. Acupuncture-related techniques have been used for treating neurocognitive dysfunctions. However, whether they help to prevent postoperative cognitive complications remains unclear. We intend to evaluate the effect of acupuncture-related techniques on the incidence of postoperative cognitive complications (PCC) in patients undergoing surgery under general anesthesia.

**Methods** Based on PRISMA guidelines, a search of PubMed, EMBASE, Web of Science, and the Cochrane Central Register of Controlled Trials and ClinicalTrials.gov was performed to identify eligible trials published from inception to June 6, 2021. The search was performed in June 2021. The inclusion criteria were prospective, randomized, controlled clinical trials that compared acupuncture-related techniques with other techniques or non-acupuncture treatment in patients undergoing surgery under general anesthesia. Pooled odds ratios (ORs), 95% CIs, and *P* values were estimated for end points using fixed and random effects statistical models.

**Results** The analysis included 12 studies with 1058 patients. Compared with patients not receiving acupuncture, patients treated with acupuncture-related techniques had a lower incidence of PCCs (OR, 0.44; 95% CI, 0.33 to 0.59; *P* < 0.001; *n* = 968) and lower levels of biomarkers, including IL-6, TNF- $\alpha$ , and S100 $\beta$ . Acupuncture with needles and without needles showed similar effects on the prevention of PCCs. The effects of acupuncture-related techniques on PCCs were observed in both English and non-English articles. Subgroup analyses showed that both agitation and/or delirium (OR, 0.51; 95% CI, 0.34 to 0.76; *P* < 0.001; *n* = 490) and delayed cognitive recovery (OR, 0.33; 95% CI, 0.21 to 0.51; *P* < 0.001; *n* = 478) were reduced after treatment with acupuncture-related techniques. In adult studies evaluating MMSE scores, the scores were not different between groups (SMD, -0.71; 95% CI, -1.72 to 0.3; *P* = 0.17; *n* = 441).

**Conclusions** Acupuncture-related techniques, including needle techniques and electrical techniques, are associated with fewer postoperative cognitive complications, suggesting that acupuncture could be considered a potential option in the perioperative setting. Additional research is needed to develop higher-quality evidence and optimal regimens.

**Trial registration** PROSPERO (CRD42021258378).

**Keywords** Acupuncture, Postoperative cognitive dysfunction, Meta-analysis

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## Background

Postoperative cognitive complications consisting of agitation and/or delirium and long-lasting postoperative cognitive dysfunction are great challenges for anesthesiologists. Patients, especially those in the aging population, who suffer from postoperative cognitive complications could be at higher risk of morbidity and mortality (Olotu 2020). Growing evidence suggests a possible role for neuroinflammation, reduced functional connectivity, reduced glucose utilisation, and neurotransmitter imbalances, particularly involving dopamine and acetylcholine, in the processes underlying postoperative cognitive complications (PCCs) (Cibelli et al. 2010; Hu et al. 2018; Subramanian and Terrando 2019; Dellen et al. 2014; Vasunilashorn et al. 2015).

Management of postoperative cognitive complications involves a multi-professional approach and consists of pharmacological and nonpharmacological components (Olotu 2020). No single medication or intervention to prevent or treat postoperative cognitive complications is available. Avoiding anesthesia that is too deep, avoiding large swings in hemodynamics, effective pain management, and early mobilization are reported to be of benefit (Guenther et al. 2016; Heinrich et al. 2021; Li et al. 2020a; Zuylen et al. 2021).

Acupuncture-related techniques have been used for the treatment of cognitive disorders such as dementia after stroke and mild cognitive impairment (Du et al. 2020; Li et al. 2019, 2020b; Min and Xu-Feng 2016; Wang et al. 2016; Yang et al. 2016). Furthermore, the role of acupuncture in the perioperative scenario are reported in both animal and clinical studies (Lu et al. 2015; Ho et al. 2020). Possible mechanisms include acupuncture modulating inflammation, oxidative stress, synaptic changes, and other cellular events to mitigate cognitive disorders (Mazidi et al. 2017; Liu et al. 2017; Yuan et al. 2014; Silva et al. 2015; Yang et al. 2018). Perioperative acupuncture reduces not only the consumption of anesthetics and analgesics but also anesthesia-related side effects (Yang et al. 2016). Subsequent studies have assessed the effects of acupuncture-related techniques on postoperative cognitive complications, but there has not been a pooling of their findings (Ho et al. 2020). Therefore, we performed a systematic review and meta-analysis of the efficacy of acupuncture-related techniques to prevent postoperative cognitive complications in patients undergoing general anesthesia. Our primary outcome was the incidence of postoperative cognitive complications, and we reported the severity of postoperative cognitive complications and changes in preinflammatory cytokines.

## Material and methods

We adhered to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for the conduct and reporting of this systematic review. The protocol was registered at PROSPERO (CRD42021258378).

A systematic search with no restriction to language and publication status was performed on June 4, 2021. We searched PubMed, EMBASE, Web of Science, the Cochrane Central Register of Controlled Trials and ClinicalTrials.gov for eligible studies. We reviewed the reference lists of the included publications and previous systematic reviews to identify additional eligible studies. The search strategy is detailed in Additional file 1: Supplemental file 1 (eMethod). We did not search the gray literature.

The inclusion criteria were prospective, randomized, controlled clinical trials that compared acupuncture-related techniques with other techniques or non-acupuncture treatment for postoperative cognitive complications in patients undergoing surgery under general anesthesia. We excluded observational studies and quasi-randomized and nonrandomized controlled trials. We excluded studies without assessment of postoperative cognition. This meta-analysis of readily available literature did not require institutional review board approval, and each respective study detailed their consent procedures.

Our primary outcomes included the incidence of postoperative cognitive complications during the hospital stay. Postoperative cognitive complications include emergence agitation and/or delirium, postoperative cognitive dysfunction, and postoperative delirium. When postoperative cognitive complications were assessed several times after surgery, the highest incidence of a postoperative cognitive complications during the hospital stay was extracted. Our secondary outcomes included the highest mini-mental state examination (MMSE) scores during the hospital stay, and levels of inflammatory cytokines and cerebral injury biomarkers, including interleukin (IL-6), tumor necrosis factor (TNF)- $\alpha$ , and S100 $\beta$ .

Data extraction was independently performed by two authors (M.Z. and J.Z.), with good interobserver agreement ( $\kappa=0.95$ ). These two authors independently screened the articles and extracted the following data from each study: patient characteristics (age, sex, and American Society of Anesthesiologists [ASA] physical status), study characteristics (country, type of surgery and anesthesia, sample size), intervention characteristics (type of acupuncture, timing and comparators), and outcomes of interest (assessment tool, type of PCC).

Z.L. and L.S. independently evaluated the risk of bias for each study included with the Cochrane risk

of bias assessment tool (Higgins and Green 2008). We also reviewed conflicts of interest or industry sponsorship. We resolved any inconsistency through discussion ( $\kappa=0.55-1.0$ ). When an email address was available, we contacted the authors of the original study for detailed information. Specifically, we attempted to retrieve information regarding the detailed methodology of each trial and the outcomes of interest that were not presented in the articles. We deemed the authors to be unresponsive if they did not reply after three consecutive attempts, based on a previous study (Kuriyama and Maeda 2019). The overall certainty of evidence for each outcome was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Balslem et al. 2011).

We calculated the odds ratios (ORs) and standardized mean differences (SMDs) for dichotomous and continuous outcomes, respectively. Pooled ORs and  $P$  values were estimated for the incidence of postoperative cognitive complications using the Mantel–Haenszel method and either a fixed or random effects statistical model. When a study presented the data as the median with interquartile range, we converted the values to the mean and standard deviation. Meta-analyses were conducted with Review Manager software (RevMan; version 5.1 for Windows; Nordic Cochrane Centre). The 95% CIs were calculated and are presented in forest plots. Statistical heterogeneity was evaluated with the  $\chi^2$  test, and inconsistency was estimated using the  $I^2$  statistic. We conducted subgroup analysis based on patient population, type of acupuncture, and type of postoperative cognitive complications. The quality of the selected randomized clinical trials was assessed based on the instrument developed by Jadad et al. (Jadad et al. 1996; Spring et al. 2016) (Additional file 1: Table S1). Sensitivity analyses were conducted to evaluate the effect of acupuncture on postoperative cognitive complications in studies published in English and non-English and in studies using different anesthetic techniques. When a trial had zero events in either arm, we performed sensitivity analyses with continuity corrections by adding 1 to each cell of the  $2 \times 2$  tables from the trial (Kuriyama and Maeda 2019; Sweeting et al. 2004).  $P$  values of 0.05 were considered statistically significant.

Egger's regression test was used to assess publication bias for the primary outcomes of this review. We also created a funnel plot for the assessment of publication bias in situations of low risk of publication bias.

## Results

### Overview of included studies

Our database search initially produced 106 titles and abstracts. Thirty-four records were finally screened.

Twenty-one non-RCT records were excluded. One record was excluded due to lack of assessment of postoperative cognition. We ultimately included 12 randomized controlled trials involving 1058 study participants for the analysis after applying the inclusion and exclusion criteria (Fig. 1). The risk of bias for each study was shown in Additional file 1: Fig. S1.

Eight and four trials included patients older than 65 years old and younger than 10 years old (1.5–8 years old for two trials, 2–10 years for one trial, 1–6 years for one trial), respectively. Eight trials were conducted in China. The types of surgery were listed as follows: ENT surgery (adenoidectomy and/or tonsillectomy, myringotomy tube placement), gastrointestinal surgery, interventional surgery, and orthopedic surgery (spine, knee replacement) (Table 1).

### Primary endpoint

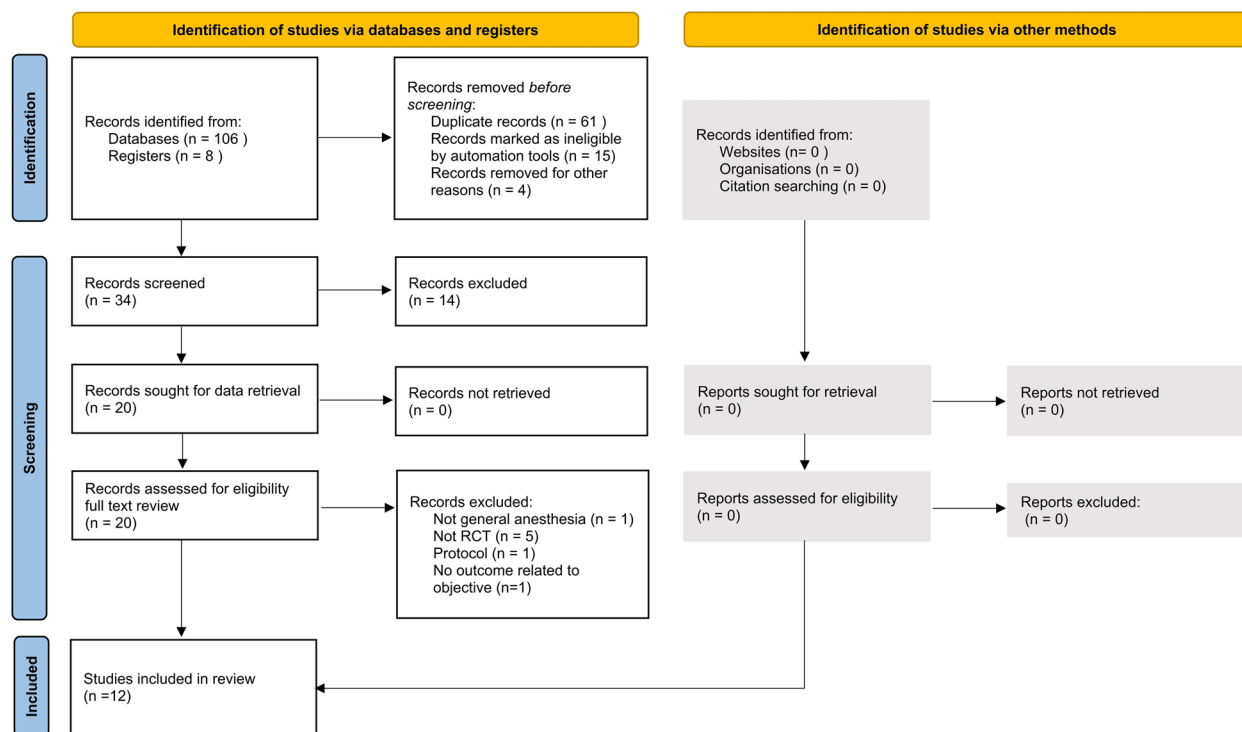
In one study (Zhang et al. 2017), only highest MMSE scores were recorded and the incidence of PPC could not be determined. Eleven studies comprising 968 participants provided data on the incidence of postoperative cognitive complications. A low certainty of evidence supported that perioperative administration of acupuncture-related techniques was associated with a lower incidence of postoperative cognitive complications (OR, 0.44; 95% CI, 0.33 to 0.59;  $P < 0.00001$ ;  $df = 10$ ;  $I^2 = 26\%$ ; Fig. 2 and Additional file 1: Table S2). Egger's regression test for assessing publication bias showed no significant bias ( $P = 0.27$ ).

### Postoperative delirium and delayed cognitive recovery

Five trials comprising 490 participants assessed postoperative delirium. Acupuncture was associated with a lower incidence of postoperative delirium (OR, 0.51; 95% CI, 0.34 to 0.76;  $P < 0.001$ ;  $df = 4$ ;  $I^2 = 64\%$ ; Additional file 1: Fig. S2). Seven trials comprising 478 participants evaluated delayed cognitive recovery. Acupuncture was associated with a lower incidence of delayed cognitive recovery (OR, 0.33; 95% CI, 0.21 to 0.51;  $P < 0.001$ ;  $df = 5$ ;  $I^2 = 0\%$ ; Additional file 1: Fig. S2).

### Acupuncture with needle and acupuncture without needle

Three trials comprising 243 participants compared acupuncture with needles and control conditions. The incidence of postoperative cognitive disorder was not different between the two techniques (OR, 0.56; 95% CI, 0.30 to 1.05;  $P = 0.07$ ;  $df = 2$ ;  $I^2 = 59\%$ ; Additional file 1: Fig. S3). Eight trials comprising 725 participants compared acupuncture without needles and control conditions. Acupuncture was associated with a lower incidence of postoperative cognitive disorder (OR, 0.38;



**Fig. 1** PRISMA flow diagram for the systematic review

95% CI, 0.27 to 0.54;  $P < 0.001$ ;  $df = 7$ ;  $I^2 = 16\%$ ; Additional file 1: Fig. S3).

#### Pediatric patients and non-pediatric patients

Subgroup analysis showed that based on the four trials comprising 370 participants compared acupuncture and control conditions in pediatric patients, acupuncture was associated with a lower incidence of postoperative cognitive complications (OR, 0.61; 95% CI, 0.38 to 0.98;  $P = 0.04$ ;  $df = 3$ ;  $I^2 = 69\%$ ; Additional file 1: Fig. S4). Seven trials comprising 598 participants compared acupuncture and control conditions in non-pediatric patients. Acupuncture was associated with a lower incidence of postoperative cognitive complications (OR, 0.36; 95% CI, 0.24 to 0.53;  $P < 0.001$ ;  $df = 6$ ;  $I^2 = 0\%$ ; Additional file 1: Fig. S4).

#### Secondary end points

Five trials in adult patients only comprising 441 participants compared the highest MMSE scores obtained during the hospital stay. No difference was observed between participants treated with acupuncture and those in the control group (SMD,  $-0.71$ ; 95% CI,  $-1.72$  to  $0.30$ ;  $P = 0.17$ ;  $df = 4$ ;  $I^2 = 96\%$ ; Fig. 3).

Five trials comprising 459 participants compared serum IL-6 levels. Acupuncture was associated with a lower level of IL-6 (SMD,  $-2.51$ ; 95% CI,  $-3.57$  to  $-0.74$ ;  $P = 0.003$ ;  $df = 4$ ;  $I^2 = 98\%$ ; Fig. 4). Five trials comprising

329 participants and 385 participants compared the levels of serum TNF- $\alpha$  and S100 $\beta$ , respectively. Acupuncture was associated with lower levels of TNF- $\alpha$  (SMD,  $-2.07$ ; 95% CI,  $-3.41$  to  $-0.73$ ;  $P = 0.003$ ;  $df = 4$ ;  $I^2 = 96\%$ ) and S100 $\beta$  (SMD,  $-0.91$ ; 95% CI,  $-1.3$  to  $-0.53$ ;  $P < 0.00001$ ;  $df = 4$ ;  $I^2 = 68\%$ ; Fig. 4). The certainty of the evidence was very low (Additional file 1: Table S2).

#### Sensitivity analysis

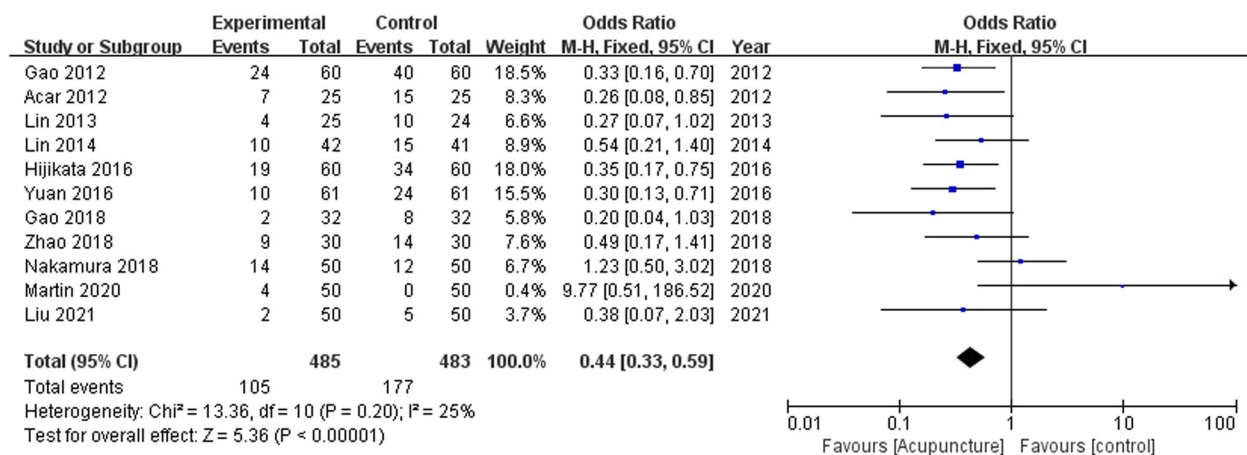
In one trial reporting the incidence of postoperative cognitive complications, the number of events in the control group was zero. For sensitivity analyses with continuity corrections, 1 was added to each cell of the  $2 \times 2$  tables from the trial. Acupuncture was associated with a lower incidence of postoperative cognitive complications (OR, 0.44; 95% CI, 0.33 to 0.60;  $P < 0.00001$ ;  $df = 10$ ;  $I^2 = 30\%$ ; Additional file 1: Fig. S5).

Seven trials were published in English, and four trials were published in non-English (all Chinese). The results of trials published in English ( $n = 594$ ; OR, 0.52; 95% CI, 0.35 to 0.79,  $P = 0.002$ ) and non-English ( $n = 394$ ; OR, 0.35; 95% CI, 0.22 to 0.55,  $P < 0.00001$ ) both showed significantly fewer postoperative cognitive complications in patients who received the acupuncture-related interventions (Additional file 1: Fig. S6).

**Table 1** Summary of the findings of the clinical trials included in the meta-analysis

Study	Age	Country	Sample size (female)	ASA	Type of Surgery	Anesthesia methods	Type of acupuncture	Parameters for stimulation	Acupoints	Comparator	Timing of acupuncture	Type of PCC	Time of PCC	Assessment tool	Primary outcome	Other outcomes
Acar et al. (2012)	2-10yrs	Turkey	50(25)	I-II	Adenoidectomy and/or tonsillectomy	Sevo	capsicum plasters	NA	bilateral HT7	inactive plasters	30 min before anesthesia induction	agitation	15 min after surgery	PAED scale	Incidence of agitation	Pain
Gao et al. (2012)	>65yrs	China	120(68)	I-III	Non-cardiac surgery	Sevo	TEAS+electroacupuncture	2/100 Hz	Hegu, Neiguan, Zusanli, Baihui	no acupuncture	30 min before anesthesia induction to end of surgery	POCD	2-4d after surgery	MMSE	Incidence of POCD	PONV, MMSE scores
Lin et al. (2013)	≥65yrs	China	124(42)	II-III	Gastro-intestinal surgery	Propofol	TEAS	2/100 Hz	Baihui, Yintang, Neiguan	no acupuncture	30 min before induction to end of surgery	POCD	3d post-op	MMSE	Incidence of POCD	S100β
Lin et al. (2014)	≥65yrs	China	83(29)	I-II	Gastro-intestinal surgery	Propofol	electroacupuncture	2/100HZ	Neiguan, Zusanli, Baihui	no acupuncture	30 min before anesthesia induction to end of surgery	POCD	3d after surgery	MMSE	Incidence of POCD	Time to awake, Remifentanyl consumption, TNF-α, IL-1β, IL-6
Hijikata et al. (2016)	18-96 months	Japan	120(37)	I-II	Minor surgery	Sevo	TEAS	1 Hz	HT7	Sham (electrode without stimulation)	during surgery	emergence agitation	during PACU	PAED, Aono's scale	Incidence of agitation	Time to tracheal extubation, PACU stay duration and postoperative pain scores
Yuan et al. (2016)	29-72yrs	China	122(ND)	I-III	Intervention neurosurgery	Propofol	TEAS	1.5 Hz	Baihui, Yintang, Neiguan	no acupuncture	before anesthesia induction	POCD	post-op 7ds, 30ds	MMSE	Incidence of POCD	NSE, S-100β, IL-1β, IL-6, TNF-α
Zhang et al. (2017)	>65yrs	China	90(42)	I-II	Spine surgery	Propofol	electroacupuncture	2/15 Hz	Baihui, Dazhui, Zusanli	no acupuncture	30 min before induction to end of surgery	POCD	post-op 3ds	MMSE	Incidence of POCD	Interleukin (IL)-6, IL-10, and S100b level; remifentanyl, propofol consumption
Gao et al. (2018)	>65yrs	China	64(31)	I-II	Spine surgery	Propofol	TEAS	2/100 Hz	Hegu, Neiguan	Sham (electrode without stimulation)	30 min before induction to end of surgery	POD	post-op 3ds	RASS, CAM	Incidence of POCD	TNF-α, IL-6, matrix MMP-9, and S100β level; remifentanyl, propofol consumption
Nakamura et al. (2018)	18-96 months	Japan	100(26)	I-II	Inguinal hernia repair or orchiopepy	Sevo	TEAS	1 Hz	HT7	Sham (electrode without stimulation)	during surgery	emergence delirium	In PACU	PAED, Aono's scale	Incidence of agitation	The severity of EA, PACU stay duration, and postoperative pain
Zhao et al. (2018)	65-75yrs	China	60(34)	Not described	Knee replacement	Propofol	electroacupuncture	2/100 Hz	Tou San-shen, Baihui, Hegu, Taichong	placebo needle	5 days before surgery, once daily	POCD	post-op 1d, 7d	MMSE	MMSE score	TNF-α, IL-6, and S100β





**Fig. 2** Forest plot for the incidence of PCC during hospital stay. The plot shows decreased incidence in patients treated with acupuncture-related techniques compared with non-acupuncture controls. Fixed-effects odds ratios are calculated using the Mantel–Haenszel test. Error bars represent 95% CI. OR=odds ratio

Six trials used propofol, and five trials used sevoflurane for general anesthesia maintenance. Acupuncture-related techniques were associated with significantly lower rates of PCCs regardless of the type of anesthetics used for general anesthesia (both  $P < 0.001$ , Additional file 1: Fig. S7).

## Discussion

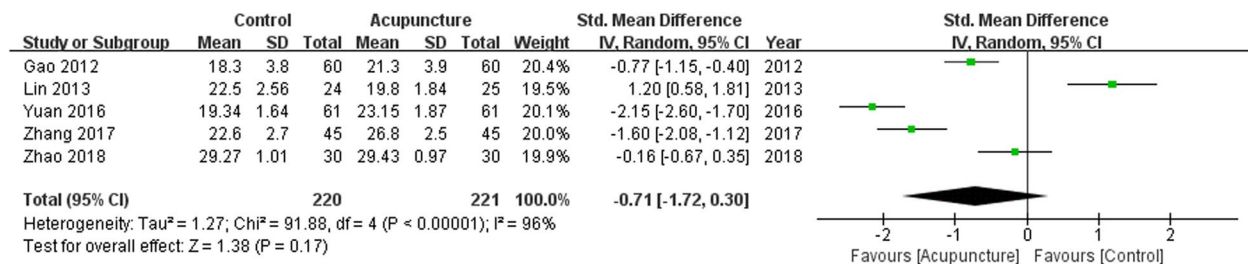
Our review of acupuncture-related techniques as interventions for postoperative cognitive complications found low-certainty evidence that showed that acupuncture-related techniques, compared with control conditions, were associated with reduced postoperative cognitive complications. Subgroup analyses reported that both acute agitation and/or delirium and delayed cognitive recovery were lower in participants who received acupuncture-related techniques. The incidence of postoperative cognitive complications was lower in participants received acupuncture in both pediatric population and non-pediatric population.

In this study, we used the mesh term ‘postoperative cognitive complications’. Another nomenclature ‘perioperative neurocognitive disorders’ was also recommended to be used as an overarching term for cognitive impairment identified in the preoperative or postoperative period (Evered et al. 2018). It includes any form of acute event (postoperative delirium) and cognitive decline diagnosed up to 30 days (delayed neurocognitive recovery) and up to 12 months (postoperative neurocognitive disorder) after the procedure. Based on this definition, the cognitive changes after surgery assessed in the included studies were acute delirium and delayed neurocognitive recovery. In the studies included, MMSE was only undertaken as the primary outcome diagnostic tool

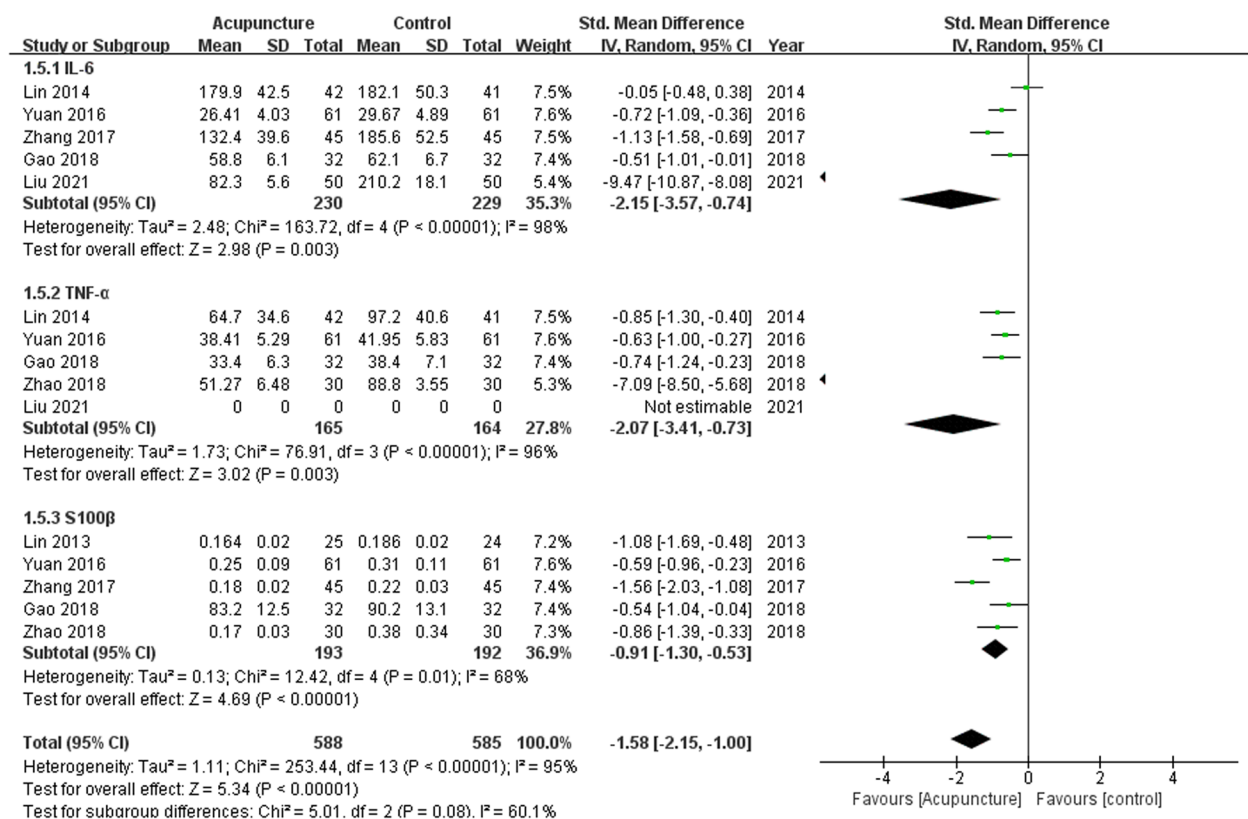
in patients older than 65 years. The MMSE is reported as the diagnostic tool for agitation and delirium in adults only, adding evidence that there are different pathologies presenting as agitations and/or delirium in older adults and in children. As indicated by the subgroup analysis, in pediatric patients, acupuncture was associated with a lower incidence of agitation and/or delirium, which is in accordance with the less cognitive complications in adults.

Our review found very low-certainty evidence that MMSE scores were higher and the levels of proinflammatory biomarkers, including serum IL-6, TNF- $\alpha$  and S100 $\beta$ , were lower in patients treated with acupuncture. This concurs with a previous report that postoperative cognitive dysfunction is correlated with the concentrations of peripheral inflammatory markers, particularly interleukin-6 and S-100 $\beta$  (Wiberg et al. 2021; Peng et al. 2013). The role of inflammation in perioperative brain function is becoming apparent (Subramaniyan and Terrando 2019). Surgery may induce a systemic inflammatory response via cytokines such as IL-1 $\beta$  (Cibelli et al. 2010), TNF- $\alpha$  (Terrando et al. 2010), and IL-6 (Hu et al. 2018), as well as S100 Ca<sup>2+</sup>-binding proteins and oxidative stress pathways. Administration of an IL-6 monoclonal antibody and targeting of TNF- $\alpha$  have been reported to prevent postoperative cognitive complications (Cibelli et al. 2010; Hu et al. 2018; Subramaniyan and Terrando 2019; Terrando et al. 2010). There is a potential benefit of acupuncture in terms of inflammatory markers and it requires further investigation.

Regardless of the type of acupuncture technique, the effect of decreasing postoperative cognitive complications could be induced by manual or electrical stimulation (transcutaneous electrical acupoint stimulation,



**Fig. 3** Forest plot for the highest MMSE scores during hospital stay. The plot shows that MMSE scores were not increased in patients treated with acupuncture-related techniques compared with non-acupuncture controls. Standard mean differences (SMD) are calculated. MMSE = Mini-mental status examination



**Fig. 4** Forest plot for the highest level of serum inflammatory cytokines and brain injury markers during hospital stay. The plot shows decreased level of markers in patients treated with acupuncture-related techniques compared with non-acupuncture controls. Standard mean differences (SMD) are calculated

TEAS). The frequency of the stimulation regimen for electroacupuncture was low (1 Hz, 2 Hz, 10 Hz, 15 Hz). Various studies have reported that high-frequency and low-frequency electroacupuncture or TEAS have clinical effects elicit through distinct mechanisms (Yang et al. 2016). For example, the suppressive effects of low-frequency electroacupuncture on carrageenan-induced edema and pain are mediated by sympathetic postganglionic neurons, while the suppressive effects of HF EA

are mediated by the sympatho-adrenal medullary axis (Kim et al. 2008). Moreover, an animal study showed that high-frequency electroacupuncture (50 Hz) more effectively exerted a protective effect against Aβ<sub>1-42</sub>-induced learning and memory deficits and synapse ultrastructure impairments (Yu et al. 2018). The most effective electroacupuncture frequency for postoperative cognitive complications remains to be explored. The comparators were no acupuncture, inactive plaster or no stimulation



electrode control (which is called mock TEAS). It was recommended that regardless of the choice of control group, it is valuable to check its adequacy (Vincent and Lewith 1995). Nevertheless, no information about verifying the adequacy of the control conditions was provided in the studies included in our review. The timing of acupuncture varies in enrolled studies. Acupuncture was given before the surgery in eight studies and during the surgery in four studies. It was speculated that acupuncture provided after anesthesia induction may not be as effective as that provided when patients were awake (Yang et al. 2016). Further studies were needed to verify the optimal timing of perioperative acupuncture.

The trials on pediatric patients were mostly performed in countries outside China, and the measured outcomes were agitation and/or delirium, which is likely an emergence delirium. The trials on non-pediatric patients were mostly on patients older than 65 years old and focused on delayed cognitive recovery. The number of acupoints chosen across interventions varied greatly, and a comparison of the effect of acupuncturing different acupoints was difficult. Baihui, Hegu, and Neiguan were the most frequently used acupoints (Baihui in 6 trials, Hegu in 4 trials, and Neiguan in 6 trials). The timing of acupuncture included preoperative, intraoperative and postoperative and a combination of the three treatment times. Seven trials administered TEAS 30 min before anesthesia induction, which is a frequently used protocol for many studies on perioperative acupuncture (Lu et al. 2021).

Our review could not adequately assess adverse events associated with acupuncture-related techniques. All studies included in our review were published after the release of the Consolidated Standards of Reporting Trials (CONSORT) statement in 1996 (Begg et al. 1996), which recommended that trial investigators report unintended effects related to interventions. However, no study provided information of adverse events. Whether acupuncture-related techniques are related to significant adverse events still needs further investigation.

The strengths of our study include the comprehensive nature of the literature search, which identified 12 publications, thus permitting sensitivity analyses. In addition, we complied with the Cochrane methodology. We attempted to contact the authors to more accurately evaluate the risk of bias and to obtain necessary unpublished data. We also confirmed the robustness of our findings with sensitivity analysis.

Our review also has limitations. First, age ranges of the participants in the enrolled trials were different. Second, the JADAD score of the eligible studies was relatively low. Seven trials had a JADAD score of 2, and one trial scored 1 (Additional file 1: Table S1). The assessment of evidence grade was low and very low for the measured outcomes

(Additional file 1: Table S2). Risk of bias and incomplete reporting were major concerns contributing to the low quality of the evidence. Risk of bias resulted from difficulty in blinding for the acupuncture intervention, though it could be partly overcome by blinded outcome assessment. Incomplete reporting was based on the failure to provide values of some effects, including the 95% CI, in some trials. There was a risk of multiple testing bias in our secondary outcomes, as a 95% CI was calculated. In relation to this, methodological bias continues to be a concern, as some trials were characterized by an unclear risk of bias. Third, the surgery type varies in the enrolled studies. Data retrieved from same surgeries may provide more potent evidence. Moreover, no data were available on postoperative cognitive disturbance-related outcomes beyond 30 days after surgery. Whether acupuncture like other non-pharmacological interventions have no effect on long-term cognitive disturbance reported after delirium needs to be verified.

## Conclusions

This systemic review and meta-analysis reports that acupuncture-related techniques may decrease postoperative cognitive complication and warrants further investigation. Nevertheless, the inherent limitations of the included studies prevent us from reaching definitive conclusions. Future large, well-designed RCTs with extensive follow-up are needed to confirm and update the findings of this analysis.

## Abbreviations

PCC	Postoperative cognitive complications
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
MMSE	Mini-mental state examination
IL	Interleukin
TNF	Tumor necrosis factor
ASA	American Society of Anesthesiologists
GRADE	Grading of Recommendations Assessment, Development and Evaluation
OR	Odds ratio
SMD	Standardized mean difference
CI	Confidence interval
RCT	Randomized clinical trial
ENT	Ear, nose and throat
TEAS	Transcutaneous electrical acupoint stimulation
CONSORT	Consolidated Standards of Reporting Trials

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13741-023-00303-5>.

**Additional file 1: Supplemental file 1 (eMethod).** Search Strategy. **Table S1.** Study Quality of Eligible Trials. **Table S2.** Grading of Recommendations Assessment, Development and Evaluation Summary of Quality of Evidence for primary and secondary Outcomes. **Figure S1.** Risk of bias summary: review authors' judgements about each risk of bias item for

each included study. **Figure S2.** Forest plot for subgroup analysis of the incidence of PND by type of PND. **Figure S3.** Forest plot for subgroup analysis of the incidence of PND by acupuncture techniques. **Figure S4.** Forest plot for subgroup analysis of the incidence of PND by age. **Figure S5.** Sensitivity analyses with continuity corrections on zero events of PND incidence. **Figure S6.** Effect of acupuncture on PND in studies published in English and non-English. **Figure S7.** Effect of acupuncture on PND under different anesthetic techniques. **Figure S8.** Funnel Plots for Studies Evaluating.

#### Acknowledgements

Not applicable

#### Authors' contributions

Zhihong Lu had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Liwen Shi, Junbao Zhang, Zhihong Lu, Zhuoma Cairen. Literature review and data extraction: Junbao Zhang and Minjuan Zhang. Bias analysis: Liwen Shi and Zhihong Lu. Statistical analysis: Manping Yang, Zhuoma Cairen. Writing of the draft: Junbao Zhang. Critical revision of the manuscript for important intellectual content: Zhihong Lu, Yun Wang. Obtained funding: Zhihong Lu. Administrative, technical, or material support: Zhihong Lu, Yun Wang. All authors read and approved the final manuscript.

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#### Availability of data and materials

All data generated or analyzed during this study are included in this published article, its supplementary information files, and the primary randomized controlled trials cited for inclusion. A copy of the raw data could be reached by requests for additional analysis. Data will be available when the manuscript published.

#### Declarations

##### Ethics and approval and consent to participate

The corresponding author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

##### Consent for publication

We have reported whether we plan to disseminate the results to study participants and or patient organizations or stated that dissemination to these groups is not possible/applicable.

##### Competing interests

All authors have completed the Unified Competing Interest form and declare: no support from any organization for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years, no other relationships or activities that could appear to have influenced the submitted work.

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