

INPLASY PROTOCOL

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None declared.

Comparative efficacy of Acupuncture-Related Techniques for Mild Cognitive Impairment : A Bayesian Network Analysis.

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Review question / Objective: Mild cognitive impairment (MCI) is a heterogenous clinical syndrome reflecting a change in cognitive function and deficits on neuropsychological testing but relatively intact activities of daily living. MCI has received increasing attention in the field of cognitive neuroscience. Previous clinical trials have shown that acupuncture is safe and effective for mild cognitive impairment. In recent years, many researchers pay attention to alternatives as adjuvant therapies to improve the outcome of patients. However, due to the great diversity of acupuncture therapies, few studies directly compare different acupuncture techniques, and it is unclear which method is optimal for treating MCI with acupuncture. As a result, determining the most effective acupuncture treatment for MCI is a challenging task. In this study, NMA will be utilized to assess and rank the data obtained so that the best acupuncture treatment for MCI may be determined.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 April 2022 and was last updated on 23 April 2022 (registration number INPLASY202240140).

INTRODUCTION

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neuroscience. Previous clinical trials have shown that acupuncture is safe and effective for mild cognitive impairment. In recent years, many researchers pay attention to alternatives as adjuvant therapies to improve the outcome of patients. However, due to the great diversity of acupuncture therapies, few studies directly compare different

acupuncture techniques, and it is unclear which method is optimal for treating MCI with acupuncture. As a result, determining the most effective acupuncture treatment for MCI is a challenging task. In this study, NMA will be utilized to assess and rank the data obtained so that the best acupuncture treatment for MCI may be determined.

Condition being studied: Acupuncture as an integral part of traditional medicines throughout the world to management Mild Cognitive Impairment(MCI) has recently drawn widespread attention and increasingly applied in clinical and scientific research. Moreover, acupuncture has advantages such as safety, convenience, very few side effects, and economical. In China, Acupuncture, with many categories such as manual acupuncture, electro- acupuncture, moxibustion therapy, auricular acupuncture and acupoint patching, are widely used to the treatment of MCI. Although there are many acupuncture-related interventions for MCI, there is still a lack of comparison on the efficacy of different acupuncture interventions and the optimal choice of acupuncture is still uncertain. MCI is defined as an intermediate stage between normal aging and Alzheimer's disease (AD), and early and easily available interventions to delay the progress of MCI to AD are necessary. Acupuncture as an integral part of traditional medicines throughout the world to management MCI has recently drawn widespread attention and increasingly applied in clinical and scientific research. Although there are many acupuncture-related interventions for MCI, there is still a lack of comparison on the efficacy of different acupuncture interventions and the optimal choice of acupuncture is still uncertain.

METHODS

Search strategy: The Bayesian Network Meta-Analyses statement and the Cochrane handbook were used to conduct this study. PubMed, Web of Science, EMBASE, China National Knowledge Infrastructure(CNKI), Cochrane Library, VIP Periodical Resource Integration Service

Platform, and Wangfang Databases were searched through till March 4th, 2022, with a combination of MeSH terms and free words.

#1 TS=(Cognitive Dysfunction or Cognitive Dysfunctions or Dysfunction, Cognitive or Dysfunctions, Cognitive or Cognitive Impairments or Cognitive Impairment or Impairment, Cognitive or Impairments, Cognitive or Mild Cognitive Impairment or Cognitive Impairment, Mild or Cognitive Impairments, Mild or Impairment, Mild Cognitive or Impairments, Mild Cognitive or Mild Cognitive Impairments or Mild Neurocognitive Disorder or Disorder, Mild Neurocognitive or Disorders, Mild Neurocognitive or Mild Neurocognitive Disorders or Neurocognitive Disorder, Mild or Neurocognitive Disorders, Mild or Cognitive Decline or Cognitive Declines or Decline, Cognitive or Declines, Cognitive or Mental Deterioration or Deterioration, Mental or Deteriorations, Mental or Mental Deteriorations)

#2 TS=((randomized controlled trial) OR (controlled trial) OR (clinical trial) OR (case-control studies) OR (case series))

#3 TS=((acupuncture*) OR (acupuncture* Treatment*) OR (acupuncture* therapy*) OR (body acupuncture*) OR (Needle* acupuncture*) OR (Manual* acupuncture*) OR (acupuncture* Point*) OR (electroacupuncture*) OR (Warm* acupuncture*) OR (electr*-acupuncture*) OR (acupoints) OR (Acupoint injection) OR (plum blossom needle) OR (filiform steel needle) OR (catgut implantation) OR (Autohemotherapy) OR (fire needle) OR (scalp acupuncture) OR (manual acupuncture) OR (autologous whole-blood acupoint injection) OR (electroacupuncture) OR (body acupuncture))

#4 #3 AND #2 AND #1.

Participant or population: The participants in this study were MCI patients who had been diagnosed with nonorganic diseases of any type of MCI using standard diagnostic criteria, such as the American Psychiatric Manual of Psychiatry and Statistics diagnostic criteria for MCI, the MCI Clinical Diagnostic Standards revised by Petersen, the Reference Standard of

Deficiency Syndrome Differentiation in traditional Chinese Medicine, The 2006 Chinese expert consensus on cognitive dysfunction and Chinese Guidelines for the Diagnosis and Treatment of Dementia and Cognitive Impairment.

Intervention: Studies that used a combination of acupuncture-related therapies and Conventional Therapy (CT) were included in the study. Classic acupuncture (with or without electrical stimulation, and manual or scalp acupuncture), ear (auricular) acupuncture, auricular pressure, BVA, abdominal acupuncture, acupoint catgut embedding and acupressure, moxibustion (including direct and indirect moxibustion, and warm needling), or acupoint injection were all included in the definition of acupuncture-related therapies. The control group received conventional therapy or placebo (sham acupuncture or other placebo treatments). These interventions were used alone or in combination. The current conventional-therapies strategy for MCI consists of conventional medicines (including Nimodipine, Huperzine, Perphenazine, Duxil, Donepezil, and Hydergine) and cognitive training.

Comparator: The control group received conventional therapy or placebo (sham acupuncture or other placebo treatments). These interventions were used alone or in combination. The current conventional-therapies strategy for MCI consists of conventional medicines (including Nimodipine, Huperzine, Perphenazine, Duxil, Donepezil, and Hydergine) and cognitive training.

Study designs to be included: All Randomized controlled trials (RCTs) of acupuncture-related therapies for MCI were used just English or Chinese as a language option, regardless of blinding, publication, status, and length of trial. Non-randomized uncontrolled trials were excluded. Additionally, case reports, animal experiments, Individual cases, research advances, expert experience, conference articles, and duplicate articles were excluded.

Eligibility criteria: 1. Types of studies: All Randomized controlled trials (RCTs) of acupuncture-related therapies for MCI were used just English or Chinese as a language option, regardless of blinding, publication, status, and length of trial. Non-randomized uncontrolled trials were excluded. Additionally, case reports, animal experiments, Individual cases, research advances, expert experience, conference articles, and duplicate articles were excluded. 2. Participants: The participants in this study were MCI patients who had been diagnosed with nonorganic diseases of any type of MCI using standard diagnostic criteria, such as the American Psychiatric Manual of Psychiatry and Statistics diagnostic criteria for MCI, the MCI Clinical Diagnostic Standards revised by Petersen, the Reference Standard of Deficiency Syndrome Differentiation in traditional Chinese Medicine, The 2006 Chinese expert consensus on cognitive dysfunction and Chinese Guidelines for the Diagnosis and Treatment of Dementia and Cognitive Impairment. 3. Interventions: Studies that used a combination of acupuncture-related therapies and Conventional Therapy (CT) were included in the study. Classic acupuncture (with or without electrical stimulation, and manual or scalp acupuncture), ear (auricular) acupuncture, auricular pressure, BVA, abdominal acupuncture, acupoint catgut embedding and acupressure, moxibustion (including direct and indirect moxibustion, and warm needling), or acupoint injection were all included in the definition of acupuncture-related therapies. The control group received conventional therapy or placebo (sham acupuncture or other placebo treatments). These interventions were used alone or in combination. The current conventional-therapies strategy for MCI consists of conventional medicines (including Nimodipine, Huperzine, Perphenazine, Duxil, Donepezil, and Hydergine) and cognitive training. 4. Outcomes: We used the MoCA and MMSE scales as the outcome indicators to assess the effects of acupuncture on cognitive function.

Information sources: The Bayesian Network Meta-Analyses statement and the Cochrane handbook were used to conduct this study. PubMed, Web of Science, EMBASE, China National Knowledge Infrastructure(CNKI), Cochrane Library, VIP Periodical Resource Integration Service Platform, and Wangfang Databases were searched through till March 4th, 2022, with a combination of MeSH terms and free words.

Main outcome(s): We used the MoCA and MMSE scales as the outcome indicators to assess the effects of acupuncture on cognitive function. The main outcomes were global cognitive function and behavioral abnormalities, which were assessed using recognized and standardized scales such as the mini-mental state examination (MMSE) score, the Montreal Cognitive Assessment (MoCA) score. Montreal Cognitive Assessment (MoCA) includes 11 items in 8 cognitive domains, namely attention and concentration, executive function, memory, language, visual structure skills, abstract thinking, computation and directivity. The total score is 30 points. If the number of years of education is less than 12 years, one point will be added to the original score. MoCA is lower than 26 indicates cognitive orientation, location orientation, immediate memory, attention and computation, delayed memory, zero for each incorrect or unknown answer. There are 30 items on the scale. One point for each correct answer, and values of normal and abnormal cognitive functions are related to the education level: the illiterate group is lower than 17 points, the primary school group lower than 20 points, the middle school group and above is lower than 24 points.

Additional outcome(s): Two reviewers (YL and LZM) independently assessed the risk of bias in included studies using Cochrane's risk of bias tool 5.1.0 in order to evaluate the methodological quality of the research. The Cochrane Risk of Bias tool contains seven items: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4)

blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; (7) other sources of bias. Each trial was graded as either "low," "high," or "unclear" risk. A third reviewer resolved conflicts during trial selection when data extraction and quality evaluation scores were inconsistent.

Strategy of data synthesis: Given the potential for clinical heterogeneity among the included studies, the datasets were merged using a random effect model. The risk of bias tool 5.1.0 from Cochrane was used to assess the quality of the studies. The Bayesian hierarchical model inference with Markov Chain Monte Carlo (MCMC) algorithm was employed in the Bayesian meta-analysis, mostly done with R software (version 3.6.3) and STATA(version 14.0). The Aggregate Data Drug Information System (ADDIS Version1.16.8) package was used to calculate this in R. We used 200,000 iterations, with the first 5,000 iterations. Four chains yielded 20,000 iterations and the factor of 2.5. Otherwise, continuous outcomes were represented by standardized mean differences (SMDs) and 95% confidence intervals (CIs). Acupuncture methods were ranked by the surface under the cumulative ranking curve (SUCRA). Finally, a cluster ranking plot was created to assess the comprehensive ability of acupuncture methods to relieve symptoms in MCI patients.

Subgroup analysis: Subgroup analyses will also be used to identify a associations between relevant study characteristics if the data is sufficient and reliable or substantial heterogeneity existed, such as sex, different ages, different occupation of people affected by MCI.

Sensitivity analysis: After conducting a quality assessment of the included studies, we will conduct a sensitivity analysis if there are studies of low quality. Sensitivity analysis will also be performed when heterogeneity testing suggests significant heterogeneity between studies.

Country(ies) involved: China.

Keywords: Acupuncture, Network meta-analysis, Mild cognitive impairment.

Contributions of each author:

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