**INTRODUCTION**

**Objective** The study aimed to provide evidence for the therapeutic use of cerebellar transcranial magnetic stimulation (TMS) in improving balance and limb motor function after stroke from clinical and neuroimaging perspectives. The study has two parts: meta-analysis on clinical studies and meta-analysis on fMRI studies. The study seeks to answer the following questions:

1. Is cerebellar TMS an effective treatment for post-stroke balance and motor impairments?
2. What neural activity alterations can be identified in stroke patients with motor or balance deficits?

**Condition being studied** Stroke is a neurological disorder characterized by the interruption of blood supply to the central nervous system (CNS), resulting in high disability and mortality worldwide. Following stroke, impairment in balance and limb motor function can profoundly impact patients' ability to carry out Activities of Daily Living (ADLs), resulting in substantial psychosocial and economic burdens on patients and their family members. The amplitude of low frequency fluctuation (ALFF) or fractional ALFF (fALFF), and regional homogeneity (ReHo) are commonly used resting-state fMRI indices in detecting the alterations of neural activity in neurological and psychiatric disorders.

**METHODS**

**Participant or population** For cerebellar TMS studies, adult stroke patients were included; for fMRI studies, adult stroke participants with balance or limb motor deficits were included.

**Intervention** For cerebellar TMS studies, stroke patients received cerebellar repetitive TMS (rTMS) or theta-burst stimulation (TBS) with possible conventional rehabilitation interventions in the treatment group.
Comparator For cerebellar TMS studies, the control group received sham stimulation or merely conventional rehabilitation therapy.

Study designs to be included For cerebellar TMS, random controlled trials (RCTs) were included; for fMRI studies, since RCTs were not applicable, we included controlled experiments.

Eligibility criteria For cerebellar TMS studies, the additional inclusion criteria included: assessment of limb motor function improvement using the Fugl-Meyer Assessment for upper extremity (FMA-UE) or lower extremity (FMA-LE), and evaluation of balance ability using the Berg Balance Scale; only including the study with the largest sample size if multiple publications used the same or similar datasets in the analysis; published on peer-reviewed articles. For fMRI studies, the inclusion criteria are as follows: inclusion of adult stroke patients (age ≥ 18 years old) in the treatment group, as well as healthy controls (HCs) in the control group; (2) resting-state fMRI studies measuring the whole-brain ALFF/fALFF or ReHo; (3) reporting of motor or balance deficits in stroke patients as part of the inclusion criteria or demographic data; for studies using the National Institutes of Health Stroke Scale (NIHSS) to assess stroke severity, the mean value of NIHSS score plus standard deviation (SD) needed to be greater than 3; (4) reporting peak coordinates in either Montreal Neurological Institute (MNI) or Talairach space; (5) including at least 6 participants in each group; (6) only extracting baseline data for studies implement interventions; (7) published on peer-reviewed articles.

Information sources We searched the Web of Science, PubMed, Cochrane Library, EMBASE, Chinese National Knowledge Infrastructure (CKNI) and Wanfang Data for cerebellar TMS studies; As for the fMRI studies, we searched the Web of Science, PubMed and Wanfang Data.

Main outcome(s) For cerebellar TMS studies, we used Berg Balance Scale (BBS), Fugl-Meyer Assessment lower extremity (FMA-LE) and Fugl-Meyer Assessment upper extremity (FMA-UE); For fMRI studies, we used ALFF/fALFF and ReHo as outcome measurements.

Quality assessment / Risk of bias analysis We used the Cochrane Risk of Bias Tool for quality assessment for cerebellar TMS studies. Seven items were measured for each study: random sequence generation, allocation concealment, blinding method, incomplete outcome data, selective outcome reporting, and other sources of bias. Within the items, each study was judged to have a low, unclear, or high risk of bias. Currently, there’s no official quality assessment guideline for fMRI meta-analysis, so we referred to the quality assessment items in previous studies, which resulted in 8 items for quality assessment. The criteria are as follows: (1) inclusion and exclusion procedure and patient demographics; (2) fMRI scanning procedure; (3) spatial normalization method; (4) reproducibility of the analysis; (5) statistical tests; (6) correction for the multiple testing problem; (7) the reliability of figures and tables; (8) quality control measures. We established a scoring system for fMRI studies where one point was assigned for a “Yes” answer, 0.5 points for “Unsure,” and 0 points for “No.” Our standard threshold for fair quality was set at a score of more than 4 points, while a score of 6.5 points indicated a good quality study. The criteria include (1) inclusion and exclusion procedure and patient demographics; (2) fMRI procedure and patient instructions; (3) spatial normalization method; (4) reproducibility of the analysis; (5) statistical tests used to substantiate the results; (6) correction for the multiple testing problem; (7) figures and tables; (8) quality control measures. We established a scoring system for fMRI studies where one point was assigned for a “Yes” answer, 0.5 points for “Unsure,” and 0 points for “No.” Our standard threshold for fair quality was set at a score of more than 4 points and a score of 6.5 points indicated a good quality study.

Strategy of data synthesis Two researchers (Zeng, YHand Zheng, WX) screened and extracted information from the retrieved articles independently. Any disagreements between the two authors were resolved through discussions in the authors’ group. We calculated the mean difference (MD) with 95% confidence intervals for cerebellar TMS studies to present the effect size. For fMRI studies, we did combined and separate analyses for ALFF/fALFF and ReHo studies using the activation likelihood estimation (ALE) meta-analysis method.

Subgroup analysis We will conduct subgroup analysis according to the type of stimulation (high frequency, low frequency or TBS) in cerebellar TMS studies. We will conduct a subgroup analysis for fMRI studies according to the post-stroke rehabilitation stage of the patients (acute, subacute or chronic stage).

Sensitivity analysis We will do the sensitivity analysis by omitting each study in turn and recalculating the MD for cerebellar TMS studies.
Country(ies) involved China, Japan.

Keywords Transcranial magnetic stimulation, Stroke, Functional Magnetic resonance imaging, Balance, Limb motor function.

Contributions of each author
Author 1 - Yuheng Zeng.
Email: tsengyuheng1999@gmail.com
Author 2 - Zujuan Ye.
Author 3 - Wanxin Zheng.
Author 4 - Jue Wang.