INPLASY PROTOCOL

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Review Stage at time of this submission: Preliminary searches.

Conflicts of interest: None declared.

INTRODUCTION

Review question / Objective: What are the clinical benefits and neurophysiological changes at spinal level associated with interlimb coordinated intervention in patients with stroke?

The clinical benefit of interlimbcoordintated intervention in gait recovery and the associated neurophysiological changes in patients with stroke: A protocol for systematic review and meta-analysis

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Review question / Objective: What are the clinical benefits and neurophysiological changes at spinal level associated with interlimb coordinated intervention in patients with stroke?

Condition being studied: Neurophysiological changes and clinical benefits of four-limb intervention in patients with chronic stroke.

Information sources: OVID, MEDLINE, PubMed, Web of Science, EMBASE and PsychINFO database were searched to retrieve the randomized controlled trials on the clinical benefit of interlimb-coordintated intervention in gait recovery and the associated neurophysiological changes in patients with stroke.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 October 2021 and was last updated on 04 October 2021 (registration number INPLASY2021100012).

> **Condition being studied:** Neurophysiological changes and clinical benefits of four-limb intervention in patients with chronic stroke.

METHODS

Search strategy: The systematic review of the literature will follow the preferred

reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. Literature will be searched and retrieved from the following databases: OVID, MEDLINE, PubMed, Web of Science, EMBASE and PsychINFO. The Boolean operators and search string are as follow: (cerebral vascular accident OR stroke) AND (arm leg cycl*) AND (gait OR walking OR lower limb function) AND (MRI OR tms or transcranial magnetic stimulation or ntms OR neurophys* OR reflex OR EMG OR electromyography). Studies published in English over the past 15 years, from August 2021, will be considered for inclusion.

Participant or population: Participants with chronic stroke (more than six months of stroke occurrence) who aged between forty to eighty and were able to stand with or without assistance will be the focus of this study.

Intervention: Intervention must include limbs coodinated task, followed by observation of gait, lower limb motor function, neurophysiological changes with the following techniques: Hoffman-reflex pathway, Electromyography.

Comparator: We aim to investigate the changes in neurophysiology in patients with stroke after four-limb intervention.

Study designs to be included: Interventional study designs such as randomized controlled trials and crossover randominzed controlled trials in which preand post-measurements are analyzed in order to determine significance of intervention will be considered for this study.

Eligibility criteria: Inclusion Criteria:1. Fulltext studies published in English 15 years prior to August 2021.2. Studies conducted on individuals aged between forty and eighty with chronic stroke (more than three months.3. Studies that investigated the neurophysiological changes in stroke patients, including peripheral nerve stimulation to assess the Hoffman-reflex pathway, Electromyography to examine the heteronymous and contralateral muscle activity on reflex amplitudes. Exclusion Criteria:1. Studies published in a language other than English.2. Studies that included unilateral intervention.3. Studies that did not mention the screening of medications that might affect affecting muscle tone4. Studies did not exclude participants with cardiovascular, musculoskeletal, respiratory, or other chronic diseases.

Information sources: OVID, MEDLINE, PubMed, Web of Science, EMBASE and PsychINFO database were searched to retrieve the randomized controlled trials on the clinical benefit of interlimbcoordintated intervention in gait recovery and the associated neurophysiological changes in patients with stroke.

Main outcome(s): Clinical functions of gait, balance, lower limb functions and neurophysiologic changes are the outcome measures of interest. These include one of the following measures: spatialtemporal parameter of gait, Berg Balance Scale, postural sway, Fugy-Meyer motor assessment, H-reflex gain and/or amplitudes elicited via nerve stimulation, EMG signals collected with surface electrodes placed in bipolar configuration over the muscle bellies of interest.

Additional outcome(s): None.

Quality assessment / Risk of bias analysis: The quality of all included articles will be assessed by the Mixed Methods Appraisal Tool (MMAT). It is a critical appraisal tools that assessed five different categories of study designs, including qualitative, randomized controlled, non-randomized controlled trial, quantitative descriptive and mixed methods. Five core criteria of each study design is evaluated by a scale of "yes" "no", and "can't tell". This tool is chosen due to its ability to assess the quality of a range of study designs. Bias assessment will be conducted by two independent reviewers and disagreements will be discussed and reaching consensus. A narrative summary of the bias risk will also be provided.

Strategy of data synthesis: Effect sizes at 95% confidence intervals will be collected to assess the relationships within data, as well as Cohen's d for estimates of effect size. Quantitative data will be extracted from each article, and a χ^2 analysis will be used to determine homogeneity between observed and expected frequencies. Statistical significance will be set at p < 0.05. A narrative synthesis will be written if a meta-analysis is not possible due to the heterogeneity of the studies.

Subgroup analysis: Not applicable.

Sensitivity analysis: The review manager was used for sensitivity analysis of results with high heterogeneity.

Country(ies) involved: China.

Keywords: Stroke; interlimb; four-limb; neurophysiology; gait function.

Contributions of each author:

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