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Motor imagery for gait rehabilitation after stroke (Protocol)

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Motor imagery for gait rehabilitation after stroke.
Cochrane Database of Systematic Reviews 2018, Issue 4. Art. No.: CD013019.
DOI: 10.1002/14651858.CD013019.

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[Intervention Protocol]

Motor imagery for gait rehabilitation after stroke

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Editorial group: Cochrane Stroke Group.
Publication status and date: New, published in Issue 4, 2018.

Citation: Silva S, Borges LRDM, Santiago L, Lucena L, Lindquist AR, Ribeiro T. Motor imagery for gait rehabilitation after stroke. *Cochrane Database of Systematic Reviews* 2018, Issue 4. Art. No.: CD013019. DOI: 10.1002/14651858.CD013019.

ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To assess the treatment effects of motor imagery for enhancing ability to walk among people following stroke.

BACKGROUND

Description of the condition

According to the World Health Organization (WHO), cardiovascular disease is the leading cause of death worldwide, accounting for 17.7 million deaths in 2015. Of these, 6.7 million were directly attributed to stroke, making it one of the main non-communicable causes of death. Stroke also represents one of the leading healthcare expenditures and the second highest cause of disability (WHO 2017). Around 15% to 30% of people with stroke exhibit persistent functional disability and only 13% of stroke survivors affected return to work (Chumney 2010; Rayegani 2016).

It is estimated that three months after stroke, 70% of stroke survivors walk at a reduced speed, and 20% remain wheelchair bound (Sakuma 2014; Dujovic 2017). Indeed, the literature reports a direct relationship between motor deficit and function (Jørgensen 1995; Langhorne 2009). Post-stroke gait disability diminishes independence, mobility, activities of daily living, and participation in community activities (Mikolajewska 2017). Thus, one of the most important goals of post-stroke rehabilitation is to restore gait pattern and achieve fast walking so that people who have had a stroke can perform their activities of daily living without complications (Chiu 2000; Whitall 2004; Ji 2015). In this respect, evidence indicates that specific high-intensity repetitive task training improves the process of gait rehabilitation (Langhorne 2009; French 2016; Mehrholz 2017).

Description of the intervention

Exercises involving direct walking practice have been used to improve gait, such as treadmill training (Mehrholz 2017), and overground physical therapy gait training (States 2009), but activities that mimic walking, including imagery/mental practice, have also been used (Barclay 2015). Movement representation techniques, also referred to as mental practice, can be defined as any type of therapy that uses the representation of movement, specifically observation or imagination, or both. These interventions are mirror therapy, action observation, and motor imagery (Thieme 2016). Mirror therapy is defined as an intervention that uses a mirror to create a reflection of the non-affected upper or lower limb, and thus provides the individual with normal visual feedback of movement (Ramachandran 1994; Thieme 2016). Action observation refers to the visual perception of a given action performed by oth-

ers. In the observation, actual performance by another person, or as video or virtual setups, can be used (Thieme 2016). In this review, we will explore the effect of motor imagery.

Motor imagery is defined as a mentally rehearsed task in which movement is imagined but is not executed (Mulder 2007; Kim 2018). The approach includes repetitive imagined body movements or rehearsing imagined acts to improve motor performance (Carrasco 2016; Li 2017). Motor imagery was initially used to improve athletic performance (Driediger 2006), and has subsequently been recommended in the rehabilitation of people with stroke to promote motor relearning (Liu 2004; Driediger 2006; Moura 2012). Motor imagery for rehabilitation can be conducted in two forms: external or visual, in which people imagine from the standpoint of an external observer (third-person imagination); and internal or kinesthetic, where people imagine the sensation of their body moving (first-person imagination) (Carrasco 2016). Motor imagery, separately or combined with physical activity (where the movement is executed), has demonstrated promising results for rehabilitating gait after a stroke (Dickstein 2004; Lamontagne 2004; Hwang 2010), such as increased gait speed (Dickstein 2004; Beyaert 2015).

How the intervention might work

Decety suggested that imagining movement activates the same brain areas that are activated when the movements are actually executed. These findings reinforce the idea that if mental stimulation of the action triggers neural activation of relevant motor areas, we can therefore 'exercise' the brain in the absence of a movement (Decety 1996).

The neurophysiological basis underlying motor imagery consists of the mirror neuron system, located in the rostral portion of the inferior parietal lobule, *pars opercularis* of the inferior frontal gyrus and the ventral portion of the premotor cortex. The units that make up this system (mirror neurons) are a class of visuomotor neurons that are activated during execution or observation of movements aimed at an objective (Garrison 2010). During motor imagery, the motor areas involved in the process are the primary motor cortex and several premotor areas, including the supplementary motor area, pre-supplementary motor area, and ventral and dorsal parts of the premotor cortex (Jeannerod 1995; Kim 2018). These areas are activated during both motor execution and motor imagery tasks; indeed, functional imaging studies have observed activation of brain regions upon motor execution and motor imagery (Lotze 1999; Johnson 2002; Wang 2016).

A number of hypotheses have been proposed to elucidate the motor imagery functioning mechanism. The first is the mental simulation theory (Munzert 2009), which states that a neural motor network is activated by imagining motor actions (Jeannerod 2001). This activation includes pre-motor and motor areas and subcortical areas of the brain (Lotze 1999) and basal ganglia (Bonda 1995). In this respect, these subliminal activations improve an individual's learning (Barclay-Goddard 2011). A second hypothesis proposes that individuals involved in motor imagery rehearse elements of the task, giving them the opportunity to foresee the outcomes of their actions based on previous experience. Therapy participants anticipate possible action trajectories, which they are more likely to use to perform when executing a real movement. As such, individuals develop more efficient ways to approach outcomes (Barclay-Goddard 2011). Although the exact motor imagery functioning mechanism has not been totally clarified, recent evidence indicates cortical reorganization in people with stroke after treatment with motor imagery, which could result in better gait recovery in this population (Guerra 2017). It is believed that cortical reorganization occurs due to increased primary motor activity, which in turn raises sensorimotor cortex recruitment, resulting in functional improvements (Sun 2013).

Why it is important to do this review

Stroke is considered to be a serious public health issue worldwide, leading to an increasing number of survivors with disabilities (Chumney 2010; Rayegani 2016). Gait recovery is a key aim of post-stroke rehabilitation, given that it enables survivors to resume most daily activities, reducing the incidence of falls, and other factors that pose a risk to this population. However, stroke survivors may undergo lengthy and challenging treatments, resulting in adoption of passive attitudes to rehabilitation. Motor imagery is an easy, safe, and less tiring technique that increases survivor participation and motivation. Furthermore, motor imagery does not require specific equipment, and is considered to be a low-cost procedure (Decety 1993; Dickstein 2004; Hosseini 2012). Nevertheless, there is currently insufficient evidence to indicate the best treatment to improve walking after stroke (Barclay 2015).

Recent studies show positive gait rehabilitation results from motor imagery, such as increased lower limb muscle strength and better walking performance in people following stroke (Oostra 2015; Kumar 2016). However, confirming the efficacy of motor imagery in post-stroke gait requires a thorough investigation of experimental studies on the issue, given that results do not appear to be consistent. Both therapy result and methodological quality of studies need to be assessed, given that treatment protocols vary considerably.

There is a wide variety of intervention protocols that differ in aspects such as frequency of exposure to motor imagery, movements and tasks performed, and duration of therapy (Carrasco 2016). Furthermore, few clinical trials on motor imagery present high methodological quality (Winstein 2016; Guerra 2017). To date, there has been no Cochrane Review exploring the effects of motor imagery on gait among stroke survivors. By conducting a systematic review and meta-analysis, and assessing the methodological quality of the studies, this review should provide support for evidence-based clinical decisions. In addition, it will also highlight where further research is needed.

OBJECTIVES

To assess the treatment effects of motor imagery for enhancing ability to walk among people following stroke.

METHODS

Criteria for considering studies for this review

Types of studies

We will include published and unpublished randomized clinical trials, including those available only in summary form. We will also include cross-over trials (using only data from the first phase), provided that allocation of interventions was random. We will exclude quasi-experimental or non-randomized studies. We will include studies regardless of publication date or language.

Types of participants

We will include studies in which participants present with a clinical diagnosis of stroke of any type (including subarachnoid hemorrhage). Participants must be at least 18 years of age, any sex, with any degree of severity of the disease, and at any stage after stroke. We will exclude studies in which participants had a mixed etiology of the disease (e.g. acquired brain injury), unless data are available for individuals who only had a stroke.

Types of interventions

We will include studies that used motor imagery for gait improvement in people with stroke. We will consider the concept of motor imagery as an approach in which the individual imagines the movement or part of it without its actual execution. Thus, we will select studies comparing:

- motor imagery alone or associated with action observation, physical activity, or functional gait training versus other therapies (including conventional physical therapy);
- motor imagery alone or associated with action observation, physical activity or functional gait training versus placebo; and
- motor imagery alone or associated with action observation, physical activity or functional gait training versus no therapy.

Types of outcome measures

We will extract the outcomes of interest from the baseline and the evaluation at the end of the intervention period (immediate effects) and follow-up (medium- or long-term effects). Measures of medium-term effects will be considered as those collected between two weeks to six months after treatment had ended, and measures of long-term effects if collected more than six months after treatment had ended.

Primary outcomes

The primary outcome is ability to walk, verified using the following continuous and dichotomous variables:

- continuous variable: independent walking speed, measured by biomechanical analysis of walking tests, or both, considering both preferable/comfortable walking speed and fastest walking speed;
- dichotomous variable: dependence on personal assistance.

According to Mehrholz and colleagues, dependence was defined "as the inability to walk indoors (with or without a gait aid) without personal assistance or supervision" (Mehrholz 2017). If reported, we will use data from functional scales related to walking to define the level of dependence. We will consider the following scales and scores (Mehrholz 2017):

- Motor Assessment Scale (Carr 1985), score of two or less for the walking item;
- Functional Independence Measure (Hamilton 1994), score of five or less for the walking item;
- Barthel Index (Collin 1988), score of three (independent, but may use any aid) or less for the ambulation item;
- Rivermead Mobility Index (Collen 1991), an answer of 'no' to the 'walking inside with an aid if necessary' item; and
- Functional Ambulation Category (Holden 1984), score of two or less.

If included studies cite walking speed and dependence on personnel assistance variables. we will consider both.

Secondary outcomes

- Walking endurance (distance covered, in meters), measured by Six-Minute Walk Test or Two-Minute Walk Test.
- Motor function, measured by the Fugl-Meyer Assessment Scale (Fugl-Meyer 1975) or Motor Assessment Scale.
- Functional mobility (including gait), measured by Rivermead Mobility Index or Timed Up and Go Test (Podsiadlo 1991).
- Adverse events (including pain, falls, and all-cause deaths).

If included studies cite more than one measure for each outcome, we will consider the Six-Minute Walk Test for walking endurance, the Fugl-Meyer Assessment Scale for motor function, and the Rivermead Mobility Index for functional mobility.

Search methods for identification of studies

See the 'Specialized register' section in the Cochrane Stroke Group module. We will search for trials in all languages and arrange for translation of relevant articles where necessary.

Electronic searches

We will search the Cochrane Stroke Group trials register and the following electronic databases:

- Cochrane Central Register of Controlled Trials (CENTRAL) (Cochrane Library; latest issue);
- MEDLINE Ovid (from 1946) (Appendix 1);
- Embase Ovid (from 1974);
- CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; from 1982);
- PsycINFO Ovid (from 1806);
- AMED Ovid (Allied and Complementary Medicine; from 1985);
- LILACS Bireme (Latin American and Caribbean Health Science Information database; from 1982);
- SPORTDiscus EBSCO (from 1949);
- PEDro (Physiotherapy Evidence Database; www.pedro.org.au/);
- REHABDATA National Rehabilitation Information Center (www.naric.com/?q=en/REHABDATA).

We developed the MEDLINE search strategy with the help of the Cochrane Stroke Group Information Specialist and will adapt it for the other databases where appropriate (Appendix 1). All search strategies deployed will be combined with subject strategy adaptations of the highly sensitive search strategy designed by Cochrane for identifying randomized controlled trials and controlled clinical trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Chapter 6 Lefebvre 2011). We will provide full search strategies for all databases and trials registers in the review appendices.

We will also search the following trials registries:

- USA National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov/);
- World Health Organization (WHO) International Clinical Trials Registry Platform (www.who.int/ictrp/en/);
- Stroke Trials Registry (www.strokecenter.org/trials/).

Searching other resources

In an effort to identify further published, unpublished and ongoing trials, we will:

- screen the reference lists of relevant studies to identify further studies for potential inclusion in the review;
- use Science Citation Index Cited Reference search for forward tracking of relevant articles;
- contact study authors, researchers and experts in the field to obtain additional information on relevant trials; and
- search for PhD and MSc theses (using ProQuest Thesis database and British Library Ethos database).

Data collection and analysis

Selection of studies

Two review authors (LS and LL) will independently screen titles and abstracts of the references obtained from our searching activities and will exclude obviously irrelevant reports. We will retrieve the full-text articles for the remaining references and the same two review authors will independently screen the full-text articles to identify studies for inclusion, and identify and record reasons for exclusion of the ineligible studies. We will resolve any disagreements through discussion, or we will consult a third person (TR) if required. We will gather multiple reports of the same study so that each study, and not each reference, is the unit of interest in the review. We will record the selection process and complete a PRISMA flow diagram.

Data extraction and management

Two review authors (LS and LL) will independently extract data from included studies. If data are lacking or details are unclear, we will contact the study authors for clarification. If there is disagreement regarding data collection, a third review author will check the data (TR). The data to be collated are:

- method used: objectives, study design, instruments used, total duration of the study, form of randomization, secrecy of the allocation, blindness of the evaluators, institutions or study centers involved, study site, withdrawal and withdrawal of the participants and year of study;
- participants: sample size, age, sex, diagnostic criteria, inclusion and exclusion criteria, severity of stroke and stage (acute/subacute and chronic);
- intervention: we will use the 'Template for intervention description and replication' (TIDieR) checklist and guide to extract data about interventions (Hoffmann 2014); we will consider all the 12 points on the TIDierR checklist;
- results: primary and secondary outcomes for each assessment and reassessment; and
- notes: funding for experimentation and notable conflicts of interest of the study authors.

Assessment of risk of bias in included studies

Two review authors (LS and LL) will independently assess risk of bias for each study using Cochrane's 'Risk of bias' tool (Higgins 2011). We will resolve any disagreements by discussion or by involving another review author (TR). We will assess the risk of bias according to the following domains:

- random sequence generation;
- allocation concealment;
- blinding of participants and personnel;
- blinding of outcome assessment;
- incomplete outcome data;
- selective outcome reporting;
- any other bias.

We will grade any identified biases using table 8.5.a of the *Cochrane Handbook for Systematic Reviews of interventions* (Higgins 2011). This table provides criteria for analysis and judgement of risk of bias in each of the seven domains. We will classify risk of bias in each domain as high, low, or unclear, and we will justify each decision and record this in the 'Risk of bias' tables.

The assessment of risk of bias for blinding of participants and personnel will depend on the influence that lack of blinding would have. If the participants and personnel are not blind, and after judging that the outcome measure could be influenced by the knowledge of participants and personnel about which intervention was provided, we will assign a high risk of bias. If we judge that the outcome measure should not influenced by the knowledge of participants and personnel about the intervention, we will assign a low risk of bias, whether or not the blinding of participants and personnel has happened.

Measures of treatment effect

We will measure treatment effects using the odds ratio (OR) for dichotomous outcomes, mean difference (MD) and standardized mean difference (SMD) for continuous outcomes with 95% confidence intervals (CI). We will perform meta-analysis using Review Manager 5 (Review Manager 2014) or newer version if available, and only if there is clinical and methodological similarity among studies so they can be pooled for analysis. We will base clinical similarity on population characteristics such as type of stroke, stage of stroke (acute, subacute, and chronic) and walking dependence (at the beginning of the study). We will consider similar methodologies when the type of intervention (motor imagery alone or motor imagery associated with action observation or physical practice), length of treatment period or treatment doses, and outcomes are repeated between studies. We will use the random-effects model for analysis.

We will group together studies and undertake meta-analyses to compare the effects of:

- motor imagery (alone or associated with action observation or physical practice) versus other therapies (including conventional physical therapy);
- motor imagery (alone or associated with action observation or physical practice) versus placebo; and
- motor imagery (alone or associated with action observation or physical practice) versus no therapies.

Unit of analysis issues

If we identify cluster-randomised studies or any non-parallel designs, we will consider their inclusion, following guidance in Chapter 16 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Dealing with missing data

We will contact authors of respective studies to request missing information. If we are unable to obtain the missing data from study authors, or if study does not report outcome data that can be used in our analysis, we will include the study only after conducting a sensitivity analysis to explore the impact of including such studies in the overall assessment of results.

Assessment of heterogeneity

We will visually assess forest plots, verifying overlap in the confidence intervals of studies (poor overlap may indicate statistical heterogeneity) (Deeks 2011). In addition, we will use the I^2 statistic to measure heterogeneity among trials in each analysis. Values of I^2 greater than 50% may represent substantial heterogeneity (Deeks 2011).

We will explore the reasons for heterogeneity (e.g. setting, participants, interventions, design, and risk of bias). If we find that heterogeneity was caused by one or two studies with peripheral results conflicting with the rest of the studies, we will carry out analyses with and without these studies as part of the sensitivity analysis.

Assessment of reporting biases

We will attempt to reduce the risk of reporting bias by performing a comprehensive search for trials. We will examine the presence of reporting bias by visual inspection of funnel plots.

Data synthesis

Two review authors (LS and LL) will independently extract data from the included studies. One review author (SS) will enter data into Review Manager 5 (Review Manager 2014). Two review authors (LS and LL) will check the entered data. When we consider studies to be sufficiently similar, we will conduct a meta-analysis by pooling the appropriate data.

GRADE and 'Summary of findings' table

We will create a 'Summary of findings' table using the following outcomes: independent walking speed, dependence on personal assistance, walking endurance, motor function, functional mobility, and adverse events.

We will create two tables to summarize the findings of the data synthesis.

- Motor imagery (alone or associated with action observation or physical practice) versus other therapies (outcomes immediately after intervention).
- Motor imagery (alone or associated with action observation or physical practice) versus other therapies (outcomes at follow-up: medium or long-term effects).

We will report the number of studies and participants, the relative effect, direction of effect, and the quality of the evidence (GRADE) for each outcome. Please see Table 1 for the template of the 'Summary of findings' table we will use for the review.
We will use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of a body of evidence as it relates to the studies that contribute data to the meta-analyses for the pre-specified outcomes (Atkins 2004). We will use methods and recommendations described in Section 8.5 and Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) using GRADEpro GDT software (GRADEpro GDT 2015). We will justify all decisions to downgrade or upgrade the quality of studies using footnotes, and we will make comments to aid the reader's understanding of the review where necessary.

Subgroup analysis and investigation of heterogeneity

We will examine the following variables in subgroup analyses:
- type of stroke: ischemic or hemorrhagic;
- post-stroke time: acute (less than one month post-stroke), subacute (between one and six months post-stroke) and chronic (more than six months after stroke);
- length of treatment period or treatment dose. We will group studies based on extracted data (a posteriori), because large variations in length of treatment period and dose are anticipated;
- type of treatment: motor imagery alone or motor imagery associated with action observation or physical practice (physical activity or functional gait training);
- walking dependence: independent or dependent of personal assistance (human support or supervision) in the beginning of study.

Sensitivity analysis

We will perform sensitivity analyses if we suspect that missing data will introduce important bias, and to assess heterogeneity caused by studies with peripheral results. Furthermore, we plan to carry out the following sensitivity analyses, excluding studies that have a high risk of bias. We will consider a study as having a high risk of bias if the following criteria are not established:
- allocation concealment;
- blinding of outcome assessment;
- random sequence generation.

ACKNOWLEDGEMENTS

We thank Joshua Cheyne for his support and assistance regarding search strategies. We also thank the Cochrane Stroke Group Editorial team for providing assistance through revision of this protocol.

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* *Indicates the major publication for the study*

ADDITIONAL TABLES

Table 1. 'Summary of findings' table template

Outcome	No. of studies/participants	Relative effect (95% CI)	Direction of effect	Quality of evidence/GRADE	Comments
Independent walking speed					
Dependence on personal assistance					
Walking endurance					
Motor function					
Functional mobility					
Adverse events					

APPENDICES

Appendix 1. MEDLINE search strategy

1. cerebrovascular disorders/ or basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp cerebral small vessel diseases/ or exp intracranial arterial diseases/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ or stroke, lacunar/ or vasospasm, intracranial/ or vertebral artery dissection/
2. (stroke$ or poststroke or apoplex$ or cerebral vasc$ or brain vasc$ or cerebrovasc$ or cva$ or [illegible]).tw.
3. ((brain$ or cerebr$ or cerebell$ or vertebrobasil$ or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or middle cerebral artery or MCA$ or anterior circulation or posterior circulation or basilar artery or vertebral artery or space-occupying) adj3 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$)).tw.
4. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraparenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or putaminal or putamen or posterior fossa or hemispher$ or subarachnoid) adj3 (h?emorrhag$ or h?ematoma$ or bleed$)).tw.
5. hemiplegia/ or exp paresis/ or exp gait disorders, neurologic/
6. (hemipleg$ or hemipar$ or paresis or paretic).tw.
7. exp brain damage, chronic/ or brain injuries/ or exp brain concussion/ or brain injury, chronic/ or diffuse axonal injury/ or craniocerebral trauma/ or exp head injuries, closed/ or exp brain abscess/
8. ((brain or head or intracran$ or cerebr$ or cerebell$ or orbit$ or brainsten$ or vertebrobasil$) adj5 (abscess$ or injur$ or contusion$ or hypoxi$ or damage$ or inflamm$ or concussion or trauma$ or fracture$ or infection$ or lesion$)).tw.
9. or/1-8
10. exp Lower Extremity/
11. foot joints/ or ankle joint/
12. (lower extremit$ or leg or legs or ankle$ or foot or feet or toe$ or toes or hip or knee or knees or thigh$).tw.
13. (walk$ or gait$ or ambulat$ or mobil$ or locomot$ or balance$ or stride or foot-drop).tw.
14. gait/ or locomotion/ or exp walking/
15. or/10-14
16. imagination/ or "imagery (psychotherapy)"/ or imitative behavior/
17. perception/ or illusions/ or visual perception/
18. exp psychomotor performance/
19. ((motor or locomot$) adj3 (imag$ or visualiz$ or ideation)).tw.
20. (action adj3 (immitat$ or observ$ or visuali$ or ideation)).tw.
21. ((cognitive or covert$ or mental) adj3 (practic$ or rehears$ or represent$ or visual$ or image$)).tw.
22. ((visual or mirror$) adj3 (reflection or illusion or feedback or therapy)).tw.
23. or/16-22
24. randomized controlled trial.pt.
25. controlled clinical trial.pt.
26. randomized.ab.
27. placebo.ab.
28. randomly.ab.
29. trial.ab.
30. groups.ab.
31. or/24-30
32. 9 and 15 and 23 and 31

CONTRIBUTIONS OF AUTHORS

Stephano Silva: developed the protocol, wrote the first draft of the protocol and made an intellectual contribution to the protocol.

Lorenna RDM Borges: made an intellectual contribution to the protocol.

Lorenna Santiago: made an intellectual contribution to the protocol.

Larissa Lucena: made an intellectual contribution to the protocol.

Ana Raquel Rodrigues Lindquist: made an intellectual contribution to the protocol.

Tatiana Ribeiro: supervised and supported the process of writing the protocol and made an intellectual contribution to the protocol.

All authors read and approved the protocol prior to publication.

DECLARATIONS OF INTEREST

Stephano Silva: none known.

Lorenna RDM Borges: none known.

Lorenna Santiago: none known.

Larissa Lucena: none known.

Ana Raquel Rodrigues Lindquist: none known.

Tatiana Ribeiro: none known.

SOURCES OF SUPPORT

Internal sources

- Department of Physical Therapy, Federal University of Rio Grande do Norte, Brazil.

External sources

- No sources of support supplied