PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Rehabilitation for balance impairment in patients after stroke: a protocol of a systematic review and network meta-analysis
AUTHORS	Li, Juan (proxy) (contact); Zhong, Dongling; Ye, Jing; He, Mingxing; Liu, Xicen; Zheng, Hui; Jin, Rongjiang; Zhang, Shao-lan

VERSION 1 - REVIEW

REVIEWER	Aurelien Hugues (1) Service de médecine physique et réadaptation, hôpital Henry-Gabrielle, Hospices Civils de Lyon, Saint-Genis-Laval, France; Plate-forme “Mouvement et Handicap”, hôpital Henry-Gabrielle, Hospices Civils de Lyon, Saint-Genis-Laval, France. (2) Equipe “ImpAct”, Centre de Recherche en Neurosciences de Lyon (CRNL), Inserm UMR-S 1028, CNRS UMR 5292, Université de Lyon, Université Lyon 1, Bron, France.
REVIEW RETURNED	12-Oct-2018

GENERAL COMMENTS	Comments Global comment Addressing to the issue of the comparative effectiveness of balance rehabilitations is relevant. There is a clinical interest for stroke patients and therapists. The method chosen is appropriate. The discussion should be complete. Abstract OK Introduction First sentence: a reference may be useful. Use of terms of “balance dysfunction” or “balance function” may be unsuitable. Indeed, balance is an activity according to the International Classification of Functioning, Disability and Health (ICF), whereas strength or proprioception are functions by example. “Balance dysfunction is one of the common daily functional problems in stroke patients, which seriously affects the patient's daily life and work” Some references may be useful. I don’t think that the reference 6 is relevant to justify the following sentence “Balance function is the ability to maintain the center of gravity within the limits of base of support as in sitting, standing, walking or position transfering”. In the reference 6, the authors give this definition of balance, by means of another reference, that seem to be more relevant.

	It may be provided more of references about the characteristics of balance disorders in stroke patients, and some of them are a little too old. I don't understand the sentence: "Modern rehabilitations usually increase balance dysfunction by creating an unbalanced plane, whether the plane is virtual (using virtual reality technology) or realistic (using balance ball or balance board)." What is the meaning? When you say "increase balance dysfunction" Is it a conclusion of effects of these rehabilitation? I am confused The paragraph beginning by "With the development of evidence-based medicine, numerous systematic reviews (SRs) have been conducted to investigate the effectiveness and safety of multiple" could be develop. Current knowledges of effects and their limitations could be explained. By example, types of rehabilitation are more detailed in the previous paragraph. However, the current state of art for the effectiveness of rehabilitations is essential to justify your project of meta-analysis. Objective is relevant. The topic of balance disorders is large and complex. Results of trials are numerous and virous. Therefore, summarizing and improving the understanding of these results is necessary and useful. This protocol is useful and relevant for clinical practice. Method Type of studies Is there any restriction on type of design for RCTs? What about crossovers? Type of interventions Do you have a definition for modern rehabilitation? Which criteria will be used to define a modern rehabilitation? After reading search strategy with the combination if key words, it appears that type of rehabilitation that will be assessed, are defined beforehand. Outcome measurements "all the following outcomes after the end of interventions and after a follow-up time will be included." I am confused. The main scales used in your meta-analysis will be continuous outcomes. For your analyses, do you summarize effects by means of final value? Or do you use the change from baseline? You explain this point in statistical paragraph but, it would be interesting to precise your sentences of outcome paragraph in order to avoid a misunderstanding. FMA: I understand that you will use only the domain of scale on balance assessment? Outcomes chosen are relevant. Risk of bias assessment Your have written: "… blind subjects, blind therapists and assessors,…" But it is, on the one hand, blind of assessor, and on the other hand, blind of patients and therapists. Assessment of blind of assessors is independent and separate from assessment of blind of patients and personnel.

	Statistical analysis “If the trial present mean values of each time point, we will adjust the outcomes by the baseline values. We will calculate the SMD directly for the trials present the values of outcomes changing from baseline.” This is not clear for me. I have a doubt on the meaning. Do you want to use both final values and change from baseline values in a same SMD analysis, in order to summarize treatment effects? If it is the case, it is not allowed. Your first sentence seems to indicate that if the trial does not present mean values of each time point, you will extract and use only final value. For me, it is not allowed to mix in a same SMD analysis some treatment effects expressed in change from baseline with some other treatment effects expressed in final values. It is allowed only for MD analysis. I am confused Assessment of publication bias Will the graphical interpretation of funnel plots be the only method to explore publication bias? A statistical test could be used in addition. All other parts of method seem to be adequate for me. Discussion The paragraphs 1, 2 and 3 of the discussion completes the introduction, justifying the objective and the relevance of this meta-analysis. The lines 5 to 14 of the discussion could answer to my comment noted in introduction (“The paragraph … project of meta-analysis.”). The paragraphs 4 and 5 could be developed. I feel that the discussion is not adequate in addressing relevant issues regarding clinical practice. It is mostly a repetition of the introduction and should be more focused on the contribution to clinical practice. What could be the different opportunities and insights that this network meta-analysis could provide?

REVIEWER	Dr. Anuja Darekar Deenanath Mangeshkar Hospital and Research Center, India
REVIEW RETURNED	22-Oct-2018

GENERAL COMMENTS	The present manuscript presents a protocol of a network meta-analysis aimed to evaluate the effectiveness of various rehabilitation interventions on balance dysfunction after stroke. I have a few major concerns about this manuscript that the authors should consider addressing before resubmitting the manuscript. The rationale for the study is not very well explained in the manuscript. The authors have identified several systematic reviews that have previously evaluated the effectiveness of rehabilitation interventions on balance dysfunction post-stroke. Why is there a need for a network meta analysis? The authors need to provide a stronger rationale for undertaking this exercise. This could be discussed in either the introduction or the discussion section of the manuscript. It does not seem like all the rehabilitation interventions were considered by the authors. For instance, virtual reality based interventions are now increasingly being used for training balance dysfunctions. These do not find a mention in the interventions included in the search strategy. Also, it is necessary to explain briefly how each intervention helps alleviate balance dysfunction (addition of a table for this purpose might be adequate).

	This will help readers understand why a specific intervention has been included in the protocol. This is also specifically important for Chinese traditional medicine interventions as not all readers would be familiar with those. The data analyses should be explained in more detail outlining the rationale for choosing specific methods and their advantages over other methods. Although, this would not be expected in a manuscript outlining the results of the network meta analyses, a proposal manuscript should explain data analyses methods in detail. Have the authors made a priori choices with regards to subgroup analyses, specifically in order to explore the degree of balance dysfunction and the appropriateness of the chosen intervention? Will the study be able to comment on this aspect? Also how will this help the clinicians in making informed choices? The entire paper should be proof read and revised for English grammar and usage. Some sentences are left incomplete without a verb, some others use improper grammar. Some words convey a completely unintended meaning and could be a source of confusion. Also, general conventions used in rehabilitation literature should be kept intact. Some examples are outlined below. I have not outlined mistakes in the entire paper (as there were too many) but the following can be used as guidelines. Examples of minor grammatical and other errors: Page 3, line 9: “(RCTs) utilized rehabilitations to treat the balance”. This should be rephrased as “(RCTs) that have utilized rehabilitation interventions to treat balance dysfunction..” Page 3, line 10: “Berg balance scale” the convention is to capitalize the first letter of every word such that is reads like ‘Berg Balance Scale’. Please consider modifying this in the manuscript. Page 3, line 11: Please insert ‘and’ after the comma after ‘(BBS) and before ‘the Fugl’. Also consider removing the phrase ‘at the end of the treatment’. It is expected that the primary outcomes would generally be measured pre and post treatment. So, mentioning only at the end of the treatment may create confusion in the readers’ mind. Page 3, line 16: please do not capitalise F in fall rates. Also, conventionally the Timed Up and Go test is abbreviated as simply the TUG and not TUGT. Please use the conventional abbreviation as far as possible. Page 3, line 29: “The findings of this network meta-analysis will summarize the direct and indirect evidence of rehabilitations on balance dysfunction after stroke..” the study results are expected to summarize the direct and indirect ‘effects’ of ‘rehabilitation interventions’ on balance dysfunction after stroke. Please make the aforementioned changes. Page 4, line 31: Does stroke often lead to ‘muscle spasms’? Or are the authors referring to spasticity here? Please clarify. Also, please elaborate on the meaning of ‘prosthetic sensory disorder’. Please review the paper using the above examples as guidelines. I am also attaching the manuscript here with highlighted areas that may need revision.

REVIEWER	Hillel Finestone Director of Stroke Rehabilitation Research, Bruyere Continuing Care Physiatrist, Elisabeth Bruyere Hospita Professor, Division of Physical Medicine and Rehabilitation, Department of Medicine, University of Ottawa
REVIEW RETURNED	31-Dec-2018

GENERAL COMMENTS	The authors primary outcome for studies assessing balance training in stroke patients is insufficient and therefore limits the ability of the reader to generalize the finding. Specifically, important outcomes eg FIST, (function in sitting test), SBS (sitting balance scale) and Ottawa Sitting Scale have not been mentioned or referenced. Without acknowledging all of the studies which looked at using these latter outcomes, the protocol is very limited. Also, although inclusion of traditional Chinese medicine studies is novel, along with others, it would have been helpful to know the authors thought about how many RCTs ("only RCTs will be included") they expected to find.

VERSION 1 – AUTHOR RESPONSE

Response for reviewer 1

Comments

Introduction

(1)First sentence: a reference may be useful.

Response: We have added 3 references. Please see page 3, line 10.

(2)Use of terms of "balance dysfunction" or "balance function" may be unsuitable. Indeed, balance is an activity according to the International Classification of Functioning, Disability and Health (ICF), whereas strength or proprioception are functions by example.

Response: "Balance dysfunction" and "balance function" have been replaced with "balance impairment" and "balance ability".

(3)"Balance dysfunction is one of the common daily functional problems in stroke patients, which seriously affects the patient's daily life and work" Some references may be useful.

Response: We rewrote this sentence and added references. Please see page 3, line 13-14.

(4)I don't think that the reference 6 is relevant to justify the following

sentence “Balance function is the ability to maintain the center of gravity within the limits of base of support as in sitting, standing, walking or position transfering”. In the reference 6, the authors give this definition of balance, by means of another reference, that seem to be more relevant.

Response: We rewrote this sentence and added a correct reference for the definition of balance. Please see page 3, line 22.

(5)It may be provided more of references about the characteristics of balance disorders in stroke patients, and some of them are a little too old.

Response: We updated the references for the characteristics of balance disorders. Please see page 3.

(6)I don’t understand the sentence: “Modern rehabilitations usually increase balance dysfunction by creating an unbalanced plane, whether the plane is virtual (using virtual reality technology) or realistic (using balance ball or balance board).” What is the meaning? When you say “increase balance dysfunction” Is it a conclusion of effects of these rehabilitation? I am confused

Response: We rewrote this paragraph. Please see page 3-4.

(7)The paragraph beginning by “With the development of evidence-based medicine, numerous systematic reviews (SRs) have been conducted to investigate the effectiveness and safety of multiple” could be develop. Current knowledges of effects and their limitations could be explained. By example, types of rehabilitation are more detailed in the previous paragraph. However, the current state of art for the effectiveness of rehabilitations is essential to justify your project of meta-analysis.

Response: we rewrote this paragraph. Please see page 4.

Method

Type of studies

(8)Is there any restriction on type of design for RCTs? What about

crossovers?

Response: Cluster RCTs and RCTs with cross-over design will be excluded. Please see exclusion criteria in page 6.

Type of interventions

(9)Do you have a definition for modern rehabilitation? Which criteria will be used to define a modern rehabilitation?

Response: Modern rehabilitations is a relative definition to traditional Chinese medicine therapies, which refer to physical therapies defined by the World Confederation for Physical Therapy (WCPT), typically including balance-specific activities (such as balance exercises, weight shift training and so on), more general activities (such as strengthening exercises, gait activities and so on), biofeedback, WBV, VR, MT, orthosis and so on. Please see Types of interventions in page 5.

(10)After reading search strategy with the combination if key words, it appears that type of rehabilitation that will be assessed, are defined beforehand.

Response: We did a literature research and consulted with the experts in rehabilitation to predefine the scope of Traditional Chinese medicine therapies and modern rehabilitations. We also revised the search strategy. Please see appendix.

Outcome measurements

(11) “all the following outcomes after the end of interventions and after a follow-up time will be included.” I am confused. The main scales used in your meta-analysis will be continuous outcomes. For your analyses, do you summarize effects by means of final value? Or do you use the change from baseline? You explain this point in statistical paragraph but, it would be interesting to precise your sentences of outcome paragraph in order to avoid a misunderstanding.

Response: We rewrote this paragraph. Please see page 5.

(12)FMA: I understand that you will use only the domain of scale on

balance assessment? Outcomes chosen are relevant.

Response: We will use the Fugl-Meyer balance Assessment (FMA (balance)). Please see outcome measurements in page 5.

Risk of bias assessment

(13)Your have written: "… blind subjects, blind therapists and assessors,…" But it is, on the one hand, blind of assessor, and on the other hand, blind of patients and therapists. Assessment of blind of assessors is independent and separate from assessment of blind of patients and personnel.

Response: We revised this sentence. Please see page 8, Line 1.

Statistical analysis

(14) "If the trial present mean values of each time point, we will adjust the outcomes by the baseline values. We will calculate the SMD directly for the trials present the values of outcomes changing from baseline." This is not clear for me. I have a doubt on the meaning.

Do you want to use both final values and change from baseline values in a same SMD analysis, in order to summarize treatment effects? If it is the case, it is not allowed. Your first sentence seems to indicate that if the trial does not present mean values of each time point, you will extract and use only final value. For me, it is not allowed to mix in a same SMD analysis some treatment effects expressed in change from baseline with some other treatment effects expressed in final values. It is allowed only for MD analysis. I am confused

Response: We rewrote this paragraph. Please see statistical analysis in page 8-9.

Assessment of publication bias

(14) Will the graphical interpretation of funnel plots be the only method to explore publication bias? A statistical test could be used in addition.

Response: We added Egger's regression test to assess the publication bias of the included studies. Please see page 10, line 17.

Discussion

(15)The paragraphs 1, 2 and 3 of the discussion completes the introduction, justifying the objective and the relevance of this meta-analysis. The lines 5 to 14 of the discussion could answer to my comment noted in introduction (“The paragraph … project of meta-analysis.”). The paragraphs 4 and 5 could be developed. I feel that the discussion is not adequate in addressing relevant issues regarding clinical practice. It is mostly a repetition of the introduction and should be more focused on the contribution to clinical practice. What could be the different opportunities and insights that this network meta-analysis could provide?

Response: We rewrote the discussion part, providing the importance of this systematic review and contributions to clinical practice.

Response for reviewer 2

The present manuscript presents a protocol of a network meta-analysis aimed to evaluate the effectiveness of various rehabilitation interventions on balance dysfunction after stroke. I have a few major concerns about this manuscript that the authors should consider addressing before resubmitting the manuscript.

(1)The rationale for the study is not very well explained in the manuscript. The authors have identified several systematic reviews that have previously evaluated the effectiveness of rehabilitation interventions on balance dysfunction post-stroke. Why is there a need for a network meta analysis? The authors need to provide a stronger rationale for undertaking this exercise. This could be discussed in either the introduction or the discussion section of the manuscript.

Response: We added the rationale for undertaking this network meta-analysis both in the introduction or the discussion section.

(2)It does not seem like all the rehabilitation interventions were

considered by the authors. For instance, virtual reality based interventions are now increasingly being used for training balance dysfunctions. These do not find a mention in the interventions included in the search strategy. Also, it is necessary to explain briefly how each intervention helps alleviate balance dysfunction (addition of a table for this purpose might be adequate). This will help readers understand why a specific intervention has been included in the protocol. This is also specifically important for Chinese traditional medicine interventions as not all readers would be familiar with those.

Response: We did a literature research and consulted with the experts in rehabilitation to predefine the scope of traditional Chinese medicine therapies and modern rehabilitation therapies. We also briefly explain how each intervention helps alleviate balance impairment in the introduction section. Please see page 3-4.

(3)The data analyses should be explained in more detail outlining the rationale for choosing specific methods and their advantages over other methods. Although, this would not be expected in a manuscript outlining the results of the network meta analyses, a proposal manuscript should explain data analyses methods in detail.

Response: We rewrote the statistical analysis to explain data analyses methods in detail. Please see statistical analysis section.

(4)Have the authors made a priori choices with regards to subgroup analyses, specifically in order to explore the degree of balance dysfunction and the appropriateness of the chosen intervention? Will the study be able to comment on this aspect? Also how will this help the clinicians in making informed choices?

Response: Subgroup analysis and meta regression will be performed based on age, sex, type of stroke, disease course of stroke, the severity of balance impairment and the duration of treatment. Please see Subgroup analysis section in page 10.

(5)The entire paper should be proof read and revised for English grammar and usage. Some sentences are left incomplete without a verb, some others use improper grammar. Some words convey a completely unintended meaning and could be a source of confusion. Also, general conventions used in rehabilitation literature should be kept intact. Some examples are outlined below. I have not outlined mistakes in the entire paper (as there were too many) but the following can be used as guidelines.

Examples of minor grammatical and other errors:

Page 3, line 9: “(RCTs) utilized rehabilitations to treat the balance”. This should be rephrased as “(RCTs) that have utilized rehabilitation interventions to treat balance dysfunction..”

Response: We have revised.

Page 3, line 10: “Berg balance scale” the convention is to capitalize the first letter of every word such that is reads like ‘Berg Balance Scale’. Please consider modifying this in the manuscript.

Response: We have revised.

Page 3, line 11: Please insert ‘and’ after the comma after ‘(BBS) and before ‘the Fugl’. Also consider removing the phrase ‘at the end of the treatment’. It is expected that the primary outcomes would generally be measured pre and post treatment. So, mentioning only at the end of the treatment may create confusion in the readers’ mind.

Response: we have inserted “and” and removed the phrase “at the end of the treatment”.

Page 3, line 16: please do not capitalise F in fall rates. Also, conventionally the Timed Up and Go test is abbreviated as simply the TUG and not TUGT. Please use the conventional abbreviation as far as possible.

Response: we have corrected “Fall rates” for “fall rates” and revised “TUGT” into “TUG”.

Page 3, line 29: “The findings of this network meta-analysis will summarize the direct and indirect evidence of rehabilitations on balance dysfunction after stroke..” the study results are expected to summarize the direct and indirect ‘effects’ of ‘rehabilitation interventions’ on balance dysfunction after stroke. Please make the aforementioned changes.

Response: We have deleted this sentence.

Page 4, line 31: Does stroke often lead to ‘muscle spasms’? Or are the authors referring to spasticity here? Please clarify. Also, please elaborate on the meaning of ‘prosthetic sensory disorder’.

Response: We have revised “muscle spasms” into “spasticity” and changed “prosthetic sensory disorder” for “vestibular impairment”.

Please review the paper using the above examples as guidelines. I am also attaching the manuscript here with highlighted areas that may need revision.

Response: We have corrected all of the highlighted areas.

Response for reviewer 3

(1)The authors primary outcome for studies assessing balance training in stroke patients is insufficient and therefore limits the ability of the reader to generalize the finding. Specifically, important outcomes eg FIST, (function in sitting test), SBS (sitting balance scale) and Ottawa Sitting Scale have not been mentioned or referenced. Without acknowledging all of the studies which looked at using these latter outcomes, the protocol is very limited. Also, although inclusion of traditional Chinese medicine studies is novel, along with others, it would have been helpful to know the authors thought about how many RCTs (“only RCTs will be included”) they expected to find.

Response: We have added function in sitting test, sitting balance scale and Ottawa Sitting Scale, the Activities-specific Balance Confidence

scale, the Overall Balance Index and the Brunel Balance Assessment and

other outcomes focus on balance ability as outcomes

VERSION 2 – REVIEW

REVIEWER	Hille M. Finestone Bruyere Continuing Care, Elisabeth Bruyere Hospital Professor, Division of Physical Medicine and Rehabilitation, Department of Medicine, University of Ottawa Mailing Address: Dept. of Physical Medicine and Rehabilitation- 2nd Flr. Bruyere Continuing Care, Elisabeth-Bruyere Hospital 43 Bruyere St., Ottawa, ON, Canada,
REVIEW RETURNED	20-Feb-2019

GENERAL COMMENTS	Much better

REVIEWER	Aurélien HUGUES Service de médecine physique et réadaptation, hôpital Henry-Gabrielle, Hospices Civils de Lyon, Saint-Genis-Laval, France; Equipe “ImpAct”, Centre de Recherche en Neurosciences de Lyon, Inserm UMR-S 1028, CNRS UMR 5292, Université de Lyon, Université Lyon 1, Bron, France.
REVIEW RETURNED	03-Mar-2019

GENERAL COMMENTS	Comments This publication is a protocol aiming at comparing the effectiveness of rehabilitation interventions relative to each other by a network meta-analysis. The issue of the recovery of balance disorders after stroke is a main topic in rehabilitation of stroke patients. There are many different rehabilitation interventions investigated in literature. The clinical practice is actually various according to the practitioner. So, the relative efficacy of rehabilitations interventions is a relevant issue to clinical practice. Introduction The sentence “Balance is the ability to maintain the line of gravity within the base of support with minimal postural sway11. The control of human balance is a comprehensive process relying on the integration of visual, vestibular and somatosensory inputs in the central nervous system” should be placed before in the text, in the first paragraph when the authors explained balance disorders after stroke. The use of studies published in Journal of Physical Therapy Science as references could be problematic because this journal is considered as predatory journal by librarian Jeffrey Beall (https://beallslist.weebly.com/). The background is well explained by the authors. Main issues of the rehabilitation are presented. The concerns of the rehabilitation the most efficacy is relevant.

	Methods The authors followed PRISMA recommendations. Even if the authors use guidelines (The Fourth National Cerebrovascular Disease Conference in 199536, A Guide to the Prevention and Treatment of Chinese Cerebrovascular Disease developed by the Chinese Medical Association in 200537, Standard for the Diagnosis and Evaluation of Stroke Difficulties formulated by the Encephalopathy Emergency Team of the State Administration of Traditional Chinese Medicine in 1996) to define stroke, they could specify in the text if ischemic transitory accidents will be included and how the diagnosis of stroke has been made (brain imagery …). Moreover, will all types of stroke lesion be included? What about location of the lesion, recurrent episode of stroke …? The authors could develop the criteria of selection about characteristics of lesion. (Major comment) The scales such as Function In Sitting Test (FIST), the Sitting Balance Scale (SBS), the Ottawa Sitting Scale, the Activities-specific Balance Confidence (ABC) scale, the Overall Balance Index (OBI) and the Brunel Balance Assessment (BBA), The MOS 36-item short-form health survey (SF-36), adverse events are not described and their use is not justified in the protocol. The search in registration websites is a good point. The search in grey literature is well planned by the authors. The authors search all studies investigating effects of rehabilitation interventions on balance after stroke. The search strategy described in Appendix combines 7 parts. The final algorithm doesn't seem to me correct because the parts 3, 4 and 5 are combined by the Boolean connector "AND". These should be combined with the connector "OR". So, the final algorithm should be: #1 AND #2 AND (#3 OR #4 OR #5) AND #7 (Major comment) The characteristics of study, participants, interventions and comparisons which will be extracted should be specify with more details. For example, "disease course and so on" is too unclear. For me, "If the P value is ≥0.1 and I2 ≤50%, we will synthesize SMD or OR with Mantel–Haenszel method (fixed effects model). If the P value is <0.1 and I2 >50%, the Der Simonian-Laird method (random-effects model) will be used." is unclear. The Mantel–Haenszel method is a method to estimate a pooled effect treatment for discontinuous data only. What "the disease course" means? Is the time post-stroke? It seems to me unclear. For subgroup analyses, how will the authors define the thresholds for the disease course and for the severity of balance impairment? Why investigate the impact of study design by sensitivity analyses when only RCTs will be included in the selection? The authors write that cross-overs will be excluded. "If the number of trials reporting the primary outcomes was 10 or more, funnel plot will be performed to assess the publication bias of the included studies." This sentence raises doubts: Will publication bias be assessed only for primary outcomes because the selection of studies will be performed according to primary outcomes only? Or will the selection of studies be made according to secondary outcomes, such as the selection criteria would suggest? Is yes, the publication bias should also be assessed for secondary outcomes by funnel and Egger's test. If no, the selection criteria should be specified in methods. (Major comment) Discussion The authors write that "However, previous meta-analyses failed to assess the comparative efficacy and acceptability of all the

	available rehabilitation therapies." But they do not explain (or try to explain) why. They write "failed": does it mean that the previous meta-analyses were unable to assess it? Or does it mean that results of these previous meta-analyses were not statistically significant? or … This explanation is needed to justify the next sentence ("NMA is needed to determine the comparative effects of these rehabilitation therapies.") The objective "to provide a ranking of these therapies for balance impairment" is very interesting. The authors should spotlight, in the discussion, the relevance of analyses on safety outcomes. It is a part of decision-making in clinical practice.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 3

Reviewer Name: Hille M. Finestone

Institution and Country: Bruyere Continuing Care, Elisabeth Bruyere Hospital

Professor,

Division of Physical Medicine and Rehabilitation, Department of Medicine,

University of Ottawa

Mailing Address:

Dept. of Physical Medicine and Rehabilitation- 2nd Flr.

Bruyere Continuing Care, Elisabeth-Bruyere Hospital

43 Bruyere St.,

Ottawa, ON, Canada,

Please state any competing interests or state 'None declared': None Declared

Please leave your comments for the authors below

Much better

Response: Thank you for your affirmation.

Reviewer: 1

Reviewer Name: Aurélien HUGUES

Institution and Country: Service de médecine physique et réadaptation, hôpital Henry-Gabrielle, Hospices Civils de Lyon, Saint-Genis-Laval, France;

Equipe "ImpAct", Centre de Recherche en Neurosciences de Lyon, Inserm UMR-S 1028, CNRS UMR 5292, Université de Lyon, Université Lyon 1, Bron, France.

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

Comments

This publication is a protocol aiming at comparing the effectiveness of rehabilitation interventions relative to each other by a network meta-analysis. The issue of the recovery of balance disorders after stroke is a main topic in rehabilitation of stroke patients. There are many different rehabilitation interventions investigated in literature. The clinical practice is actually various according to the practitioner. So, the relative efficacy of rehabilitations interventions is a relevant issue to clinical practice.

Response: We appreciate for your affirmation.

Introduction

The sentence “Balance is the ability to maintain the line of gravity within the base of support with minimal postural sway11. The control of human balance is a comprehensive process relying on the integration of visual, vestibular and somatosensory inputs in the central nervous system” should be placed before in the text, in the first paragraph when the authors explained balance disorders after stroke.

Response: Thank you for your constructive comments. We have adjusted the order of this sentence.

The use of studies published in Journal of Physical Therapy Science as references could be problematic because this journal is considered as predatory journal by librarian Jeffrey Beall (https://beallslist.weebly.com/).

Response: Thank you for your advice, we have deleted the reference.

The background is well explained by the authors. Main issues of the rehabilitation are presented. The concerns of the rehabilitation the most efficacy is relevant.

Response: Thank your for your affirmation.

Methods

The authors followed PRISMA recommendations.

Even if the authors use guidelines (The Fourth National Cerebrovascular Disease Conference in 199536, A Guide to the Prevention and Treatment of Chinese Cerebrovascular Disease developed by the Chinese Medical Association in 200537, Standard for the Diagnosis and Evaluation of Stroke Difficulties formulated by the Encephalopathy Emergency Team of the State Administration of Traditional Chinese Medicine in 1996) to define stroke, they could specify in the text if ischemic transitory accidents will be included and how the diagnosis of stroke has been made (brain imagery …). Moreover, will all types of stroke lesion be included? What about location of the lesion, recurrent episode of stroke …? The authors could develop the criteria of selection about characteristics of lesion. (Major comment)

Response: Thank you for your constructive comments. We have specified the diagnosis of stroke as required. All types of stroke will be included. As for types of stroke, location of lesion, times of strokes, we will perform subgroup analysis to investigate the influence on the results. We also mentioned in the subgroup analysis part.

The scales such as Function In Sitting Test (FIST), the Sitting Balance Scale (SBS), the Ottawa Sitting Scale, the Activities-specific Balance Confidence (ABC) scale, the Overall Balance Index (OBI) and the Brunel Balance Assessment (BBA), The MOS 36-item short-form health survey (SF-36), adverse events are not described and their use is not justified in the protocol.

Response: We appreciate for your suggestion. The details of the scales mentioned above has been justified.

The search in registration websites is a good point. The search in grey literature is well planned by the authors.

Response: We appreciate for your affirmation.

The authors search all studies investigating effects of rehabilitation interventions on balance after stroke. The search strategy described in Appendix combines 7 parts. The final algorithm doesn't seem to me correct because the parts 3, 4 and 5 are combined by the Boolean connector "AND". These should be combined with the connector "OR". So, the final algorithm should be: #1 AND #2 AND (#3 OR #4 OR #5) AND #7 (Major comment)

Response: We appreciate for your constructive comment. We have revised our search strategy.

The characteristics of study, participants, interventions and comparisons which will be extracted should be specify with more details. For example, "disease course and so on" is too unclear.

Response: Thank you for your suggestion. The characteristics of included studies has been supplemented.

For me, "If the P value is ≥0.1 and I2 ≤50%, we will synthesize SMD or OR with Mantel–Haenszel method (fixed effects model). If the P value is <0.1 and I2 >50%, the Der Simonian-Laird method (random-effects model) will be used." is unclear. The Mantel–Haenszel method is a method to estimate a pooled effect treatment for discontinuous data only.

Response: Thank you for your comment. We have revised the statistical analysis.

What "the disease course" means? Is the time post-stroke? It seems to me unclear.

Response: Disease course means the time post stroke.

For subgroup analyses, how will the authors define the thresholds for the disease course and for the severity of balance impairment?

Response: The thresholds for the disease course is six month, since six months after stroke is the sequela period; For the severity of balance impairment, BBS will besed to identify the severity of balance impairment, 0~20: poor balance ability; 20~40: fair balance ability; 41~56: good balance ability.

Why investigate the impact of study design by sensitivity analyses when only RCTs will be included in the selection? The authors write that cross-overs will be excluded.

Response: Thank you for your comment. We have changed "study design" to "study quality".

"If the number of trials reporting the primary outcomes was 10 or more, funnel plot will be performed to assess the publication bias of the included studies." This sentence raises doubts: Will publication bias be assessed only for primary outcomes because the selection of studies will be performed according to primary outcomes only? Or will the selection of studies be made according to secondary outcomes, such as the selection criteria would suggest? Is yes, the publication bias should also be

assessed for secondary outcomes by funnel and Egger's test. If no, the selection criteria should be specified in methods. (Major comment)

Response: Thank you so much for your constructive comment. The funnel plot will be performed only for primary outcome. We have rewritten this sentence to avoid ambiguity.

Discussion

The authors write that "However, previous meta-analyses failed to assess the comparative efficacy and acceptability of all the available rehabilitation therapies." But they do not explain (or try to explain) why. They write "failed": does it mean that the previous meta-analyses were unable to assess it? Or does it mean that results of these previous meta-analyses were not statistically significant? or … This explanation is needed to justify the next sentence ("NMA is needed to determine the comparative effects of these rehabilitation therapies.")

Response: Thank you so much for your comment. We have rewritten this sentence.

The objective "to provide a ranking of these therapies for balance impairment" is very interesting. The authors should spotlight, in the discussion, the relevance of analyses on safety outcomes. It is a part of decision-making in clinical practice.

Response: Thank you so much for your suggestion. We have supplied the safety outcomes.

VERSION 2 – REVIEW

REVIEWER	AURELIEN HUGUES Service de médecine physique et réadaptation, hôpital Henry-Gabrielle, Hospices Civils de Lyon, Saint-Genis-Laval, France; Plate-forme "Mouvement et Handicap", hôpital Henry-Gabrielle, Hospices Civils de Lyon, Saint-Genis-Laval, France; Equipe "ImpAct", Centre de Recherche en Neurosciences de Lyon, Inserm UMR-S 1028, CNRS UMR 5292, Université de Lyon, Université Lyon 1, Bron, France.
REVIEW RETURNED	09-May-2019

GENERAL COMMENTS	Comments All comments made for the last reviewing have been modified. Introduction: Clear and correct. Methods: The authors have written "No restrictions on language or publication date." It is "No restriction ..." Discussion: correct.