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Review

Do exercise therapies restore the deficits of joint position sense in patients with chronic ankle instability? A systematic review and meta-analysis

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ABSTRACT

To determine whether existing exercise therapies can restore the joint position sense (JPS) deficits of patients with chronic ankle instability (CAI) when compared with controlled non-training patients. Seven databases were searched using ankle, injury, proprioception, and exercise-therapy-related terms. Peer-reviewed human studies in English that used the absolute errors score of joint position reproduction (JPR) test to compare the JPS of injured ankles in CAI patients before and after exercise therapy and non-training controls were included and analyzed. Demographic information, sample size, description of exercise therapies, methodological details of the JPR test, and absolute error scores were extracted by two researchers independently. Meta-analysis of the differences in JPS changes (i.e., absolute errors after treatment minus the baseline) between the exercise therapies and non-training controls was performed with the weighted mean difference (*WMD*) and 95% confidence interval (*CI*). Seven studies were finally included. Meta-analyses revealed significantly higher improvements in passive JPS during inversion with, $WMD = -1.54^{\circ}$ and eversion, of, $WMD = -1.80^{\circ}$, after exercise therapies when compared with non-training controls. However, no significant changes in the impaired side active JPS were observed with regard to inversion and eversion. Existing exercise therapies may have a positive effect on passive JPS during inversion and eversion, but do not restore the active JPS deficits of injured ankles in patients with CAI when compared with non-training controls. Updated exercise components with a longer duration that focus on active JPS with longer duration are needed to supplement the existing content of exercise therapies.

Introduction

Ankle sprains are among the most frequently-incurred musculoskeletal traumas that are related to physical and sports activity, with an incidence of approximately 2–7 sprains/1 000 person-years according to data relating to emergency department visits.[1] Of major concern is the fact that while commonly viewed as an innocuous injury, up to 74% of patients who sustain an initial sprain will proceed to develop chronic ankle instability (CAI) with ongoing symptoms (e.g. repeated sensation of the ankle "giving way", persistent pain, and recurrent sprains).[1,2] Long-term joint instability in CAI is also associated with the onset and progression of ankle osteoarthritis, thus leading to a heavy socioeconomic burden.[3,4] Although there have been numerous treatments for CAI, the clinical outcomes are still far from satisfactory.[3,5] Therefore, it is important for both patients with CAI and orthopedic clinicians to investigate more effective therapeutic approaches to manage CAI.

The current consensus of opinion suggests that it is the combination of mechanical insufficiencies and sensorimotor dysfunction that leads to the symptoms of CAI and that mechanical factors might provide a weaker contribution.[2,4] Of the sensorimotor factors, proprioception deficits were first recognized by Freeman et al. in 1965, when these authors suggested that the concurrent destruction of proprioceptors within the ligamentous tissues may result in neural deafferentation.[6] However, subsequent evidence has suggested that the impaired ligamentous proprioceptors alone are insufficient to cause CAI symptoms and that it is maladaptive neuroplasticity in the central nerve system (CNS) caused by prolonged deafferentation that leads to the dysfunction of proprioceptors beyond

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Abbreviations

JPS	joint position sense
CAI	chronic ankle instability
JPR	joint position reproduction
WMD	weighted mean difference
CI	confidence interval
CNS	central nerve system
PEDro	Physiotherapy Evidence Database
IAC	International Ankle Consortium

joints (e.g. the fibular muscle spindles), therefore acting as a key factor in persistent functional instability.[7–10] A recent review on this topic also suggested that patients with CAI did have deficits of proprioception in their injured ankle, especially with regard to their perception of ankle joint position, an attribute referred to as joint position sense (JPS).[11,12] It is JPS that allows us to maneuver our way around obstacles out of view. Higher ankle JPS deficits are associated with worse balance impairments and an increased risk of sprain recurrence.[13–15] As a result, JPS deficits might represent a potential therapeutic target for CAI.

To measure JPS, the Joint Position Reproduction (JPR) test is the most representative and reliable approach to measure the JPS; therefore, to improve the homogeneity of outcomes, only outcomes arising from the JPR test were selected and pooled in the present study.[16] In the JPR test, the researcher presents a predefined target angle to the tested ankle and then asks the participants to reproduce the angle actively or passively (active and passive JPR/JPS, respectively).[11,12] The absolute deviation between the target angle and the reproduced angle would be defined as the absolute error, and a higher absolute error represents a worse JPS.[11,12] Participants would also use blindfolds and earplugs to minimize confounding factors caused by visual and auditory issues.[11,12] Focusing on the JPR test, the Xue et al. paper indicated that the unstable ankle of the CAI patients have significant deficits in active JPS, while passive JPS was intact when compared with healthy controls.[12]

Clinical guidelines advocate that patients with CAI should take non-surgical treatments for at least 3–6 months initially and that exercise therapy is an integral component in the management of CAI and its proprioception deficits.[3,5,17] Over recent years, some researchers have summarized the effect of exercise therapy on CAI, but most of these researchers have only focused on the results of self-report questionnaires and balance tests (e.g. reaching distance in the Y-balance test), which might lack physiological specificity.[16,18,19] With regard to proprioception and the subdivided JPS, it is evident that despite the design of various exercise strategies to restore the proprioception deficits in CAI, no consensus has been achieved regarding their exact effects. This may be due to the small sample size, the absence of controls, and the heterogeneous testing methodology.[9,20] Recently, Han et al. performed a review on this problem, but they also pooled the results with heterogeneous JPS test methodology (i.e. active or passive JPS, JPR test or sloped-surface block method).[21] As a result, we believe that summarizing the proprioceptive effects of existing exercise therapies on CAI with a more detailed meta-analysis could have the potential to offer better guidelines for the future development of more mechanism-targeted treatments for CAI.

Therefore, the purpose of this systematic review was to determine whether existing exercise therapies can restore the JPS deficits of patients with CAI when compared with non-training controls. We hypothesized that existing exercise therapies are able to restore ankle JPS deficits in patients with CAI.

Material and methods

Study design

This systematic review with meta-analysis was designed and carried out in accordance with the guidelines of Preferred Reporting Items for Systematic reviews and Meta-Analyses.[22] The study protocol was prospectively registered in the International Platform of Registered Systematic Review and Meta-analysis Protocols platform (ID INPLASY202110032).

Search strategy and article selection

Seven electronic databases (PubMed, Embase, Cochrane, CINAHL, Web of Science, SPORTDiscus, and Scopus) were searched from inception to the 17th of February 2022. Four strings of keywords grouped with 'AND' were composed as the search strategy, using terms related to (1) ankle, (2) injury, (3) proprioception, and (4) exercise therapy. Within each string, the included terms were connected by 'OR'. The full search strategy for PubMed is presented in Supplementary Appendix A.

Two researchers (TW, Xu-X) independently screened the titles and abstracts of all searched records for any potentially relevant articles with the following inclusion criteria: peer-reviewed human studies in English that used the JPR test to compare the JPS of injured ankles in CAI patients before and after exercise therapy and non-training controls. If the course of treatment was only one session that focused on an immediate effect, the article would be excluded. The reference lists of each included article would also be manually checked for any missed records. When screening, if an article was included by either researcher, its full text would be assessed for eligibility; while for article inclusion, if the discrepancies remained unsolved after discussion, a third researcher (HY) would be consulted. If the full text could not be downloaded, the corresponding authors would be contacted.

Data extraction

The included studies were reviewed by two researchers (WY and GX) independently. The following contents were extracted: demographic information, sample size, description of exercise therapies, methodological details of the JPR test (e.g., movement direction, target angle, devices), and absolute errors (means and standard deviation). If there were multiple target angles in the same study and movement direction, the largest one that started from a neutral ankle position would be extracted to evaluate the vulnerable proprioceptors at the extreme limits of ankle movement.[11,16] The components of each exercise therapy were summarized and categorized by referring to the standards described previously by Clark et al.[17] and the results of a single study were also summarized as either positive or negative. If the outcomes were confusing or not fully reported, the corresponding authors would be contacted.

Quality assessment

All researchers discussed the criteria for each item prior to formal quality assessment. Then, two researchers (XX, TW) evaluated the included studies independently. Disagreements would be resolved by discussion and consultation with a third author (HY).

The Physiotherapy Evidence Database (PEDro) scale was used to assess the risk of bias; this consists of 11 items that evaluate the quality and validity of each trial, and was scored as 'Yes' (1 point) or 'No' (0 points) for each item.[23] The mean score of items 2–11 was used to determine the overall study quality (10 points in total) and a PEDro score of six or higher was considered to indicate good/excellent methodological quality.[23] Publication bias was allowed because no analyses could be performed for the relatively few studies included in each pooling analysis (fewer than 10).[24]

The recommendations of the International Ankle Consortium (IAC) were used to assess the selection criteria of CAI among the included studies.[2] The standard inclusion criteria for patients with CAI were required to meet five items: (1) a history of at least 1 ankle sprain; (2) injury resulting in pain, swelling, and the interruption of physical activity for at least one day; (3) the initial ankle sprain occurred at least 12 months prior to the study; (4) no history of ankle sprain in the previous three months; and (5) at least one out of the following three functional instability symptoms: at least two episodes of the ankle ‘giving way’ in the past six months, or ankle sprain recurrence, or self-reported ankle instability confirmed by a validated questionnaire.[2] Each item was classified as “reported and met the standard”, “reported but did not meet the standard”, or “not reported”.[2]

Statistical analysis

Meta-analysis of the differences in JPS changes (i.e., outcomes after treatment minus the status at baseline) between the exercise therapies and non-training controls was performed in Stata V.14 (Stata Corp LP, College Station TX, USA). The weighted mean difference (*WMD*) and 95% confidence interval (*CI*) of absolute errors were calculated in degrees (°) for the between-group differences. A larger negative *WMD* implied greater positive effects of exercise therapies than non-training controls with regard to ankle JPS. Considering the inherent heterogeneity of CAI criteria and training content among the studies, a random-effects model was used to pool the results from single studies. The heterogeneity of the pooled results was estimated by I^2 statistics; an I^2 of 75% or greater indicated high heterogeneity and was interpreted with caution.

In this study, only subgroup results of the same types of JPR (i.e. actively or passively reproduced) and ankle movement directions were taken into account. This was because most proprioceptors only work monotonically in one specific joint direction.[15] Furthermore, no further subgroup analysis on the types of exercise therapy was performed due to the limited number of included studies. The one-study-removed method of sensitivity analysis was used to evaluate the stability of the pooled results (consisting of more than two studies) by removing the included studies one by one. If the statistical significance was changed, the pooled result was interpreted with caution.

Results

Study selection and characteristics

The systematic search identified 9 966 potentially eligible studies, and 7 studies were finally included.[9,25–30] The steps of selection and the reasons for exclusions are presented in Fig. 1. There were 257 patients with CAI included in this review, and the mean age of the included participants ranged from 19.6 to 40.6 years. Among the included studies, muscle strengthening (5/7), balance (4/7), coordination (2/7), and

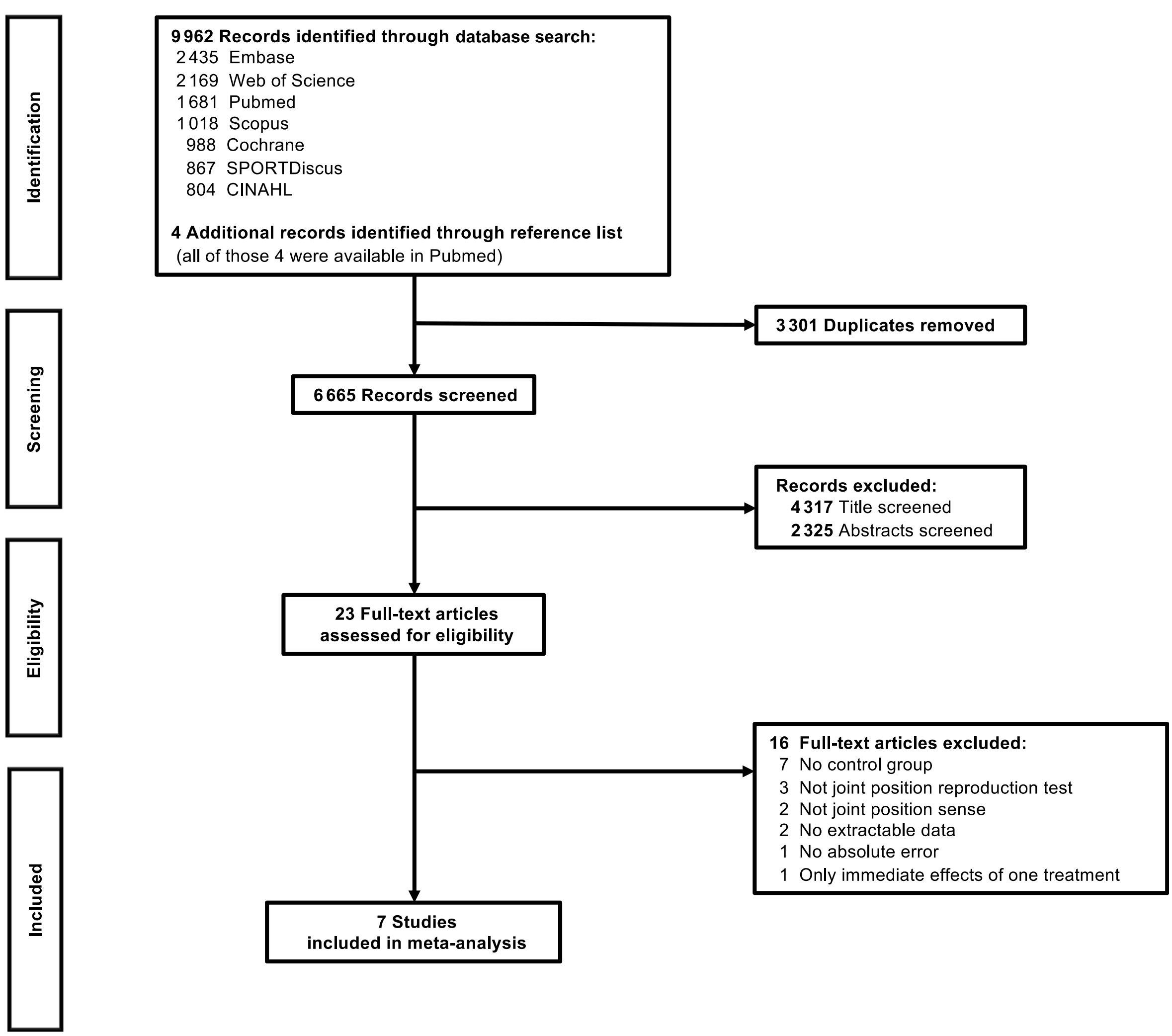

Fig. 1. Flow chart of the systematic review selection process.

vibration (1/7) were used in the exercise therapies over a course of 4–6 weeks. With regards to JPS evaluation, both active (3/7) and passive (6/7) JPR were used in all four ankle movement directions (i.e., dorsiflexion, eversion, inversion, and plantarflexion). Further study characteristics, including demographic data, sample size, a description of participants and exercise therapies, and methodological details of the JPR test, are presented in Supplementary Appendix B.

Quality assessment

Scores on the PEDro scale ranged from 5 to 8 out of 10 points. All the included studies ensured between-group similarity at baseline and performed between-group statistical comparisons, with both point measures and variability data provided. Furthermore, all of the studies (7/7) ensured their dropout rates were less than 15% and that their patients received the intervention as allocated. However, only 2/7 studies described the concealed allocation and blinded assessor, and none of the studies (0/7) performed participant or therapist blinding due to the utilization of exercise therapy. Further details regarding the PEDro scale are given in Supplementary Appendix C.

As regards the selection criteria of CAI, all the studies (7/7) required the patients to have sustained at least one ankle sprain and have at least one of the IAC-standardized functional instability symptoms. However, for the initial ankle sprain, only 2/7 studies met the required severity, and only 1/7 study set the time limit as > 12 months. Further detail relating to the rating scales are provided in Supplementary Appendix D.

Joint position sense

Three studies applied the active JPR test to measure the proprioceptive effect of exercise therapy.[9,25,26] Docherty et al. previously suggested that no significant effect of exercise therapy on active JPS in dorsiflexion was observed when compared to non-training controls and that the significant positive effect in plantarflexion exhibited wide variation.[25] Furthermore, no significant effects were observed in eversion by two studies[9,25] and in inversion by three studies.[9,25,26] (Fig. 2).

Six studies applied the passive JPR test to measure the proprioceptive effect of exercise therapy.[9,26–30] The significant positive effects of exercise therapy on passive JPS were observed in eversion by three studies[9,28,29] and in inversion by four studies[9,26,28,29] when compared to non-training controls. In dorsiflexion, four pooled studies showed a significant positive effect on passive JPS, although the heterogeneity was high ($I^2 = 90.2\%$).[27–30] No significant effect on passive JPS was observed in plantarflexion according to four studies.[27–30] (Fig. 3).

Sensitivity analysis

The pooled results of active JPS in inversion and passive JPS in all four ankle movement directions underwent sensitivity analysis. The pooled result for active JPS in inversion was significant when the study by Bernie et al.[9] was removed while the significant result for passive JPS in dorsiflexion was unstable when the study by Eils et al.[27] was removed or when the study by Chang et al.[29] was removed. The pooled results for passive JPS in inversion and eversion remained significant, while the pooled results for plantarflexion remained non-significant, regardless of which study was removed. An overall forest plot of the sensitivity analysis is provided in Supplementary Appendix E.

Discussion

The most important finding of this study was that existing exercise therapies might have a positive effect on JPS when compared with non-training controls. However, whether these improvements restore the JPS deficits in CAI still need further validation (Fig. 4).

Joint position sense and exercise therapy

Generally, the ankle-foot complex is the only part of the body contacting the ground during physical activity in humans, and ankle stability plays an essential role in the execution of movements and the avoidance of falls.[12] The functional stability of the joints is achieved through sensory input, CNS processing, and motor output.[11,14] With regards to the

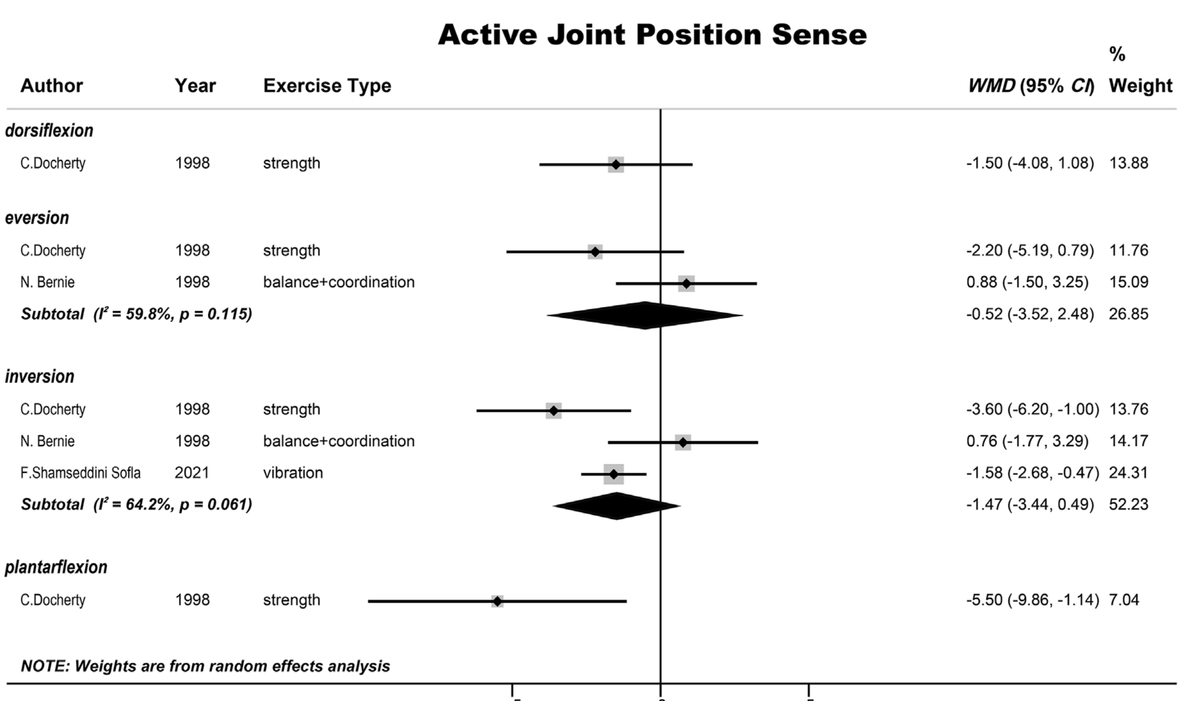

Fig. 2. Differences of the joint position sense changes from the baseline to the end of exercise therapy between the exercise therapies and non-training controls in the injured ankles of patients with chronic ankle instability; negative *WMD* indicates higher positive effect (less error) of exercise therapy on improving active joint position sense in degrees (°) than controls. *WMD*, weighted mean difference.

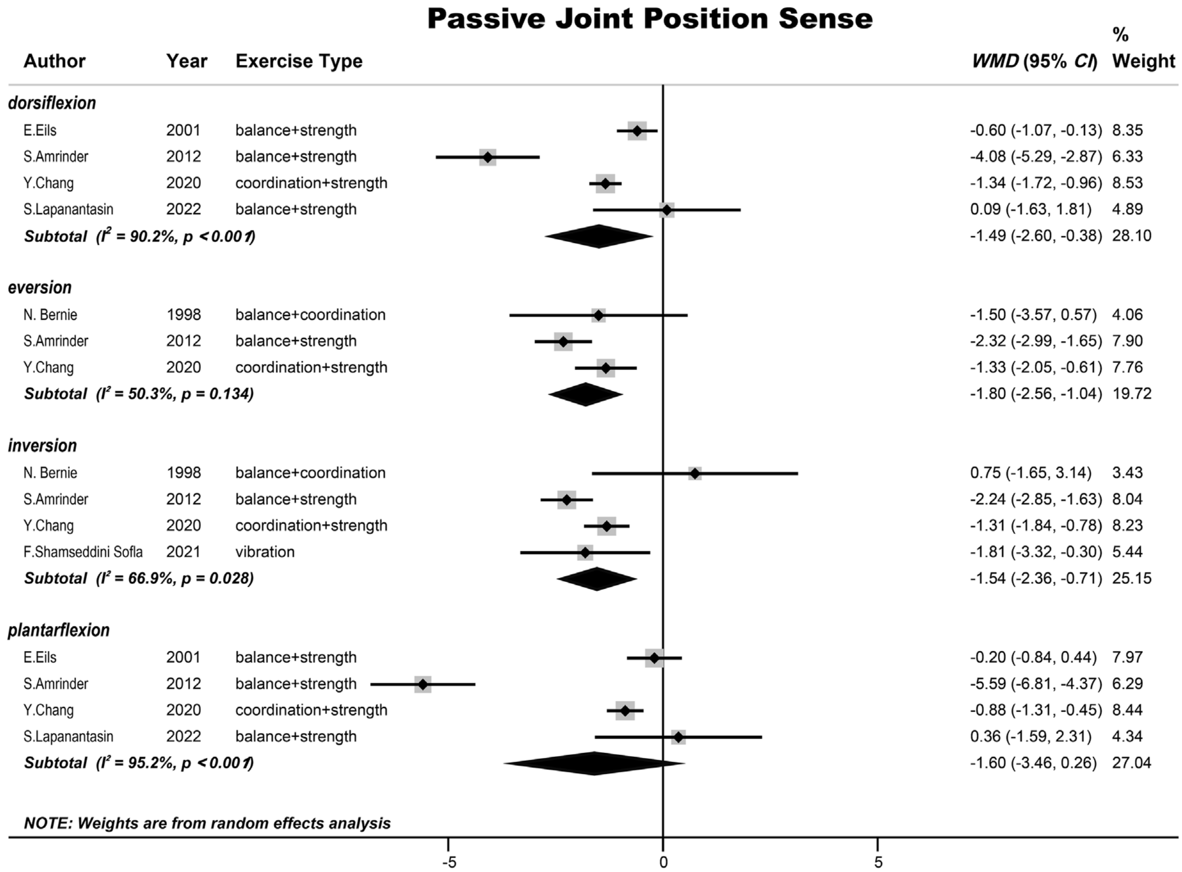

Fig. 3. Differences of the joint position sense changes from the baseline to the end of exercise therapy between the exercise therapies and non-training controls in the injured ankles of patients with chronic ankle instability; negative *WMD* indicates higher positive effect (less errors) of exercise therapy on improving passive joint position sense in degrees (°) than controls. *WMD*, weighted mean difference.

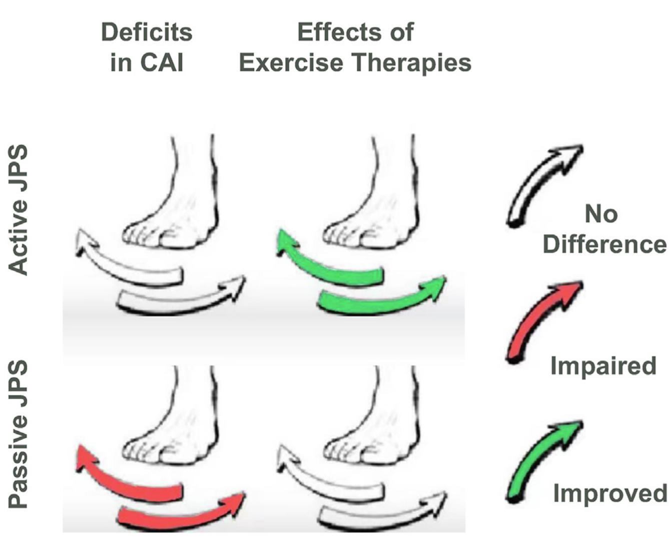

Fig. 4. Summarized JPS deficits and the effects of the existing exercise therapy in CAI. JPS, joint position sense; CAI, chronic ankle instability.

physiological basis of JPS, the Ruffini endings within ligaments and the tibial/fibular muscle spindles are known to contribute to both active and passive JPS, whereas central processing provides more support to active JPS.[15] As mentioned earlier, joint deafferentation is only a minor factor; the corresponding central maladaptive neuroplasticity may be the major factor underlying the pathogenesis of CAI.[4,7] As mentioned above, the most recent review also suggested that patients with CAI did have significant deficits of active JPS during ankle inversion and eversion, rather than passive JPS when compared with healthy controls.[12]

Any exercise will stimulate proprioceptors and generate neuromuscular impulses from the musculoskeletal tissues to the CNS; therefore, any type of exercise therapy can theoretically be considered as "proprioceptive training".[16,17] Considering clinical outcomes, previous reviews have suggested that either balance or strengthening training could improve self-reported functional instability and dynamic balance in CAI. Some researchers further suggested that their approaches may have restored the proprioception deficits of CAI.[18,19,27] According to our meta-analysis, existing exercise therapies only improve the "passive" JPS of injured ankles during eversion (approximately 1.80°) and inversion (approximately 1.54°). These findings are not consistent with the "active" JPS deficits found in the latest review of CAI proprioception.[12] Clearly, the positive effect of existing exercise therapies was "enhancing" intact JPS, rather than "restoring" the JPS deficits in CAI.

The effect of existing exercise therapies on JPS deficits in CAI

Since exercise is commonly considered to be an effective way to train both passive and active JPS in healthy people, the pathological features of CAI could be blamed for such conflict.[17] With regards to the partially blocked peripheral proprioceptors in CAI, previous studies suggested that exercise could improve passive JPS by increasing the sensitivity of these receptors and the amount of gamma-efferent activity, and these findings are consistent with our pooled results.[9,28] However, active JPS would be additionally influenced by the CNS, and recent evidence suggested that both the sensorimotor cortex and cerebellum are abnormal after ankle sprains.[7,8] According to the results of this study, we speculate that existing exercise therapies might fail to induce positive neuroplasticity and restore active JPS in a significant manner, and that this might be due to their relatively short courses (4–6 weeks) and non-specific training contents. Since our results were only based on the phenomena observed from the few existing clinical trials, these speculations still need to be investigated in greater detail.

On the other hand, the characteristics of the included studies could also represent potential factors responsible for this conflict. Not all types of exercise therapy were included in this review. Although these therapies are heterogeneous in terms of their components according to the category, and because no subgroup analyses were performed, we were unable to detect a significant effect of any type of component on the trend in the pooled results following sensitivity analysis.[17] Thus, we suggest that the addition of more JPS-targeted components to existing exercise therapies was needed, in the restoration of JPS deficits in CAI. With regards to sample size, only 10–40 participants/group were enrolled in a single study, and the number of the included studies that applied active JPR was relatively small (1–3 studies in each direction). This may have led to reduced statistical power to detect any curative effects of exercise therapy for active JPS. Furthermore, in the cross-sectional review that did not find impaired passive JPS in CAI, the pooled studies that applied passive JPR were also limited (2–4 studies in each direction).[12] Both of these factors could be potential obstacles and prevent tackling the problem in a robust manner. We can only note that existing exercise therapies did not restore the JPS deficits in CAI and that more high-quality original evidence with larger sample sizes and updated exercise components is needed to allow a more robust analysis.

Clinical relevance

Clinical guidelines suggest that deficits of ankle proprioception should be identified in clinics and considered in rehabilitation to reduce the risk of recurrent sprains.[5] According to our review, existing exercise therapies might not necessarily restore proprioception deficits, thus highlighting the importance of developing more JPS-targeted strategies for CAI, especially for active JPS during inversion and eversion. For example, the reproduction of repeated joint positioning itself could be effective if errors were able to be adjusted by feedback. This may improve the JPS in patients with chronic neck pain and uninjured individuals.[17] In addition, innovative CNS stimulation technology could also be a potential supplement to rehabilitation to restore maladaptive changes, although further exploratory studies on active JPS and CNS features are still needed.[31] By updating the literature on the proprioceptive effect of existing exercise therapies on CAI, a first step has been taken toward the need for newly developed proprioceptive training.

It should be mentioned that this review does not deny the clinical importance of the included exercise components. Muscle strength, response, and other deficits of CAI can all contribute to the formation of CAI and need to be restored.[4,5] Strength, coordination, and balance training are important in the improvement of ankle function and the prevention of ankle re-injury, although these strategies might not restore JPS deficits directly.[5,18,19] Furthermore, the improvement of passive JPS and other potential sensory improvements might also be a compensatory mechanism for the impaired active JPS. In clinical practice, there is a need for further emphasis on the functional requirements of specific deficits. It is also necessary to apply the combination of various exercise components to achieve optimal outcomes.[16]

Study limitations

There are several limitations associated with this study that need to be considered. First, this study only involved studies that considered JPS and used non-training controls and ignored other subtypes of proprioception and exercise controls due to the lack of available original studies. Second, although the JPR test without weight bearing is designed to reduce the bias caused by visual and vestibular supplements, it might not reflect the performance of the proprioceptive system in real situations, thus reducing its clinical meaning.[11] Third, the target angles and the device used for JPR tests were not further explored by subgroup analysis because of the limited number of studies available, although a previous review suggested that these factors would not significantly influence the possibility of detecting JPS deficits in patients with CAI.[12] Fourth, it was not possible to perform further subgroup analysis of the exercise components, thus rendering our conclusion less specific. Finally, both the unblinded accessors and the low fill rate of the IAC standard might influence the strength of our conclusions. To improve the transparency and homogeneity of CAI studies, we advise the authors of future trials to apply the PEDro scale and IAC standards in their study designs.

Conclusion

Existing exercise therapies might have a positive effect on passive JPS during inversion and eversion but do not restore the deficits of active JPS in the injured ankles of patients with CAI when compared with non-training controls. Updated exercise components that focus on active JPS and with longer duration are needed to supplement the existing content of exercise therapies.

Submission statement

All authors have read and agree with manuscript content. The manuscript has not been published and is not under consideration for publication elsewhere.

Authors' contribution

XX, TW, and Xu-X carried out the study design, literature search and selection, quality rating, and manuscript writing; JZ and LQ carried out statistical analysis and manuscript reviewing; WY and GX carried out the data collection; WR and HY carried out the study design, supervision of the literature search, data collection, and manuscript reviewing. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors. XX, TW, Xu-X contributed equally to this study as co-first authors; HY and WR contributed equally to this study as co-corresponding authors.

Conflict of interest

The authors have no direct or indirect interests that are in direct conflict with the conduction of this study.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.smhs.2023.01.001.

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