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Pressure Pain Sensitivity over Nerve Trunk Areas and Physical Performance in Amateur Male Soccer Players with and without Chronic Ankle Instability

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Abstract

Objective: Chronic ankle instability (CAI) is reported after ankle sprain. Our aim was to assess differences in mechanical pain sensitivity of lower extremity nerve trunks and physical performance between amateur soccer players with and without CAI.

Design: A cross-sectional case-control study.

Setting: Amateur soccer teams.

Participants: Fifty-five male soccer players, 28 with and 27 without CAI participated.

Main outcome measures: The perceived instability was assessed with the Cumberland Ankle Instability Tool (CAIT). Pressure pain thresholds (PPTs) on the common peroneal and tibialis nerve trunks, vertical jump, lateral step-down test and joint position sense of the knee were assessed by a blinded assessor.

Results: Soccer players with CAI showed lower PPTs over the common peroneal nerve than those without CAI (between-groups mean difference: $-1.0 \pm 0.8 \text{ kg/cm}^2$, $P < 0.001$).

No differences for PPT over the tibialis posterior ($P = 0.078$) or any physical performance outcome (knee joint positioning sense [$P = 0.798$], lateral step-down test [$P = 0.580$] and vertical jump variables [all, $P > 0.310$]) were found. PPT over the common peroneal nerve exhibited a significant moderate correlation with the CAIT score ($r = 0.528$, $P < 0.001$).

Conclusion: Amateur soccer players with CAI have higher pressure pain sensitivity over the common peroneal nerve but exhibit similar physical performance to amateur soccer players without CAI.

Key words: Soccer player, pressure pain, chronic ankle instability, physical.

Pressure Pain Sensitivity over Nerve Trunk Areas and Physical Performance in Amateur Male Soccer Players with and without Chronic Ankle Instability

Introduction

The incidence of an ankle sprain in individuals on soccer teams is approximately 7.9% (Waterman, Owens, & Davey, 2010). In professional soccer players, ankle sprains account for 13-14.5% of all injuries (Waldén, Hägg, & Ekstrand, 2005; Ekstrand, Hägg, & Waldén, 2011; Noya Salces & Silletto, 2012a; Noya Salces & Sillero, 2012b; Noya Salces, Gómez-Carmona, & Gracia-Marco, 2014). It has been reported that ankle sprains occur at a rate of 0.809 per 1000 hours of sport-practice, with 12.2% happening during sports competition and 15.7% during training (Noya Salces, Gómez-Carmona & Gracia-Marco, 2014). In Spanish amateur soccer players, the incidence of ligament injury represents 32.1% of the total injuries and the ankle joint is the second location affected with 12.4% of the overall injuries (Herrero, Salinero, & Coso, 2014). Sixty seven percent of the total injuries need medical attention and result in the inability to participate in subsequent soccer training or match plays (Herrero, Salinero, & Coso, 2014). Injuries in amateur soccer players have a high economic impact with ankle injuries accounting for an average cost of 2153€ (Gerbert, Gerber, & Pühse, 2018). In the general population, 70-80% of individuals suffering an ankle sprain will develop chronic instability (Hiller, Kilbreath, & Refshauge, 2011; Gribble, et al, 2016). In fact, soccer exhibits a high rate of recurrent ankle sprains (61%) and instability (38%) (Attenborough, Hiller, & Smith, 2014). Therefore, further studies investigating underlying mechanisms of chronic ankle instability (CAI) in soccer players are needed.

The tibial and peroneal nerves can potentially be injured during an inversion ankle sprain (Nitz, Dobner, & Kersey, 1984; Baima, & Krivickas, 2008). In fact, peroneal and tibial nerve lesions have been previously observed after severe ankle sprains (Mitsiokapa,

Mavrogenis, & Drakopoulos, 2017). Lorenzo-Sánchez-Aguilera et al (Lorenzo-Sánchez-Aguilera et al, 2019) reported sensitivity to pressure pain over muscle tissues (e.g. tibialis anterior, peroneus longus, or peroneus brevis) and nerves (common peroneus and tibialis) of the lower extremity in individuals with CAI. These studies would suggest a potential nerve involvement in ankle injuries; however, both studies were conducted in non-sport players; therefore, we do not know if physical demands related to soccer could influence these results.

Soccer is a sport which high demands are placed on the lower extremity where balance, speed, strength, and coordination are physical qualities needed. Some studies have observed that dynamic postural balance, range of motion, muscle strength, and joint position sense of the ankle are affected in sport players with CAI (Fu & Hui-chan, 2005; Kunugi, Masunari, & Koumura, 2018); however, other did not find difference in dynamic balance and muscle strength between sport players with and without CAI (Shiravi, Shadmehr, & Moghadam, 2017). It is important to understand that functional tasks of the lower extremity performed during soccer, such as running, jumping or landing, not only involve the ankle, but also the knee and hip. For instance, there is evidence showing that people with CAI adopt different movement strategies of the hip and the knee than subjects with no history of ankle sprains during functional tests such as the star excursion balance test (Hoch, Gaven, & Weinhandl, 2016). A recent meta-analysis found that reduced ankle dorsi flexion is associated with a dynamic knee valgus suggesting that deficits in knee control could be intrinsically related to the ankle (Lima, Ferreira, & de Paula Lima, 2018). In fact, patients with CAI exhibit decreased knee flexion than those without CAI (Theisen, & Day, 2019). We do not currently know if soccer players with CAI also exhibit proprioceptive deficits in the knee and not only in the ankle.

Therefore, the main objective of the current study was to compare the differences in mechanical sensitivity to pressure pain over peripheral nerves of the lower extremity between soccer players with and without CAI. A secondary objective was to determine differences between physical performance (dynamic postural balance, countermovement jump and joint position sense of the knee) between soccer players with and without CAI. We hypothesized that soccer players with CAI will exhibit higher pressure pain sensitivity and worse physical performance than those soccer player without CAI.

Methods

Study Design

A case-control study following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement was conducted (von Elm, Altman, & Egger, 2014). All participants read and signed the informed consent form before their inclusion. The local Ethic Committee of the University of Alcalá de Henares (CEID-HU-2018-04) approved the study design.

Participants

Fifty-five amateur soccer players, 28 subjects with CAI and 27 without previous history of ankle sprain were recruited to participate in this study. All participants were required to be active in this season and training regularly over the past months. Participants were volunteers recruited from three regional soccer teams in Madrid. To be included within the CAI group, soccer players had to present with: 1, history of one significant ankle sprain in the last 12 months; 2, self-reported feeling of instability in the ankle joint in the previous months; (Gribble et al, 2013) and, 3, a score of ≤ 27 on the Cumberland Ankle Instability Tool (Hiller, Refshauge, & Bundy, 2006; Cruz-Díaz, Hita-Contreras, & Lomas-Vega, 2013).

The Cumberland Ankle Instability Tool (CAIT) is a questionnaire with nine items used to identify and rate the self-perception of ankle instability (Hiller, Refshauge, & Bundy, 2006; Cruz-Díaz, Hita-Contreras, & Lomas-Vega, 2013). The maximum score is 30, and a value ≤ 27 is indicative of CAI (Hiller, Refshauge, & Bundy, 2006). In this study, the Spanish version of the CAIT, which has shown high reliability and internal consistency, was used (Cruz-Díaz, Hita-Contreras, & Lomas-Vega, 2013).

To be included in the non-CAI group, soccer players could not have experienced an ankle sprain over the previous year and report no sensation of instability. Participants in both groups were excluded if: 1, any ankle sprain event within the 3 months before the study; 2, fracture in the lower extremity; 3, lower extremity trauma or surgery pathology; 4, low back pain the previous 6 months; or, 5, any systemic medical disease (e.g. arthritis, diabetes).

Outcome measures

All outcomes were evaluated by an assessor blinded to the subject's condition and were assessed in the following order: pressure pain thresholds over the nerve trunks, vertical jump, lateral step-down test, and joint position sense in closed-kinetic-chain of the knee. A 2min rest period followed each test.

Primary Outcome

The primary outcome in the current study was pressure pain threshold. Pressure pain threshold (PPT), i.e., the minimal amount of pressure to be perceived first as painful, was assessed over the common peroneal nerve (behind the head of the fibula) and the tibialis posterior nerve (at the popliteal fossa, in the middle point just lateral to the popliteal artery) on the affected leg within those with CAI and on the dominant leg within those without CAI (Walsh, Kenneally, & Hall, 2010; Fingleton, Dempsey, & Smart, 2014). For PPTs assessment, an electronic algometer was used. The algometer was calibrated prior

to data collection. The pressure was applied perpendicularly to each point at a rate of approximately 1kg/s with 1 cm² tip; therefore, PPTs are expressed as kg/cm². Three measures were obtained from each site with a 10sec rest-period between measurements. The mean of the 3 trials was used for the analysis. This procedure has exhibited moderate to excellent intra- (ICC: 0.64-0.9) and inter- (ICC: 0.56-0.82) rater reliability (Fingleton, Dempsey, & Smart, 2014).

Secondary Outcomes

The knee joint positioning sense in closed-kinetic-chain of the affected/dominant leg was assessed by using a digital inclinometer (0.3° precision Limit® mini, 50 mm x 50 mm x 32 mm, Alingsas, Sweden) following the method proposed by Romero Franco et al (Romero-Franco, Montaña-Munuera, & Jiménez-Reyes, 2016). Participants wore a mask throughout the entire test to assure they were using their vision. The dominant leg was propped on a 5 cm high inclined surface and the non-dominant leg was propped on a 30 cm high step. Participants started with their dominant limb's knee extended. Next, the knee was led to the target position (knee flexion angle of 45° of the assessed limb), and they had the chance to remember this position for a total time of 5 seconds (**Fig 1A**). Following this, they returned to the initial position and were asked to actively bend the knee until the target position was achieved (**Fig 1B**). The participants had 3 attempts with 2sec-rest between each attempt. The range of knee flexion during the reposition task in each attempt was recorded. The average of the three trials was compared to the target position, which was used to obtain the absolute angular error (AAE) and the relative angular error (RAE) according to these formulas:

$$\text{AAE: } [(target\ position - trial\ 1) + (target\ position - trial\ 2) + (target\ position - trial\ 3)] / 3$$

$$\text{RAE: } [(trial\ 1 - target\ position) + (trial\ 2 - target\ position) + (trial\ 3 - target\ position)] / 3$$

This procedure has shown good reliability to obtain proprioceptive errors (Romero-Franco et al, 2014; Romero-Franco, Montaña-Munuera, & Jiménez-Reyes, 2016).

The lateral step-down test was assessed as follows. A 1cm marker was attached to each participant's tibial tuberosity and another marker was attached to the step at the level of the second toe. The test was explained to participants to make certain they knew how to perform it before the actual test. In preparation, participants had 3 practice attempts before the real measurement started. Five consecutive real trials were performed. During the test, the examiner was located 3m from the participant and provided instructions about the motion/speed and recorded their performance on video. Each participant placed his non-dominant leg on one side of a 20cm height step and positioned their hands on both hips (**Fig. 2A**). On the examiner's cue, each participant stepped down, maintained the position once they touched the floor (**Fig. 2B**) and stepped up also on the examiner's cue. Participants followed the examiner's instructions which lasted 2sec to step down and 2sec to step up. Also, they were asked to not move their foot once the heel touched the floor. Subsequently, the examiner evaluated the test performance and recorded it on a 7-point scale (0-6). According to the criteria established by Piva et al. (Piva et al, 2006) a score 0-6 is considered 'good' movement quality, a score of 2-3 is considered 'moderate' movement quality and a score of ≥ 4 is considered 'bad' movement quality. This test has adequate reliability to assess dynamic postural balance during a functional task (Piva et al, 2006; Rabin, & Kozol, 2010; Rabin, Kozol, & Moran, 2014); and the minimal detectable change (MDC) has been found to be 0.6 score (Bagherian, Ghasempoor, Rahnema, & Wikstrom, 2018).

Finally, the application MyJump2 was used to assess the vertical jump performance and it was recorded with an iPhone 6S with a 720p camera at 240 fps. This app has shown a high level of correlation with force plate measurements and it is a reliable and valid tool

to assess jump (Rogers et al, 2018). The test was performed following the protocol suggested by Balsalobre-Fernández et al (Balsalobre-Fernández, Glaister, & Lockey, 2015). The vertical jump was evaluated using the maximum jumping height (cm) reached in two attempts and the following variables were recorded: height, time, strength and speed of the vertical jump.

Sample size calculation

Sample size determination and calculations were based on detecting a moderate-large effect size of 0.80 between soccer players with and without CAI on the primary outcome (PPTs), a 2-tailed test, with an alpha level (α) of 0.05, and a desired power (β) of 90%. This generated a sample size of at least 25 participants per group.

Statistical analysis

The statistical analysis was conducted with SPSS for Windows (SPSS IBM, Chicago, IL, USA), version 22.0. The normal distribution of the quantitative variables was tested using the Shapiro-Wilk test. Data are described as means with their standard deviations (SD) for quantitative variables and as absolute frequency and percentage for qualitative variables. Differences in clinical variables (age, weight, height, BMI, years practicing amateur soccer, CAIT) between groups were compared using the independent Student's t-tests. Independent Student's t-tests were conducted to determine between-groups differences for the primary (PPTs) and secondary (knee joint positioning sense, lateral step-down test and vertical jump measurements) outcomes. To determine clinical relevance of between-groups differences, standardized mean differences (SMD) were calculated by dividing the between-group difference by the pooled standard deviation to enable comparison of effect sizes. Values were considered as trivial when ranging from 0.0 to 0.2, small from 0.2 to 0.49, moderate from 0.5 to 0.79, and large when greater than 0.8 (Sullivan, & Feinn, 2012). In addition, correlation analyses using Spearman's Rho (r_s)

were conducted to evaluate the potential relationships between PPTs (sensory outcome), physical performance (motor outcomes) and the degree of CAI (CAIT score) (Mukaka, 2012). In general, a P-value<0.05 was considered statistically significant, but for multiple comparisons (Student's t-tests), a Bonferroni-corrected alpha level of 0.025 (2 points of PPT assessment) was considered significant.

Results

Twenty-seven amateur soccer player without CAI and 28 amateur soccer players with CAI were finally included. No significant between-groups differences were found in demographic and clinical variables, except for the CAIT (**Table 1**).

Pressure pain Sensitivity in Soccer Players with and without CAI

The analysis found significant differences between groups for PPTs over the common peroneal ($t=5.236$, $P<0.001$), but not over the tibialis posterior ($t=1.795$, $P=0.078$), nerve: soccer players with CAI exhibited higher pressure pain hyperalgesia (between-groups mean difference: $-1.0 \pm 0.8 \text{ kg/cm}^2$) over the common peroneal nerve compared to soccer players without CAI. **Table 2** shows PPT over the common peroneal and tibialis posterior nerves in amateur soccer players with and without CAI.

Physical Performance in Soccer Players with and without CAI

No significant between-groups differences between amateur soccer players with and without CAI were reported for any secondary outcome: AAE knee joint positioning sense ($t=0.257$, $P=0.798$), RAE knee joint positioning sense ($t=1.371$, $P=0.176$), lateral step-down test ($t=0.557$, $P=0.580$), and height ($t=1.023$, $P=0.311$), time ($t=0.982$, $P=0.331$), strength ($t=0.973$, $P=0.335$), speed ($t=0.960$, $P=0.341$), and power ($t=0.358$, $P=0.722$), of the vertical jump (**Table 2**).

Correlation between Pressure Pain Sensitivity and Physical Performance

No significant association between PPTs and physical performance outcomes was observed (all, $P > 0.20$). There was a significant moderate correlation between PPT over the common peroneal nerve and the CAIT score ($r = 0.528$, $P < 0.001$): the lower the CAIT score, i.e., the greater the probability of CAI, the lower the PPT on the common peroneal nerve (**Fig. 3**).

Discussion

The primary objective of the current study was to evaluate the differences between neural mechanical sensitivity in male amateur soccer players with and without CAI. Our findings indicate the presence of pressure pain hypersensitivity, i.e., lower PPTs, over the common peroneal, but not over the tibialis posterior, nerve in amateur soccer players with CAI. Our secondary aim was to evaluate the differences in physical performance between amateur soccer players with and without CAI. No significant between-groups differences in any of the secondary outcomes related to physical performance were observed.

The presence of pressure pain hyperalgesia in subjects with ankle sprain has been previously investigated in two studies. Ramiro-González et al (2012) found lower PPTs over the affected anterior talofibular and calcaneofibular ligaments in subjects with an acute ankle sprain, whereas Lorenzo-Sánchez-Aguilera et al (2019) found lower PPTs over the common peroneal and tibialis posterior nerve in people with chronic ankle sprain. These studies support the presence of localized pressure pain hyperalgesia, but not generalized or widespread pressure pain sensitivity, of different ankle tissues in people after an inversion ankle sprain. Our study is the first one investigating the presence of pressure pain hyperalgesia in people with CAI. This is important since acute ankle sprain is generally associated to peripheral drive whereas chronic ankle sprain or CAI should be

more related to central sensitization. We observed localized pressure pain hyperalgesia on the common peroneal, but not on the tibialis posterior, nerve in amateur soccer players with CAI. These results support the presence of localized, but not widespread, pressure pain sensitivity over the affected ankle tissues, e.g., ligament, muscle or nerve, in subjects after an ankle injury, supporting the presence of peripheral, but not central, sensitization in ankle injury, independently of the chronicity of the condition. In fact, according to prior studies on pain mechanisms, localized pressure pain sensitivity, as expressed by lower PPTs, over the surrounding tissues of the affected ankle could be explained as a result of different biological changes. For instance, those inflammatory substances that originally sensitize ligaments could also extend to the other tissues, e.g., common peroneal nerve, producing a pain response to pressure. Another factor may be an increased spontaneous activity of nociceptive fibers from different tissues in the ankle region. A third mechanism could involve changes in the spinal cord neurons of innervated related segments. These changes could enhance nociceptive afferent input from the corresponding dermatome (L5-S1) and therefore stimulating sensitivity to pressure pain in their associated tissues (Woolf, 2011). Additionally, current and previous studies support the thoughts that this nerve trunk pressure pain hyperalgesia is not related to physical demands, since previous studies were conducted on non-sport players, whereas the current study was performed on amateur sport players.

Current findings support the presence of sensitivity to pressure pain in the common peroneal nerve, the main nerve innervating the lateral aspect of the ankle, leading to a suspicion of a potential injury of this peripheral nerve in the lower extremity in soccer players with CAI. It is possible that potential injury of the common peroneal nerve could be related to the delayed peroneal reaction time on the affected ankle observed in people with CAI (Hoch, & McKeon, 2014). This muscle-nerve interaction has several clinical

implications. For instance, a potential role of the common peroneal nerve trunk sensitivity in the complex presentation observed in people with CAI would suggest the necessity of evaluation and appropriate treatment targeting the nerve tissue in people with CAI. In line with this hypothesis, Plaza-Manzano et al (2016) reported that the inclusion of neural mobilization interventions into an exercise program was effective for improving strength, range of motion, function and pain in subjects with recurrent ankle sprains. However, current Clinical Practice Guidelines for ankle injury/sprain does not include interventions targeting nerve tissues (Vuurberg et al 2018). Therefore, it is possible that the inclusion of therapeutic interventions aiming to desensitize nerve tissues, particularly the common peroneal nerve, would prepare ankle structures to posterior treatment strategies used in the management of this condition such as proprioception, reaction time or strength deficit.

The secondary objective of the current study was to determine the differences in the physical performance of amateur soccer players with and without CAI. We did not find significant differences in error in knee joint positioning sense, dynamic balance and vertical jump parameters between amateur sport players with and without CAI. The ankle joint is intimately related to several injuries of the lower extremity (Murphy, Connolly, & Beynnon, 2003; van Seters, van Rijn, & van Middelkoop, 2017). For example, a deficit in ankle dorsiflexion range of motion has been related to a greater risk of suffering a knee injury (Amraee, Alizadeh, & Minoonejhad, 2017). Our study is the first investigating deficits in knee joint positioning sense and CAI. Current results suggest no differences in knee proprioception between amateur soccer players with and without CAI. It is possible that biomechanical alterations in the knee in a specific task, for example in landing after a jump, in individuals with CAI would be more related to proprioceptive and range of motion deficits of the ankle joint rather to proprioceptive deficits in the knee (Mason-

Mackay, Whatman, & Reid, 2017; Lima, Ferreira, & de Paula Lima, 2018; Theisen, & Day, 2019).

The lateral step-down test (LSDT) assesses dynamic balance (Piva et al, 2006) and several authors have related the quality of movement with range of motion deficits in the ankle joint (Grindstaff, Dolan, & Morton, 2017). In our study, only four amateur soccer players exhibited a poor quality of movement during the LSDT. Since our sample consisted of trained soccer players, it is possible that physical condition can potentially compensate deficits on LSDT. Additionally, we did not measure ankle range of motion, an important outcome to appreciate, as it may be associated with physical performance. Similar to our results, Ko et al have not either observed differences in dynamic balance between subjects with and without CAI (Ko Rae, Lee, & Lee 2018).

This is the first study examining vertical jump outcomes between amateur soccer players with and without CAI. Again, we did not find any significant difference between groups. Our results differ from those previously reported by Kunugi et al. (Kunugi, Masunari, & Koumura, 2018) who observed differences in jump height between soccer players with and without CAI; however, this study only examined measurements during a single-leg rebound jump. Theisen & Day found differences in jump landing between people with CAI and healthy subjects (Theisen, & Day, 2019). Moreover, the power of a single-leg vertical jump seems to be a risk factor for lower extremity injury in amateur soccer players (Henry, Evans, & Snodgrass, 2015). It is possible that the physical performance outcomes used in our study, i.e., LSDT, vertical jump or JPS of the knee, are not affected in individuals with CAI, whereas other outcomes such as the excursion balance test or landing task may be potentially more appropriate to detect deficits in athletes with CAI.

We examined the correlation between mechanical sensitivity of nerve trunks in the lower extremity and physical performance with self-perceived instability. We only observed a correlation between the CAIT score and mechanical pain sensitivity over the common peroneal nerve, the nerve showing pressure pain hyperalgesia, suggesting that that lower localized PPT (a suggestive finding of peripheral sensitization) was associated with lower CAIT scores (a suggestive finding of more CAI). This association could be bidirectionally explained. For instance, we do not currently know if higher sensitivity to pressure pain over the common peroneal nerve is consequence of repetitive ankle sprains leading to development of potential CAI; or the opposite, higher pressure pain sensitivity over the common peroneal nerve could be a potential risk factor for further development of CAI. Longitudinal studies should investigate the direction of this potential association.

Finally, some limitations exist in the current study. First, the cross-sectional nature of the study design does not permit us to clarify the association between the observed pressure pain hypersensitivity and CAI. Second, we included a subgroup of male amateur soccer players; so, our results should not be extrapolated to female soccer players or non-sport subjects with CAI. Third, we did not assess ankle dorsiflexion range of motion, which could also be affected in amateur soccer players with CAI.

Conclusions

This study found that amateur soccer players with CAI exhibit hypersensitivity to pressure pain over the common peroneal, but not over tibialis posterior, nerve compared to those soccer players without CAI. Amateur soccer players with and without CAI did not show differences in physical performance, as measured by the LSDT, vertical jump, and knee joint positioning sense.

Legend of Figures

Figure 1: Knee joint positioning sense assessment. (A) Initial targeted position of the knee (flexion angle of 45°); (B) Attempt of the subject to get the initial targeted knee position.

Figure 2: Lateral step-down test (A) Initial position of the non-dominant leg on one side of a 20cm height step; (B) The subject stepped down, maintained the position once they touched the floor and stepped.

Figure 3: Correlation between PPT in the common peroneal nerve and CAIT score

References

- Amraee, D., Alizadeh, M.H., Minoonejhad, H., Razi, M., & Amraee, G.H. (2017). Predictor factors for lower extremity malalignment and non-contact anterior cruciate ligament injuries in male athletes. *Knee Surgery, Sports Traumatology, Arthroscopy*, 25,1625-31. doi:10.1007/s00167-015-3926-8.
- Attenborough, A.S., Hiller, C.E., Smith, R.M., Stuelcken, M., Greene, A., & Sinclair, P.J. (2014). Chronic Ankle Instability in Sporting Populations. *Sports Medicine*, 44, 1545-56. doi:10.1007/s40279-014-0218-2.
- Bagherian, S., Ghasempoor, K., Rahnama, N., & Wikstrom, E. (2018). The effect of core stability training on functional movement patterns in collegiate athletes. *Journal of Sport Rehabilitation*, 0,1-22. doi:10.1123/ijsp.2017-0214.
- Baima, J., & Krivickas, L. (2008) Evaluation and treatment of peroneal neuropathy. *Current Reviews in Musculoskeletal Medicine*, 1, 147-53. doi:10.1007/s12178-008-9023-6.
- Balsalobre-Fernández, C., Glaister, M., & Lockey, R.A. (2015). The validity and reliability of an iPhone app for measuring vertical jump performance. *Journal of Sports Sciences*, 33,1574-9. doi:10.1080/02640414.2014.996184.
- Cruz-díaz, D., Hita-contreras, F., Lomas-Vega, R., Osina-Pérez, M., & Martínez-amat, A. (2013). Cross-cultural adaptation and validation of the Spanish version of the Cumberland Ankle Instability Tool (CAIT): an instrument to assess unilateral chronic ankle instability. *Clinical Rheumatology*, 32, 91-8. doi:10.1007/s10067-012-2095-0.
- Ekstrand, J., Hägglund, M., & Waldén, M. (2011). Injury incidence and injury patterns in professional football: the UEFA injury study. *British Journal of Sports Medicine*, 45, 553–8. doi:10.1136/bjsm.2009.060582.

- Fingleton, C.P., Dempsey, L., Smart, K., & Doody, C.M. (2014). Intraexaminer and Interexaminer Reliability of Manual Palpation and Pressure Algometry of the Lower Limb Nerves in Asymptomatic Subjects. *Journal of Manipulative & Physiological Therapeutics*, 37, 97–104. doi:10.1016/j.jmpt.2013.12.006.
- Fu, A.S.N., & Hui-chan, C.W.Y. (2005). Ankle Joint Proprioception and Postural Control in Basketball Players With Bilateral Ankle Sprains. *The American Journal of Sports Medicine*, 33, 1174-82. doi:10.1177/0363546504271976.
- Gerbert, A., Gerber, M., Pühse, U., Gassmann, P., Stamm, H., & Lamprecht, M. (2018). Costs resulting from nonprofessional soccer injuries in Switzerland : A detailed analysis. *Journal of Sport and Health Science*, 00, 1-8. doi:10.1016/j.jshs.2018.08.001.
- Gribble, P.A., Bleakley, C.M., Caul, B.M., Docherty, C.L., Fourchet, F., Fong, D.T., et al. (2016). Evidence review for the 2016 International Ankle Consortium consensus statement on the prevalence , impact and long-term consequences of lateral ankle sprains. *British Journal of Sports Medicine*, 50,1496-505. doi:10.1136/bjsports-2016-096189.
- Gribble, P.A., Delahunt, E., Bleakley, C., Caulfield, B., Docherty, C., Fourchet, F.R., et al. (2013). Selection Criteria for Patients With Chronic Ankle Instability in Controlled Research : A Position Statement of the International Ankle Consortium. *Journal of Orthopaedic & Sports Physical Therapy*, 43, 585-91. doi:10.2519/jospt.2013.0303.
- Grindstaff, T.L., Dolan, N., & Morton, S.K.. (2017). Ankle dorsiflexion range of motion influences Lateral Step Down Test scores in individuals with chronic ankle instability. *Physical Therapy in Sport*, 23, 75-81. doi:10.1016/j.ptsp.2016.07.008.

- Henry, T., Evans, K., Snodgrass, S.J., Miller, A., & Callister, R. (2015). Risk Factors for Noncontact Ankle Injuries in Amateur Male Soccer Players. *Clinical Journal of Sport Medicine*, 26, 251–8. doi:10.1097/jsm.0000000000000240.
- Herrero, H., Salinero, J.J., & Coso, J Del.(2014). Injuries among Spanish male amateur soccer players: a retrospective population study. *The American Journal of Sports Medicine*, 42, 78–85. doi:10.1177/0363546513507767.
- Hiller, C.E., Kilbreath, S.L., & Refshauge, K.M. (2011). Chronic ankle instability: Evolution of the model. *Journal of Athletic Training*, 46,133-41. doi: 10.4085/1062-6050-46.2.133.
- Hiller, C.E., Refshauge, K.M., Bundy, A.C., Herbert, R.D., & Kilbreath, S.L. (2006). The Cumberland Ankle Instability Tool: A Report of Validity and Reliability Testing. *Archives of Physical Medicine and Rehabilitation*, 87, 1235-41. doi:10.1016/j.apmr.2006.05.022.
- Hoch, M.C., & Mckeen, P.O. (2014). Peroneal reaction time after ankle sprain: A systematic review and meta-analysis. *Medicine Science*, 46,546-56. doi:10.1249/MSS.0b013e3182a6a93b.
- Hoch, M.C., Gaven, S.L., & Weinhandl, J.T. (2016) Kinematic predictors of star excursion balance test performance in individuals with chronic ankle instability. *Clinical Biomechanics*, 35, 37-41. doi: 10.1016/j.clinbiomech.2016.04.008
- Ko Rae, K., Lee, H., Lee, W.Y., & Sung, K.S. (2018). Ankle strength is not strongly associated with postural stability in patients awaiting surgery for chronic lateral ankle instability. *Knee Surgery, Knee Surgery, Sports Traumatology, Arthroscopy*, 1-8. doi:10.1007/s00167-018-4960-0.

- Kunugi, S., Masunari, A., Koumura, T., & Fujimoto, A. (2018). Altered lower limb kinematics and muscle activities in soccer players with chronic ankle instability. *Physical Therapy in Sport*, 34, 28-35. doi:10.1016/j.ptsp.2018.08.003.
- Lima, Y.L., Ferreira, V.M.L.M., de Paula Lima, P.O., Bezerra, M.A., de Oliveira, R.R., & Almeida, G.P.L. (2018). The association of ankle dorsiflexion and dynamic knee valgus: A systematic review and meta-analysis. *Physical Therapy in Sport*, 29, 61-9. doi:10.1016/j.ptsp.2017.07.003.
- Lorenzo-Sánchez-Aguilera, C., Rodríguez-Sanz, D., Gallego-Izquierdo, T., Lázaro-Navas, I., Plaza-Rodríguez, J., Navarro-Santana, M., et al. (2019). Neuromuscular Mechanosensitivity in Subjects with Chronic Ankle Sprain : A Cross-Sectional Study. *Pain Medicine*, 0, 1-8. doi:10.1093/pm/pny299.
- Mason-Mackay, A.R., Whatman, C., & Reid, D. (2017). The effect of reduced ankle dorsiflexion on lower extremity mechanics during landing: A systematic review. *Journal of Science and Medicine in Sport*, 20, 451-8. doi:10.1016/j.jsams.2015.06.006.
- Mitsiokapa, E., Mavrogenis, A.F., & Drakopoulos, D. (2017). Peroneal nerve palsy after ankle sprain : an update. *European Journal of Orthopaedic Surgery & Traumatology*, 27, 53-60. doi:10.1007/s00590-016-1845-0.
- Mukaka, M.M. (2012). Statistics Corner: A guide to appropriate use of Correlation coefficient in medical research. *Malawi Medical Journal*, 24, 69-71.
- Murphy, D.F., Connolly, D.A.J., & Beynnon, B.D. (2003). Risk factors for lower extremity injury: a review of the literature. *British Journal of Sports Medicine*, 37, 13-29. doi: 10.1136/bjism.37.1.13

- Nitz, A.J., Dobner, J.J., & Kersey, D. (1984). Nerve injury and Grades II and III ankle sprain. *The American Journal of Sports Medicine*, 13, 177-82. doi: 0.1177/036354658501300306
- Noya Salces, J.N., Gómez-Carmona, P.M., Gracia-Marco, L., Moliner-Urdiales, D., & Sillero-Quintana, M. (2014). Epidemiology of injuries in First Division Spanish football. *Journal of Sports Sciences*, 32, 1263–70. doi:10.1080/02640414.2014.884720.
- Noya Salces, J., & Silletto, M. (2012)a. Incidencia lesional en el fútbol profesional español a lo largo de una temporada : días de baja por lesión. *Apunts Medicina de l'Esport*, 47, 115-23. doi:10.1016/j.apunts.2011.10.001.
- Noya Salces, J., & Sillero, M. (2012)b. Epidemiology of injuries in professional football in Spain during the 2008-2009 season. *Archivos de Medicina del Deporte*, XXIX, 750–66.
- Piva, S.R., Fitzgerald, K., Irrgang, J.J., Jones, S., Hando, B.R., Browder ,D.A., et al. (2006). Reliability of measures of impairments associated with patellofemoral pain syndrome. *BMC Musculoskeletal Disorders*, 7, 1-13. doi:10.1186/1471-2474-7-33.
- Plaza-Manzano, G., Vergara-Vila, M., Val-Otero, S., Rivera-Prieto, C., Pecos-Martin, D., Gallego-Izquierdo, T., et al. (2016). Manual therapy in joint and nerve structures combined with exercises in the treatment of recurrent ankle sprains : A randomized, controlled trial. *Manual Therapy*, 26, 141-9. doi:10.1016/j.math.2016.08.006.

- Rabin, A., & Kozol, Z. (2010). Measures of Range of Motion and Strength Among Healthy Women With Differing Quality of Lower Extremity Movement During the Lateral Step-Down Test. *Journal of Orthopaedic & Sports Physical Therapy*, 40, 792-800. doi:10.2519/jospt.2010.3424.
- Rabin, A., Kozol, Z., Moran, U., Efergan, A., Geffen, Y., & Finestone, A.S. (2014). Factors Associated With Visually Assessed Quality of Movement During a Lateral Step-down Test Among Individuals With Patellofemoral Pain. *Journal of Orthopaedic & Sports Physical Therapy*, 44,937-46. doi:10.2519/jospt.2014.5507.
- Ramiro-González, M.D., Cano-de-la-Cuerda, R., De-la-Llave-Rincón, A., Miangolarra-Page, J.C., Zarzoso-Sánchez, R.A., & Fernández-de-las-Peñas, C. (2012). Deep tissue hypersensitivity to pressure pain in individuals with unilateral acute inversion. *Pain Medicine*,13,361-7. doi: 10.1111/j.1526-4637.2011.01302.x
- Rogers, S.A., Hassmén, P., Hunter, A., Alcock, A., Crewe, S.T., Strauts, J.A., et al. (2018). The Validity and Reliability of the MyJump2 Application to Assess Vertical Jumps in Trained Junior Athletes. *Measurement in Physical Education and Exercise Science*, 00, 1-9. doi:10.1080/1091367X.2018.1517088.
- Romero-Franco, N., Martínez-López, E.J., Hita-Contreras, F., Lomas-Vega, R., & Martínez-Amat, A (2014). Short-term effects of anaerobic lactic exercise on knee proprioception of track and field Athletes. *Isokinetics and Exercise Science* 22, 205-210. doi: 0.3233/IES-140540
- Romero-Franco, N., Montaña-Munuera, J., & Jiménez-Reyes, P. (2016). Validity and Reliability of a Digital Inclinator to Assess Knee Joint Position Sense in a Closed Kinetic Chain. *Journal of Sport Rehabilitation*, 24, 1-16. doi:10.1123/ijsp.2017-0214.

- Shiravi, Z., Shadmehr, A., Moghadam, S.T., & Moghadam, B.A. (2017). Comparison of dynamic postural stability scores between athletes with and without chronic ankle instability during lateral jump landing. *Muscles Ligaments Tendons J*, 7, 119-24. doi: 10.11138/mltj/2017.7.1.119
- Sullivan, G.M., & Feinn, R. (2012). Using effect size-or why the P value is not enough. *The Journal of Graduate Medical Education*, 4, 279-82. doi: 10.4300/JGME-D-12-00156.1
- Theisen, A., & Day, J. (2019). Chronic ankle instability leads to lower extremity kinematic changes during landing tasks : A Systematic Review. *International Journal of Exercise Science*, 12, 24-33.
- van Seters, C., van Rijn, R.M., van Middelkoop, M., & Stubbe, J.H. (2017). Risk Factors for Lower-Extremity Injuries Among Contemporary Dance Students. *Clinical Journal of Sport Medicine*, 0,1-7. doi: 10.1097/JSM.0000000000000533
- von Elm, E., Altman, D.G., Egger, M., Pocock, S.J., Gøtzsche, P.C., & Vandenbroucke, J.P. (2014). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement : Guidelines for reporting observational studies. *International Journal of Surgery*, 12, 1495-9. doi:10.1016/j.ijsu.2014.07.013.
- Vuurberg, G., Hoorntje, A., Wink, L.M., van der Doelen, B.F.W., van den Bekerom, M.P., Dekker, R. et al (2018). Diagnosis, treatment and prevention of ankle sprains: update of an evidence-based clinical guideline. *British Journal of Sports Medicine* 52, 956. doi: 10.1136/bjsports-2017-098106.
- Waldén, M., Hagglund, M., & Ekstrand, J. (2005). UEFA Champions League study: a prospective study of injuries in professional football during the 2001–

2002 season. *British Journal of Sports Medicine*, 39, 542–6.
doi:10.1136/bjism.2004.014571.

- Waterman, B.R., Owens, B.D., Davey, S., Zacchilli, M.A. & Belmont, P.J. (2010). The Epidemiology of Ankle Sprains in the United States. *The Journal of Bone and Joint surgery*, 92, 2279-84. doi:10.2106/JBJS.I.01537.
- Walsh, J., Kenneally, M., & Hall, T (2010). Pressure pain thresholds of the sciatic, tibial and common peroneal nerves in asymptomatic subjects. *Irish Society of Chartered Physiotherapists*, 31, 23-7. doi:https://psycnet.apa.org/doi/10.1037/0022-006X.62.2.281.
- Woolf, C.J. (2011) Central sensitization: Implications for the diagnosis and treatment of pain. *Pain* 152, S2-15. doi: 10.1016/j.pain.2010.09.030.





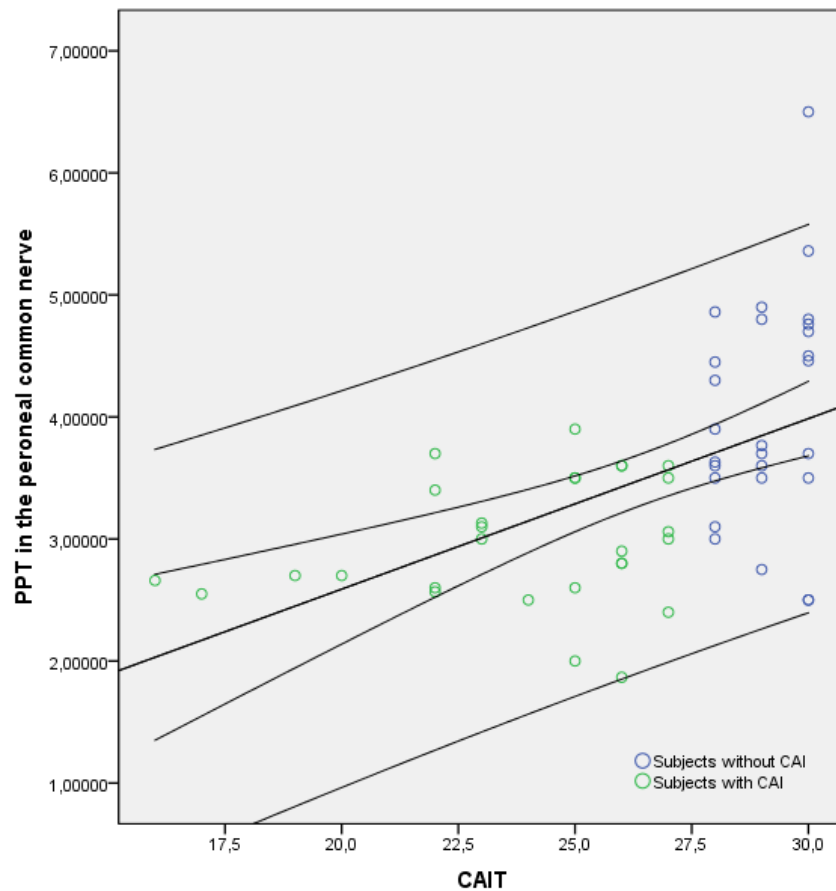
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Figure 3: Correlation between PPT in the common peroneal nerve and CAIT score



The solid line reflects the lineal regression, dashed line shows the 95%CI% of the linear regression model and dotted line expressed the 95%CI% of the participants of the study. The blue points indicate the subjects in the control groups and green triangle the subjects in the cases groups.

CAI: Chronic Ankle Instability; PPT: Pressure Pain threshold; PN: Peroneal Nerve.

Table 1: Clinical and Demographic Data of Soccer Players with and without Chronic Ankle Instability (CAI)

Variable		Soccer players with CAI (n=28)	Soccer players without CAI (n=27)	P value
Age (years)		25 ± 4	24 ± 4	0.388
Weight (kg)		73.5 ± 7.8	72.0 ± 8.7	0.615
Height (m)		176.5 ± 7.0	176.0 ± 7.0	0.577
BMI kg/m ²		23.5 ± 1.1	23.2 ± 1.0	0.489
Experience (years)		17.5 ± 6.5	18.0 ± 5.0	0.732
CAIT		24 ± 3	29 ± 1	0.001
Dominant Extremity	Right	17	17	
	Left	11	10	
Symptomatic Extremity	Right	20	-	
	Left	8	-	
Player's Position	Goalkeeper	3	3	
	Full-back	3	4	
	Center	4	3	
	Midfielders	8	8	
	Wingers	3	3	
	Withdrawn striker	3	2	
	Center - Forwards	4	4	

Data are expressed as means ± standard deviation

CAIT: Cumberland Ankle Instability Tool

Table 2: Differences in Pressure Pain Thresholds (PPT) and Physical Performance Outcomes between Soccer Players with and without Chronic Ankle Instability (CAI)

Variable	Soccer players with CAI (n=28)	Soccer players without CAI (n=27)	Between-groups difference	Size effect
PPT TN (Kg/cm ²)	3.5 ± 0.8	3.9 ± 1.0	-0.4 (-1.4; 0.6)	0.45
PPT PN (Kg/cm ²) *	3.0 ± 0.5	4.0 ± 0.9	-1.0 (-1.5; -0.5)	1.1
AAE JPS	4.6 ± 2.8	4.4 ± 2.9	0.2 (-1.6; 2.0)	0.10
RAE JPS	1.45 ± 4.8	-0.55 ± 5.1	2.0 (-0.9; 4.9)	0.36
LSDT	2.1 ± 0.6	2.0 ± 0.7	0.1 (-0.2; 0.4)	0.14
Jump Height (cm)	35.4 ± 5.0	36.9 ± 5.5	-1.5 (-4.4; 1.4)	0.27
Jump Time (ms)	536.0 ± 37.7	546.7 ± 43.0	-10.7 (-32.5; 11.1)	0.25
Jump Strength (N)	1527.5 ± 193.5	1584.5 ± 238.0	-57.0 (-174.2; 60.2)	0.27
Jump Speed (m/s)	1.3 ± 0.1	1.35 ± 0.1	0.05 (-0.02; 0.12)	0.25
Jump Power (W)	2090.0 ± 401.0	2054.0 ± 338.0	36.0 (-165.3; 237.3)	0.10

Abbreviations: PPT: Pressure Pain Threshold; TN: Tibial Nerve; PN: Common Peroneal Nerve; AAE: Absolute Angular Error; RAE: Relative Angular Error; JPS: Joint Position Sense; LSDT: Lateral Step-Down Test

Data are expressed as means ± standard deviations for group scores and means (95% confidence interval) for between-groups differences

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Pressure Pain Sensitivity over Nerve Trunk Areas and Physical Performance in Amateur Soccer Players with and without Chronic Ankle Instability

Conflict of Interest File

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Pressure Pain Sensitivity over Nerve Trunk Areas and Physical Performance in Amateur Soccer Players with and without Chronic Ankle Instability

Ethical Approval

All participants read and signed the informed consent form before their inclusion. The local Ethic Committee of the University of Alcalá de Henares (CEID-HU-2018-04) approved the study design.