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ABSTRACT

HOCH, M. C., and P. O. MCKEON. Peroneal Reaction Time after Ankle Sprain: A Systematic Review and Meta-analysis. *Med. Sci. Sports Exerc.*, Vol. 46, No. 3, pp. 546–556, 2014. **Background**: Many studies have examined the temporal response of the peroneal muscles to sudden inversion perturbation in patients with a previous ankle sprain. The purpose of this systematic review with meta-analysis was to synthesize the evidence and determine whether peroneal reaction time (PRT) impairments are present after ankle sprain. **Methods**: An electronic search was conducted using PubMed Central and EBSCOhost (1965–January 2013). Articles were included if they 1) examined the PRT to sudden inversion perturbation in patients with a history of ankle sprain using a mechanical tilt platform, 2) made comparisons with a control group or contralateral limb with no history of ankle sprain, and 3) provided data for the calculation of effect sizes (ES). In addition to examining the overall effect of sustaining an ankle sprain on PRT, the effects of study design and subject characteristics on PRT were evaluated. Bias-corrected Hedges *g* ES and 95% confidence intervals (CI) were calculated to make comparisons across studies. **Results**: A total of 23 studies met the inclusion criteria. The overall ES was 0.67 (95% CI = 0.37–0.95, $P < 0.001$), indicating that a previous ankle sprain, regardless of study design or subject characteristics, resulted in moderate-to-strong PRT deficits. Further analyses determined studies with patients classified as having chronic ankle instability demonstrated large magnitude PRT deficits in between groups (ES = 0.72, 95% CI = 0.29–1.14, $P = 0.001$) and side-to-side (ES = 1.24, 95% CI = 0.70–1.79, $P < 0.001$) comparisons, whereas patients with all other ankle sprain histories demonstrated weak PRT alterations in between groups (ES = −0.21, 95% CI = −1.01 to 0.59, $P = 0.61$) and side-to-side (ES = 0.21, 95% CI = −0.19 to 0.60, $P = 0.31$) comparisons. **Conclusions**: Overall, this meta-analysis determined that individuals with a previous ankle sprain exhibit delayed PRT. Further analyses determined that these deficits are more evident in patients with chronic ankle instability when compared with the contralateral uninvolved limb or a healthy control group. **Key Words:** CHRONIC ANKLE INSTABILITY, NEUROMUSCULAR CONTROL, ELECTROMYOGRAPHY, SENSORIMOTOR SYSTEM, LATENCY

APPLIED SCIENCES

Lateral ankle sprains are among the most frequently occurring injuries in sports-related activity (23), the military (2), and hospital emergency rooms (29). It is estimated that 23,000 ankle sprains occur daily in the United States with an estimated 4.4 billion dollars spent annually on treatment for these injuries (29,47). In addition to the frequency of acute ankle sprains, approximately 70% of individuals who sustain an acute ankle sprain will experience additional sprains, recurrent joint instability, residual symptoms, and decreases in functional capacity for up to 2 yr after the initial injury (19,21,27). These negative sequelae are associated with a health condition known as chronic ankle instability (CAI) and can lead to the development of posttraumatic ankle osteoarthritis (16,50). Understanding the clinical consequences of ankle sprains is imperative for developing successful rehabilitation strategies that reduce residual symptoms and restore functional capacity.

Several alterations in sensorimotor system function have been investigated after acute ankle sprain as possible contributing factors for recurrent ankle sprains and CAI (19). One such aspect is the ability of the peroneal muscles to create a dynamic defense mechanism to protect the ankle during sudden inversion perturbation. Previous investigators (17,32) have referred to this phenomenon using a variety of terms including peroneal reaction time (PRT), peroneal onset time, or peroneal latency. For the purposes of this systematic review, the temporal reaction of the peroneal muscles to an inversion perturbation will be referred to as PRT and defined as the time between ankle perturbation and the onset of peroneal muscle activity. This aspect of function is typically collected by measuring the timing of peroneal activation in response to a sudden inversion perturbation using electromyography and a trapdoor mechanism.

Measuring PRT after sudden inversion perturbation examines closed-loop neuromuscular control (17). This mechanism may be altered as a result of deleterious changes in the transmission of afferent input or in the ability of the central nervous system to generate an appropriate motor response (17). Delayed PRT has been examined prospectively as a risk

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factor for ankle sprain; however, no studies have identified any significant association (4,22,53,54). This suggests that delayed PRT may manifest as a consequence of trauma after lateral ankle sprain. PRT has been assessed in individuals with a variety of different ankle sprain histories (ASH), ranging from an initial acute sprain to CAI (17,32). Also, several different inversion tilt platform protocols have been used to create inversion perturbations along with several different methods of determining the activation thresholds for deriving PRT, which have confounded the ability to draw clear interpretations from the literature. These inconsistencies make it difficult to determine whether this aspect of sensorimotor system function should be a clinical consideration during the rehabilitation of patients who have sustained an ankle sprain.

Previous systematic reviews with meta-analysis (38,40) have been performed on this area of research. Munn et al. (40) concluded that PRT was unaffected in those with CAI, whereas Menacho et al. (38) determined that delays in PRT were present in studies which examined a range of ASH. In the case of both systematic reviews, the number of included studies could be substantially increased because additional evidence has become available, which may ultimately change the overall conclusions that can be derived from this body of research. Therefore, providing a comprehensive systematic review with meta-analysis, which critically appraises the research literature, may provide a better indication if PRT alterations are present in those with a history of ankle sprain(s). Therefore, the purpose of this systematic review with meta-analysis was to determine whether PRT impairments are present in individuals with a history of lateral ankle sprain. Specific variables that were evaluated included the type of 1) study comparisons and 2) subject characteristics of the included studies.

METHODS

Search Strategy

In January 2013, we performed a computerized search of EBSCOhost (MEDLINE, Sports Discus, and CINAHL) and PubMed Central entries from January 1, 1965, to January 1, 2013, to identify studies that examined PRT in individuals with a history of ankle sprain (Table 1). Search strategies were limited to studies that were written in English, involved humans, and were reported in peer-reviewed journals. Relevant articles were also identified by cross-referencing the citation lists of the articles identified in the electronic search.

TABLE 1. Search strategy.

Step	Search Terms	Boolean Operator	EBSCOhost	PubMed
1	Chronic Recurrent History Frequent Multiple Functional Lateral	OR	219,263	1,926,841
2	Ankle		12,596	29,292
3	Injury Sprain Strain Instability Insufficiency	OR	88,158	707,631
4	1, 2, 3	AND	2468	4528
5	Muscle		57,862	346,140
6	Reaction time Onset Latency	OR	29,491	343,313
7	Inversion Supination Perturbation Trapdoor	OR	3135	22,333
8	5, 6, 7	AND	220	500
9	4, 8	AND	57	37
Duplicates			19	29

Criteria for Selecting Studies

Only studies assessing PRT in participants using a mechanical tilt (trapdoor) platform to induce a sudden ankle inversion perturbation in individuals with a history of ankle sprain were included. We chose to investigate studies using mechanical tilt platforms, which induced an inversion perturbation during quiet standing or walking because we were most interested in examining the PRT to "sudden" or "unexpected" perturbations, and this form of testing is most commonly described in the literature. To be included, a study had to address the purpose of this systematic review and provide adequate results for calculation of effect size (ES). In cases where median and range were presented, they were converted to estimate means and standard deviations for the purpose of meta-analysis (25).

Assessment of Methodologic Quality

Included studies were evaluated using a quality index for nonrandomized studies (11). This quality index created by Downs and Black (11) encompasses components of the Strengthening the Reporting of Observational Studies in Epidemiology statement and has demonstrated high internal consistency and interrater reliability. An adapted, 16-question version of the original index described by Munn et al. (40) was used to assess methodologic quality in this systematic review. On the basis of the recommendations of Munn et al. (40), studies meeting <60% criteria were considered low quality, 60%–74.9% moderate quality, and >75% high quality. Each author independently performed the quality assessment for each of the included studies. Consensus regarding the quality index score for each study was agreed upon by both authors. In addition, a sensitivity analysis using the one-study-removed method (5) for the effect of study design quality was performed. This analysis was performed to determine whether the results of one particular study substantially influenced the cumulative effect.

Data Extraction and Statistical Analysis

Study variables. Study comparison refers to the comparison design within each study. The two levels coded for

this variable included 1) side-to-side comparison (1,3,10,12, 24,26,28,30,33–35,39,41,42,44) and 2) between-group comparison (3,6,13,14,18,24,26,28,31,35,39,46,48,49). Side-to-side comparisons were studies that included the uninvolved limb as the control limb for comparison. Group comparisons used a healthy control group to compare subjects with a history of injury. It was not possible to make between-group and side-to-side comparisons in all included studies.

Subject characteristics refer to the type of subjects included in the study based on the available inclusion and exclusion criteria. The two levels coded for this variable included 1) CAI (1,10,13,18,24,30,31,34,35,39,44,48,49) and 2) ASH (3,6,12,14,26,28,33,41,42,46). Studies which labeled subjects with chronic, mechanical, or functional instability or provided evidence of repeated ankle sprains were classified collectively as CAI. Studies with all other histories of ankle sprain, including acute sprains or studies with nondescript subject information, were classified as ASH.

These variables were also combined to examine possible interactions between study comparison and subject characteristics. The four levels coded for this analysis included 1) CAI between-group comparison (13,18,24,31,35,39,48,49), 2) CAI side-to-side comparison (1,10,24,30,34,35,39,44), 3) ASH between-group comparison (3,6,14,26,28,46), and 4) ASH side-to-side comparison (3,12,26,28,33,41,42). The criteria for coding studies in this analysis were a combination of the previously described criteria for each variable.

Meta-analysis. Separate meta-analyses were performed on each of the study variables. For each meta-analysis, a random-effects model was used. Individual measures across the multiple variables were pooled from the included studies using a bias-corrected Hedges *g* ES and 95% confidence interval (CI) to examine the magnitude and precision of the difference from side-to-side or between-group comparisons (5). The calculated Hedges *g* ES is a unitless measure and represents an effect that exists on a parametric distribution (5). A positive ES indicated delayed PRT in pathologic subjects or limbs as compared with controls or the uninvolved limb. For all studies, pooled standard deviations associated with the involved limb or either the uninvolved limb or the healthy control group was used in the calculation of ES. In studies that assessed multiple different measures associated with the temporal response of the peroneal muscles to inversion perturbation, we included the measure that was most closely associated with our definition of PRT. When applicable, ES was calculated for both peroneus longus and brevis muscles. In studies where multiple comparisons were made, each comparison was treated independently within the statistical analyses. ES were interpreted as *weak* if they were less than 0.40, *moderate* if between 0.41 and 0.69, or *strong* if greater than 0.70 (8,36). ES and CI were interpreted as significant if the P value of the effect was <0.05. All statistical analyses were completed using a comprehensive meta-analysis version 2.2.034 (Biostatic, Inc., Englewood, NJ). In addition to statistical comparisons, a qualitative assessment of subgroup ES and CI was performed for each variable by examining the differences in ES estimates between groups or if CI crossed zero to further describe trends in the pooled data.

Assessment of Publication Bias

To assess the robustness of the observed overall effects of moderators on PRT, we used Orwin's fail-safe N test. The fail-safe N test determines the number of studies with trivial ES that would be required to counter the pooled ES of the included studies. To assess the likelihood of publication bias, we generated a funnel plot of all included comparisons. In addition, the trim-and-fill method of imputing potentially missing studies was used for an additional assessment of publication bias.

Level of Evidence

The quality, the quantity, and the consistency of the included studies were assessed using the Oxford Centre for Evidence-Based Medicine–Levels of Evidence (CEBM). This taxonomy was used to determine the quality of the included studies and generate the strength of recommendation.

RESULTS

Evidence synthesis. The computerized literature search using all databases yielded 94 articles. After the removal of 48 duplicate results across all databases, the final search resulted in 46 articles to be reviewed. Seven additional articles were identified through a hand search of cross-listed articles. The literature search resulted in 23 relevant studies (1,3,6,10,12–14,18,24,26,28,30,31,33–35,39,41,42,44,46, 48,49). Three of the articles (1,6,46) were included after hand measuring means and standard deviations from figures, and one study (44) was included after additional information was provided by the authors. A complete list of search terms, Boolean operators, and results are presented in Table 1. A flow diagram of the study selection process is presented in Figure 1. Reasons for rejection included irrelevant methods, outcome methods, or subjects or inadequate data reporting. With the exception of Hopkins et al. (24), all studies used a bipedal stance trapdoor platform with similar testing procedures to create sudden inversion perturbations. Hopkins et al. (24) used a trapdoor platform that created a sudden inversion perturbation while walking.

The mean quality index score for the included studies was 60.60% (range = 37.50%–81.25%), indicating that the average level of study quality was moderate. Of the 23 included studies, 11 were classified as low quality, 7 were classified as moderate quality, and 5 were classified as high quality. When classifying studies as low, moderate, or high quality based on their respective quality index score, an analysis of the individual influences of methodologic-quality determined that the quality of study design did not influence the overall result (Q_2 = 2.20, P = 0.33); however, it should be noted that several low quality CAI studies were associated with large ES. Most studies were retrospective cross-sectional or case–control

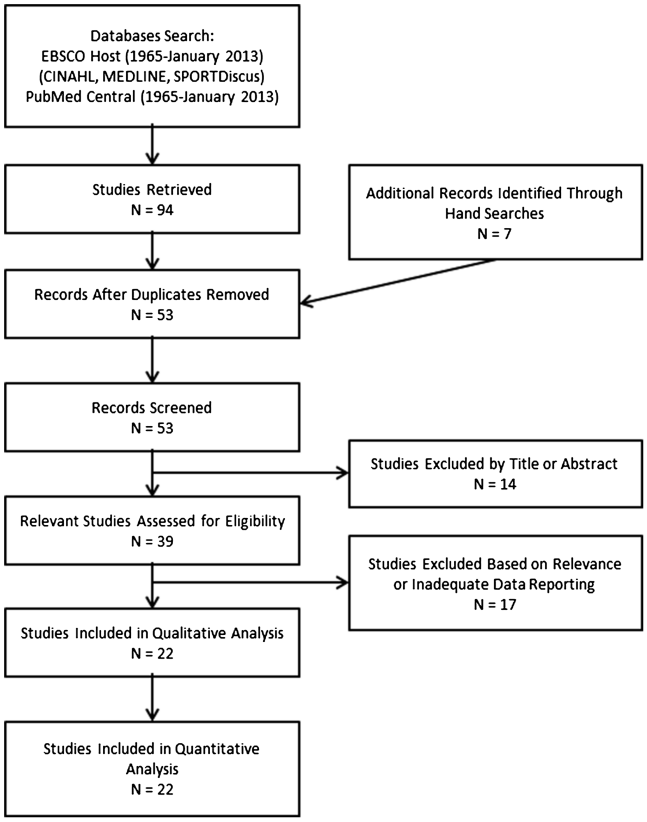

FIGURE 1—Flow chart illustrating the study selection process.

designs, indicating level 3 evidence based on the Oxford CEBM. A breakdown of each study is presented in Table 2.

Overall summary effect. Across the multiple studies and the two variables examined, the overall effect was 0.67 (95% CI = 0.37–0.95, $P < 0.001$), indicating that having a previous ankle sprain, regardless of a side-to-side or between-group comparison, demonstrated a moderate-to-strong deficit in PRT. The individual ES and the cumulative effect are presented in Figure 2 and Table 3.

Summary effects of individual study variables. No difference was detected between the two levels of study comparisons ($Q_1 = 3.72$, $P = 0.07$). On the basis of these findings, it can be concluded that either type of comparison may be useful in detecting PRT deficits after ankle sprain. However, from a qualitative perspective, the effect of side-to-side comparisons was strong, with a CI that did not encompass zero (ES = 0.88, 95% CI = 0.49–1.26, $P < 0.001$), whereas the effect of the between-group comparisons was weak with a CI which narrowly encompassed zero (ES = 0.36, 95% CI = −0.05 to 0.78, $P = 0.08$). Therefore, side-to-side comparisons may be a stronger design for detecting PRT deficits.

A significant difference was detected between the two levels of subject characteristics ($Q_1 = 13.78$, $P < 0.001$). Studies labeled as ASH demonstrated a weak effect with a CI which encompassed zero (ES = 0.06, 95% CI = −0.31 to 0.43, $P = 0.77$), whereas studies labeled as CAI demonstrated a strong effect with a CI which did not encompass zero (ES = 1.04, 95% CI = 0.68–1.41, $P < 0.001$). Therefore, the magnitude and consistency of PRT deficits are greater in studies with CAI compared with those included with ASH. For subject characteristics, significant differences were detected between the 4 levels of study comparison ($Q_3 = 13.24$, $P = 0.004$). For those studies with CAI subjects, between-group (ES = 0.72, 95% CI = 0.29–1.14, $P = 0.001$) and side-to-side comparisons (ES = 1.24, 95% CI = 0.70–1.79, $P < 0.001$) demonstrated strong effects with CI, which did not encompassed zero. Studies labeled as ASH between-group (ES = −0.21, 95% CI = −1.01 to 0.59, $P = 0.61$) and side-to-side comparison (ES = 0.21, 95% CI = −0.19 to 0.60, $P = 0.31$) demonstrated weak effects with CI which encompassed zero. Overall, CAI studies demonstrated large magnitude and consistent PRT deficits in both types of study comparisons, whereas ASH studies demonstrated weak, inconsistent PRT alterations in both types of study comparisons.

Publication bias. Publication bias was assessed with a funnel plot using Duval and Tweedie's trim-and-fill method (Fig. 3). On the basis of the relative symmetry and distribution of the studies, it is unlikely that publication bias played an important role in the results. This is supported by the trim-and-fill analysis, which exhibited agreement between the observed and the estimated overall summary effect. In addition, the results of the Orwin fail-safe N test indicated that a range of 142–324 additional studies with weak ES (Hedges g ranging from 0.05 to 0.10) would be needed to nullify the overall summary effect.

Sensitivity analysis. The results of the one-study-removed method indicated that ES remained moderate to strong and ranged from 0.61 to 0.72. The lowest lower bound of the 95% CI was 0.34, and the greatest upper bound of the 95% CI was 1.00. All P values were $P < 0.001$, indicating that there was no single comparison that substantially influenced the overall summary effect.

DISCUSSION

The main findings of the meta-analysis revealed that people who have sustained an ankle sprain exhibit delayed PRT to inversion perturbation when compared with an uninvolved limb or a healthy control group. However, secondary analyses determined PRT is significantly delayed in subjects classified with CAI while it was not significantly affected in studies with other ASH regardless of between-group or within-group comparisons. Therefore, the subject characteristics and study design are important considerations for examining PRT in individuals who have sustained a previous ankle sprain.

The results of this study contradict the results of the meta-analysis performed by Munn et al. (40), which concluded that PRT was unaffected in those with CAI when compared with a control group or the uninvolved limb. Although Munn et al. (40) did identify large pooled estimates of mean difference suggesting PRT was delayed in those with CAI, the CI of the pooled estimates crossed zero and the random-effects meta-analyses yielded nonsignificant P values, which ultimately led to the conclusion that this aspect of sensorimotor system

TABLE 2. Characteristics for each of the included studies.

Study	Inclusion Criteria	Involved Subjects	Comparison Subjects	Degrees of Perturbation	Dependent Variables	Study Design	Quality Index Score (%)
Chronic ankle instability studies							
Han and Ricard (18)	One or more ankle sprains resulting in pain during weight bearing for at least 1 day in the past 12 months and two or more sprains that resulted in pain during weight bearing for at least 1 d in the past 36 months. No pain or swelling at time of study	20	20	37° inversion	PL latency	Randomized controlled trial	68.75
Donahue (10)	Unilateral CAI associated with an acute ankle sprain in previous 3–10 months	18	–	35° inversion	PL latency	Cross sectional	68.75
Hopkins et al. (24) [a]	Unilateral FAI determined through the Functional Ankle Instability Questionnaire and Ankle Instability Instrument	21	21	30° inversion	PL latency	Case–control	68.75
Eechaute et al. (13)	CAI defined as a history of traumatic lateral ankle sprain interfering with physical activity for ≥3 wk requiring ≥2 medical consultations, repetitive lateral ankle sprains for at least 6 months, presence of giving way, and decreased physical activity	40	30	50° inversion	PL latency	Cross sectional	81.25
Mitchell et al. (39)	FAI defined as a history of at least two ankle sprains and at least three residual symptoms of ankle instability	19	19	3° inversion, 20° PF	PL reaction time (1), PB reaction time (2)	Case–control	75.00
Akhbari et al. (1)	FAI defined as at least one significant ankle sprain, no history of ankle fracture, and at least one repeated ankle sprain or episodes of "giving way"	15	–	10°, 20°, 30° inversion	PL onset (1, 2, 3)	Cross sectional	68.75
Vaes et al. (48)	History of ankle sprain followed by pain, swelling, and inability to participate in recreational activity for 3 wk; repetitive ankle sprains and insecure feeling of the ankle "giving way"	40 (48 ankles)	41 (46 ankles)	15° inversion, 40° PF	PL latency	Cross sectional	62.50
Vaes et al. (49)	At least one ankle sprain requiring immobilization, with reported pain, swelling, stiffness for 3 wk; the feeling of instability or complaints of repetitive sprains	8 (16 ankles)	7 (14 ankles)	15° inversion, 40° PF	PL latency	Cross sectional	81.25
Rosenbaum et al. (44)	History of ankle inversion trauma and feeling of ankle instability. Subjects with mechanical instability were determined through radiographic imaging and anterior drawer test	30 MI, 35 FI	–	30° inversion	FAI PL latency (1), FAI PB latency (2), MAI PL latency (3), MAI PB latency (4)	Cross sectional	68.75
Khin-Myo-Hla et al. (31)	Patients with three of more episodes of ankle sprain and complained of feeling that the ankle was giving way	18 (21 ankles)	8 (9 ankles)	30° inversion	PB reaction time	Cross sectional	50.00
Löfvenberg et al. (35)	Chronic lateral instability for at least 12 months	13 (15 ankles)	15	30° inversion	PL reaction time	Cross sectional	37.50
Karlsson and Andreasson (30)	Unilateral CAI for at least 6 months caused by supination trauma resulting in reduced sports activity	20	–	30° inversion	Peroneal reaction time	Repeated measures	56.25
Konradsen and Ravn (34)	Functional instability defined by subjects who complained of frequent sprains and/or sensations of the ankle giving way	15	–	30° inversion	PL reaction time, PB reaction time	Cross sectional	37.50
Ash studies							
Shima et al. (46)	Ankle sprain requiring medical treatment. Hypermobility assessed thought stress radiograph with talar tilt.	10 (16 ankles)	8 (10 ankles)	25° inversion	Peroneal latency injured—hypermobile (1), injured—normal (2)	Cross sectional	56.25
Osborne et al. (42)	A history of nonrehabilitated, unilateral, inversion ankle sprain sustained between 6 and 18 months before study	9	–	20° inversion	PL onset latency	Repeated measures	81.25
Fernandes et al. (14)	Athletes with a history of ankle sprain and/or subsequent ankle instability	24 (43 ankles)	10 (25 ankles)	10, 15, 20° inversion	PL latency	Cross sectional	68.75

(Continued on next page)

TABLE 2. *(Continued)*

Study	Inclusion Criteria	Involved Subjects	Comparison Subjects	Degrees of Perturbation	Dependent Variables	Study Design	Quality Index Score (%)
Konradsen et al. (33)	Grade II or grade III acute ankle inversion sprains marked swelling, inability to bear weight, or the presence of instability	44	–	30° inversion	PL reaction time week 3 (1), week 6 (2), and week 12 (3)	Repeated measures	81.25
Ebig et al. (12)	History of unilateral inversion ankle sprain requiring protective weight bearing and/or immobilization to the injured ankle	13	–	20° inversion	Peroneal response time	Cross sectional	56.25
Beckman and Buchanan (3)	History of at least one inversion ankle sprain in the last 2 yr and hypermobility defined by a minimum of 10 of excessive right ankle/foot inversion (hypermobile)	10	10	30° inversion	Peroneal onset latency	Case–control	37.50
Johnson and Johnson (28)	Recurrent ankle sprains diagnosed as second degree or greater with most recent sprain no sooner than 3 months prior to data collection	7	11	35° inversion	Peroneal latency	Cross sectional	56.25
Brunt et al. (6)	Grade II ankle sprain in previous year diagnosed by examination and x-ray	5	10	10.5° inversion	PL response latency	Cross-sectional	37.50
Isakov et al. (26)	At least one ankle sprain and positive anterior drawer test	11	–	20° inversion	Peroneal latency	Cross sectional	43.75
Nawoczenski et al. (41)	Unilateral inversion ankle sprain within the previous 3–10 months	15	–	35° inversion	PL onset	Cross sectional	50.00

[a] iinversion perturbation was created while walking.
CAI, chronic ankle instability; FAI, functional ankle instability; MAI, mechanical ankle instability; PL, peroneus longus; PB, peroneus brevis; PF, plantarflexion;

function was not affected in those with CAI. However, it should be noted that the *P* values reported by Munn et al. (40) associated with the between-group ($P = 0.10$) and side-to-side ($P = 0.17$) comparisons were trending toward statistical significance and the CI narrowly crossed zero. The meta-analysis

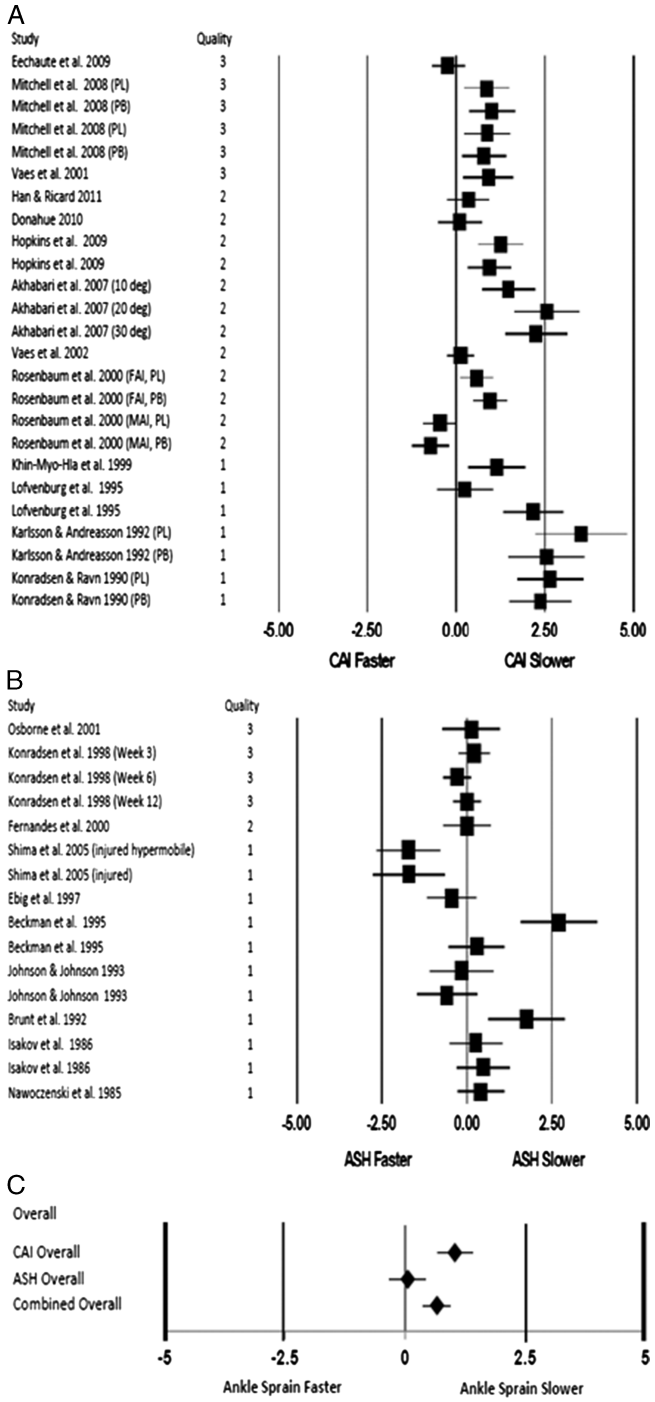

FIGURE 2—Hedges *g* ES and 95% CI for chronic ankle instability (CAI) studies (A), ankle sprain history (ASH) studies (B), and summary measures (C). The quality column represents the quality index score assigned to each study (1 = low, 2 = moderate, 3 = high). Positive ES represent peroneal muscle response deficits in those with a history of ankle sprain. Negative ES represent slower peroneal muscle responses in the control group.

TABLE 3. Characteristics of included comparisons.

Study	Comparison	Hedges *g*	Lower limit	Upper limit	*P*
Chronic ankle instability studies					
Eechaute et al. (13)	Between groups	−0.23	−0.70	0.24	0.33
Mitchell et al. (39)	PL, side to side	0.85	0.21	1.49	0.009
	PB, side to side	1.01	0.36	1.66	0.002
	PL, between groups	0.86	0.22	1.50	0.009
	PB, between groups	0.78	0.15	1.41	0.016
Vaes et al. (49)	Between groups	0.90	0.18	1.62	0.014
Han and Ricard (18)	Between groups	0.34	−0.27	0.95	0.27
Donahue (10)	Side to side	0.09	−0.54	0.72	0.78
Hopkins et al. (24)	Side to side	1.24	0.60	1.88	<0.001
	Between groups	0.92	0.30	1.54	0.003
Akhabari et al. (1)	10°, Side to side	1.47	0.70	2.24	<0.001
	20°, Side to side	2.56	1.64	3.48	<0.001
	30°, Side to side	2.26	1.38	3.14	<0.001
Vaes et al. (48)	Between groups	0.12	−0.28	0.52	0.56
Rosenbaum et al. (44)	FAI, PL, side to side	0.58	0.11	1.05	0.016
	FAI, PB, side to side	0.96	0.47	1.45	<0.001
	MAI, PL, side to side	−0.46	−0.96	0.04	0.07
	MAI, PB, side to side	−0.73	−1.24	−0.22	0.005
Khin Myo et al. (31)	Between groups	1.14	0.35	1.66	0.005
Lofvenburg et al. (35)	Side to side	0.24	−0.55	1.03	0.55
	Between groups	2.17	1.31	3.03	<0.001
Karlsson and Andreasson (30)	PL, side to side	3.53	2.22	4.84	<0.001
	PB, side to side	2.54	1.44	3.64	<0.001
Konradsen and Ravn (34)	PL, side to side	2.65	1.71	3.59	<0.001
	PB, side to side	2.37	1.48	3.26	<0.001
CAI summary effect	All CAI comparisons	1.04	0.68	1.41	<0.001
ASH studies					
Osborne et al. (42)	Side to side	0.13	−0.73	0.99	0.78
Konradsen et al. (33)	3 wk, side to side	0.22	−0.24	0.68	0.35
	6 wk, side to side	−0.28	−0.69	0.13	0.19
	12 wk, side to side	0.00	−0.41	0.41	0.99
Fernandes et al. (14)	Between groups	0.00	−0.71	0.71	0.99
Shima et al. (46)	Injured hypermobile, between groups	−1.72	−2.68	−0.76	<0.001
	Injured, between groups	−1.70	−2.77	−0.63	0.002
Ebig et al. (12)	Side to side	−0.45	−1.19	0.29	0.23
Beckman and Buchanan (3)	Side to side	2.71	1.58	3.84	<0.001
	Between groups	0.29	−0.53	1.12	0.49
Johnson and Johnson (28)	Between groups	−0.15	−1.09	0.79	0.76
	Side to side	−0.59	−1.48	0.30	0.20
Brunt et al. (6)	Between groups	1.75	0.63	2.86	0.002
Isakov et al. (26)	Side to side	0.26	−0.53	1.05	0.52
	Between groups	0.48	−0.31	1.27	0.24
Nawoczenski et al. (41)	Side to side	0.41	−0.28	1.10	0.25
ASH summary effect	All ASH comparisons	0.06	−0.31	0.43	0.77
Overall summary effect	All comparisons	0.67	0.39	0.95	<0.001

FAI, functional ankle instability; MAI, mechanical ankle instability; PL, peroneus longus; PB, peroneus brevis.

in the current study may have generated different results because a greater number of studies examining PRT in those with CAI were included allowing more subjects to be entered into the analysis. As well, Hedges *g* estimates of ES were used as compared with the unstandardized mean difference. The current meta-analysis also examined these deficits using a different search strategy and inclusion criteria. Lastly, we used a different theoretical perspective by initially including all studies which examined PRT in patients with a history of ankle sprain and then created the CAI and the ASH subcomparisons. The combination of these factors likely led to the differing results between studies.

It was determined that those with CAI had delayed PRT to inversion perturbation; however, this was not detected in the studies included in the ASH group. One potential explanation for the lack of consistency in the findings of the ASH group may have been because these studies potentially examined a broader spectrum of patients with diverse histories of ankle sprain. In addition, several of these studies may have contained subjects that would have been considered to have CAI creating a mixed pool of subjects and possibly

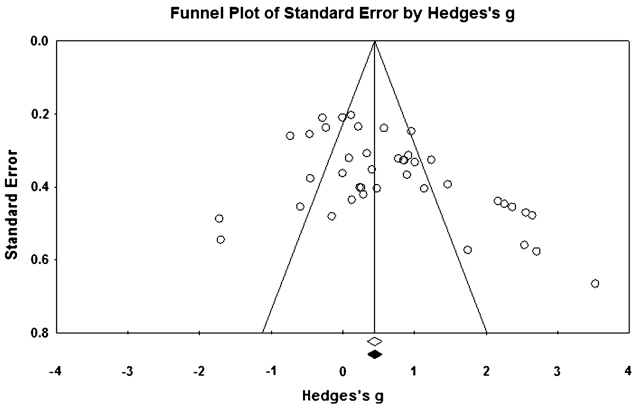

FIGURE 3—Funnel plot analysis for publication bias.

overestimating the ES in certain ASH studies. Because subject characteristics, ASH, and stability status were often unclear or not specified, it was difficult to consistently stratify these studies into groups that may have provided clearer recommendations regarding PRT deficits. Conversely, the inclusion criteria for CAI studies were generally more clearly delineated, which may have facilitated more consistent findings across studies. In most studies, subjects had to report a history of more than one ankle sprain, self-reported episodes of ankle "giving way," and self-reported disability in physical activity or activities of daily living as a result of ankle sprain trauma. These findings suggest that the inclusion criteria used to classify individuals with a history of lateral ankle sprain(s) may create a sensitive dependence on the ability to consistently detect sensorimotor system impairments. This concept is supported by the work of Hiller et al. (20) and Delahunt et al. (9), who stress the importance of reporting subject characteristics for individuals with a history of ankle sprain to draw clearer interpretations of the finding leading to more precise clinical recommendations. Therefore, providing more stringent and detailed information on the inclusion of individuals with other ASH, such as patients with a first-time acute sprain, may elucidate clearer trends in these groups.

This meta-analysis determined that side-to-side comparisons may be more beneficial than between-group comparisons for detecting PRT deficits when CAI and ASH studies were pooled. However, subsequent analyses determined that much of the variability in the between-group comparisons were the result of ASH studies. When examining the combination of study comparison and subject characteristics, it was determined that CAI studies demonstrated strong ES indicative of delayed PRT in both types of study comparison, whereas ASH studies did not demonstrate significant differences in PRT in either type of study comparison. From our results, we cannot determine which study comparison is more effective at identifying PRT deficits in those with CAI because both study designs exhibited strong ES, and the CI were overlapping. Our findings differ from a recent meta-analysis (36), which examined that joint position recognition deficits in those with CAI and determined between-group comparisons were recommended over side-to-side comparisons. Furthermore, another recent meta-analysis (51) determined that postural control deficits were present on the uninvolved limb of individuals with CAI compared with healthy subjects. While it is unclear why PRT side-to-side comparisons yielded large magnitude differences in the CAI group compared with past meta-analyses (36,51), it suggests that PRT may provide a unique neurophysiologic perspective to examine sensorimotor function in those with CAI. Although we do not believe that this aspect of this meta-analysis should support performing side-to-side comparisons over between-group comparisons, we do believe these findings further reinforce the idea that the more clearly defined CAI group elicits deficits more effectively than the ASH group.

Although this study identified delayed PRT in those with CAI, the causal-link between alterations in PRT and CAI have yet to be established because of retrospective study designs and limited evidence regarding concurrent changes in other aspects of sensory or motor function. The current methods of estimating PRT examine the ability of the sensorimotor system to utilize feed-back loops to manage a perturbation. Deficits in this aspect of function permit speculation that PRT alterations could be associated with the ability to detect the perturbation and/or generate the appropriate motor response once the perturbation is detected. This suggests that delayed PRT may be related to decreases in somatosensory system acuity after repetitive damage to structures surrounding the ankle, previously referred to as partial articular deafferentation (7,15,17,32). This is supported by a meta-analysis (36), which determined that those with CAI have impaired ankle joint position recognition. Also, supraspinal adaptations in peroneal motoneuron excitability have been observed in those with CAI, which may inhibit various aspects of muscle function (37,43,45). Collectively, this evidence points toward sensorimotor system impairments, which may impact several aspects of lower extremity function. Ultimately, these sensorimotor alterations may dictate who develops into an ankle sprain coper with relatively no residual impairments versus individuals with CAI after an ankle sprain. Further examining how underlying sensorimotor impairments influence PRT and the development of CAI requires additional investigation.

With the exception of Hopkins et al. (24), all studies used a bipedal stance trapdoor platform with similar testing procedures to create sudden inversion perturbations. Hopkins et al. (24) assessed PRT through unexpected inversion perturbations created during (52) walking gait. This investigation exhibited large ES for both side-to-side and between-group comparisons with CI, which did not encompass zero. Although this is the only investigation that has used a dynamic technique, examining PRT during activity warrants further investigation. Inducing inversion perturbations during dynamic activity may provide a greater challenge to the sensorimotor system because of increased task complexity and more unpredictable environments. In addition, subjects do not have consistent somatosensory information because the plantar cutaneous receptors are not in constant contact with the ground and articular and musculotendinous receptors are moving through a large range of motion during the gait cycle. Therefore, subjects are required to adapt to the rapidly changing spatiotemporal aspects of movement at the time of perturbation which may be more challenging then static stance. Further examining PRT using similar methods may identify even more consistent and larger magnitude deficits in those with CAI and other ASH.

Although this meta-analysis did identify delayed PRT in those with CAI, several aspects of this impairment in this patient population require further study. It remains unclear how delayed PRT may relate to deleterious changes in levels of activity and participation that may be meaningful to patients with CAI. This suggests that the mere presence of a PRT impairment may have no bearing on the magnitude or progression of CAI as perceived by the individual. Furthermore, the lack of a causal

link between CAI and PRT indicates that improving PRT may not prevent future ankle sprains or influence disability. In addition to examining underlying changes in sensory and motor function, examining the response of the peroneal muscles along with more proximal muscles, such as the gluteus medius, would begin to provide a better depiction if this phenomenon is local or global in nature. Gaining a greater understanding of the extent of PRT deficits in patients with CAI from both a patient-centered and disease-oriented perspective may lead to clinical intervention strategies that can address this particular impairment as well as larger-scale issues such as decreased functional capacity and degenerative joint conditions. Finally, future studies that investigate sensorimotor function in individuals with a history of ankle sprain should provide detailed descriptions of the included subjects based on the sensitive dependence of this information for detecting sensorimotor alterations in this study.

Limitations

Electronic searches were conducted in the databases that we considered to be the most relevant to impairments associated with ankle sprain, which was followed by a hand search of the identified studies. However, it is possible that other evidence is available, which was not indexed in the selected search databases or identified through hand searching. We also limited our search to studies published in English, but we do not believe any relevant articles were excluded with this search parameter.

For the purposes of meta-analysis we decided to group studies based on subject characteristics, study design, and study quality. Several other variables such as velocity of the trapdoor perturbation, the end range angle of the trapdoor, if subjects were blindfolded or wore headphones, the methods of EMG normalization, and the parameters and methods used to determine muscle onset may influence the PRT observed in each study. We selected not to use these variables to further group studies because they varied considerably across studies and certain elements were often not reported. Although this meta-analysis was able to determine the influence of subject characteristics, study design, and study quality on PRT, several of the aforementioned variables require careful consideration when designing future studies.

We chose to use standardized ES versus the unstandardized mean differences in the time domain (ms) to answer the questions posed in this systematic review. We believe the use of standardized ES was more appropriate than unstandardized mean differences because although these studies were homogenous in several ways, they were also methodologically different in several ways, which were identified in the previous paragraph. Also, the time domain values varied considerably across studies (range = 51–106 ms), and some studies exhibited high levels of dispersion around the measures of central tendency. Cumulatively, we believe that ES was a more prudent method to answer the question posed in this systematic review. The limitation to our meta-analysis technique is that we cannot specify the mean latency differences between groups or limbs. We believe calculating this information may not be directly useful for future studies on this topic because it may not be consistent with the values obtained in individual studies. However, the ES estimates provided in this study indicate large magnitude PRT deficits are present in individuals with CAI, which suggests these deficits are clinically relevant and supports further investigating this aspect of function in these patients.

CONCLUSIONS

The overall results of this meta-analysis determined that individuals with a previous ankle sprain exhibit impaired PRT. Further analyses determined that those with CAI have a delayed PRT when compared with the contralateral uninvolved limb or a healthy control group. However, individuals with all other ASH did not demonstrate significant deficits in PRT. On the basis of the CEBM guidelines, the strength of recommendation associated with PRT deficits in patients with CAI is grade B based on the consistency of the findings from primarily level 3 evidence. However, the strength of recommendation associated with PRT deficits in people with ASH is grade C based on the inconsistency of the findings and extrapolations from level 3 and level 4 evidence. Gaining deeper insights into underlying sensory or motor alterations responsible for delayed PRT, the role of delayed PRT in activity limitation and participation restriction, and the extent to which delayed PRT contributes to CAI progression will elucidate the clinical relevance of this impairment and clinical intervention strategies to address these deficits.

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