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Personal influencing factors for pressure pain threshold in healthy people: A systematic review and meta-analysis

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ABSTRACT

All studies that investigated personal factors influencing pressure pain threshold (PPT) in healthy people were synthesized. Data was summarized, and risk of bias (RoB) and level of evidence were determined. Results were pooled per influencing factor, grouped by body region and included in meta-analyses. Fifty-four studies were eligible. Five had low, nine moderate, and 40 high RoB. Following meta-analyses, a strong conclusion was found for the influence of scapular position, a moderate for the influence of gender, and a weak for the influence of age (shoulder/arm region) and blood pressure on PPT. In addition, body mass index, gender (leg region), alcohol consumption and pain vigilance may not influence PPT. Based on qualitative summary, depression and menopause may not influence PPT. For other variables there was only preliminary or conflicting evidence. However, caution is advised, since the majority of included studies showed a high RoB and several were not eligible to include in meta-analyses. Heterogeneity was high in the performed meta-analyses, and most conclusions were weak. More standardized research is necessary.

1. Introduction

Pain is defined as “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage” (Raja et al., 2020), and is one of the most common reasons why people opt for medical help (Mäntyselkä et al., 2001). Pain has a huge impact on a person’s functioning and quality of life, but also on society, as pain usually results in high medical costs or other socio-economic problems (Blyth et al., 2019).

The somatosensory system processes nociceptive signals that can lead to the sensation of pain (Yam et al., 2018). Psychophysical testing, such as quantitative sensory testing (QST), can be used to assess sensitivity of the somatosensory system and associated pathways, in which measuring pain thresholds is an indispensable part (Backonja et al., 2009). Based on patients’ self-reported sensory experience, pain thresholds for mechanical, thermal, vibration and electrical stimuli can identify allodynia and hyperalgesia (Cruz-Almeida and Fillingim, 2014).

These are regarded as signs of altered somatosensory processing (Jaber et al., 2018). In clinical practice and research, the most feasible way to assess pain thresholds is measuring pressure pain thresholds (PPTs), which refer to the minimum amount of pressure necessary to induce pain (Hall et al., 2015). A pressure sensation stimulates C- or A δ -fibres in the skin, of which a signal goes through the anterior spinothalamic tract until it reaches the thalamus in the brain, which processes the information before sending it out to various parts of the cortex (Yam et al., 2018). To determine the PPT, usually an algometer is used, which is found to be reliable and valid (Frank et al., 2013). To date, PPT values could be a useful measure for possible signs of altered somatosensory processing, and thus to detect differences between healthy and patient populations (diagnostic) or changes over time (e.g., before and after treatment, responsive) (Jaber et al., 2018; Arendt-Nielsen and Yarnitsky, 2009; Walton et al., 2011).

In order to adequately interpret PPT values, normative values are necessary (Arendt-Nielsen et al., 2018; Vardeh et al., 2016). The first

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step is to focus on the diagnostic goal, as these normative values are the only way to assess whether a patient presents altered somatosensory processing or not. However, to date, no clear normative values for PPT are available and determining them seems to remain challenging. Some literature of normative data in healthy people exists, but even when groups based on age and measurement location were considered, a broad range of PPT values is still presented (Waller et al., 2016; Pfau et al., 2014; Sterling et al., 2002; Tuveson et al., 2006). This variation could be explained by other factors influencing PPT as well.

Systematic reviews and meta-analyses found that age (4 studies) (Tumi et al., 2017), and gender (33 (Racine et al., 2012) and 5 studies (Riley et al., 1998)) influenced PPT in healthy people. Unfortunately, other reviews, also focusing on influencing factors (such as the use of alcohol, gender role, or menstrual cycle), only reported analyses combining all pain thresholds for different modalities (Martin, 2009; Iacovides et al., 2015; Horn-Hofmann et al., 2015; Alabas et al., 2012). These modalities stimulate different fibres through different pathways: e.g. mechanical (pressure) and thermal stimuli stimulate C- or A δ - fibres through the anterior and lateral spinothalamic tract, respectively (Yam et al., 2018). Tumi et al (Tumi et al., 2017). confirmed this by finding a difference in the influence of age between heat pain threshold and PPTs, and Riley et al. (1998) found larger gender differences for PPT compared to thermal stimuli in healthy people. Thereupon, differences in the targeted anatomical structure and tissue depth exist (Fillingim, 2002). Aforementioned differences could lead to different responses to pain threshold testing, and therefore it is important to analyse a certain pain threshold modality separately. As such, the influence of other personal variables (other than age and gender) on PPT specifically remains unclear. Moreover, the last review of the influence of gender on PPT dated from 2012 (Racine et al., 2012), so an update seems necessary as well.

To date, no guidelines are available in scientific literature for which influencing factors to consider when determining normative values for PPT. It is important to know which factors influence the PPT, because this information can be useful for the diagnosis of patients with altered central somatosensory processing. These normative values can thus be used to detect an indication of the presence of mechanical hyperalgesia. As such, more research to detect the influence of different factors on PPT separately is necessary. This review will focus on all personal clinically measurable influencing factors, because measurements can be standardized regarding environmental factors and time of measurement throughout the day, but also because invasive and medical lab tests (e.g., to test the influence of genetics, fat mass) are not always available in clinical practice (such as physiotherapists cabinet).

Therefore, the aim of this systematic review was to synthesize all studies that had the purpose to explore which clinically measurable personal factors might influence PPTs in healthy people. This way, these personal factors can be considered in future studies on normative values of PPT, and can be considered for diagnosis of patients with mechanical hyperalgesia.

2. Methods

This systematic review and meta-analysis was conducted according to the updated Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021).

2.1. Eligibility criteria

Studies were included if they evaluated clinically measurable personal factors (I) possibly influencing PPT (O) in a healthy population (P). Personal influencing factors were defined as moderators, predictors or correlating personal characteristics for PPT values, or as mean difference PPT values between groups divided based on the personal factor. The eligibility criteria can be found in Table 1.

Table 1
Eligibility criteria related to PICO.

| | Inclusion | Exclusion |
|----------|---|--|
| P | 1. Healthy human subjects free of pain, illness or disease (included in intervention or control group) 2. > 18 years of age | 1. Animal studies |
| I | 1. Clinical, non-invasive measurable personal factors influencing the PPT (e.g., gender, strength, psychosocial factors) | 1. Other factors such as environmental factors (e.g., attention, type of assessor)/genetics |
| C | 1. No comparison with another population, comparison with a non-healthy population or comparison between two healthy populations (e.g. men vs women) 2. Separate statistical analyses for the healthy subjects | 1. Statistical analyses only of mixed population (e.g., patient population and healthy subjects) |
| O | 1. PPT measured with pressure algometer or other material that can measure the amount of pressure objective | 1. Vibration, electrical, thermal, ischemic pain threshold 2. Vibration, electrical, thermal, sensory, ischemic, mechanical detection threshold |
| S | 1. All sorts of study designs in a longitudinal setting | 1. Reviews, Meta-analyses, Abstracts, Letters, Congress proceedings, case reports, cross-sectional or case-control studies (PPT measured on only one time point) |
| L | 1. Articles written in English, Dutch, German or French | 1. Articles written in any other language |

Abbreviations: P, population; I, intervention; C, comparison; O, outcome; S, study design; L, language

2.2. Information sources and search strategy

The electronic databases PubMed (MEDLINE), Web of Science (WoS) and Embase were searched for eligible literature up to 11th January, 2022. Additionally, the references of previous reviews (Tumi et al., 2017; Martin, 2009; Horn-Hofmann et al., 2015; Alabas et al., 2012) and the references of the included articles retrieved through the search strategy were screened for relevant studies. To answer the research question, three different sets of key words (P, I and O) were composed following the Patient (P), Intervention (I), Comparison (C), Outcome (O) and Study design (S) model and combined using 'AND' and 'OR' (Eriksen and Frandsen, 2018). The search strategy for PubMed can be found in Table 2, the strategies for WoS and Embase can be found in table S1. No additional search filters were added.

2.3. Selection process

All studies retrieved from the electronic databases were imported in Endnote 20 (\$author1\$ et al., 28. </id><AuthGrp><Author><au>The

Table 2
Search Strategy related to PICO in PubMed.

| Population | Intervention | Outcome |
|---|---|--|
| ("Healthy Volunteers"[Mesh]) OR Healthy volunteer* OR healthy people OR healthy subject* OR healthy perso* OR healthy individua* | ("Prognosis"[MeSH Terms] OR "effect modifier, epidemiologic"[MeSH Terms]) OR Predict* OR moderat* OR modif* OR Prognos* OR "epidemiologic effect modifier" OR influenc* | ("Pain Threshold"[Mesh] OR "Pain Measurement"[Mesh] OR "Pain Perception"[Mesh]) OR "pain threshold" OR "pain measurement" OR "pain perception" OR "quantitative sensory testing" OR "sensory testing" OR qst OR pressure algomet* OR "mechanical pain threshold" OR pressure pain threshold OR ppt |

Abbreviations: QST, Quantitative Sensory Testing

Table 3
Level of evidence and strength of recommendation scoring.

| Level of evidence | | Strength of recommendation | |
|-------------------|---|----------------------------|---|
| LoE 1 * | Systematic review of randomized trials | SoR I (very strong) | At least one LoE 1 study or three LoE 2 studies |
| LoE 2 * | Randomized trial | SoR II (strong) | At least one LoE 2 study or three LoE 3 studies |
| LoE 3 * | Non-randomized controlled cohort/follow-up study | SoR III (moderate) | At least one LoE 3 study or three LoE 4 studies |
| LoE 4 * | Case-series, case-control, or historically controlled studies | SoR IV (weak) | At least one LoE 4 study or three LoE 5 studies |
| LoE 5 * | Mechanism-based reasoning | SoR V (N/A) | At least one systematic review of descriptive and qualitative studies |
| | | SoR VI (N/A) | At least a single descriptive or qualitative study |
| | | SoR VII (very weak) | At least one LoE 5 study |
| | | Preliminary SoR | Based on only one study |
| | | Conflicting conclusion | Conflicting results |

Abbreviations: RCT, Randomized Controlled trial; LoE, Level of Evidence; SoR, Strength of recommendation; N/A, not applicable

*Level of evidence can be graded down due to study quality or other methodological issues.

EndNote Team (Author) and identified duplicates were removed. The remaining studies were independently screened on title and abstract by two reviewers (SV and VH) with the help of Rayyan (Ouzzani et al., 2016). Subsequently, potentially eligible studies were additionally screened on full text by both reviewers independently in the following order of exclusion: language > study design > outcome > population > intervention. Conflicts during the whole process were resolved by consensus and in case of doubt, the last author was contacted.

2.4. Data collection and items

Data of all included studies were extracted into an evidence table. Information about (Raja et al., 2020) Author, year and origin; (Mäntyselkä et al., 2001) Study design; (Blyth et al., 2019) Participants, such as group composition and characteristics, and eligibility criteria; (Yam et al., 2018) Device, speed of the pressure build-up and analysis of PPT, including the reported signal and patient position; (Backonja et al., 2009) Location of PPT; (Cruz-Almeida and Fillingim, 2014) Influencing factor and measurement method; and (Jaber et al., 2018) Results was collected. The first reviewer (SV) completed the evidence table and the second reviewer (VH) checked the table independently.

2.5. Risk of bias in individual studies

Risk of bias (RoB) in the individual studies was assessed using the quality in prognostic studies (QUIPS) checklist (Hayden et al., 2013), as the aim of our review was to find the prognostic factors for PPT. The checklist consists of six domains that can be scored either as a 'high risk', 'moderate risk' or 'low risk' of bias: 1) Study Participation, 2) Study Attrition, 3) Prognostic Factor Measurement, 4) Outcome Measurement, 5) Study Confounding, and 6) Statistical Analysis and Reporting. Risk of bias assessment was performed independently by two reviewers (SV and VH), and conflicts were resolved by consensus. To assure uniform RoB scoring, guidelines for interpretation of each item were discussed beforehand through a calibration exercise. The overall RoB judgement of a study was based on all domains; ranging from overall 'low' RoB if all domains were scored 'low' or maximum one 'moderate'; to an overall 'high' RoB if at least one domain was scored as 'high' or ≥ 3 as 'moderate'. All other studies were judged as having an overall 'moderate' RoB.

Additionally, the overall level of evidence per study was evaluated by the first author (SV) based on RoB score and study design with the Centre for Evidence-Based Medicine (CEBM) guidelines (Explanation of the, 2011). Different level of evidence (LoE) scores were given based on their study design, methodology and RoB score (Table 3).

The RoB scoring was completed independently and in a double-blind manner by two reviewers (SV and VH). Finally, results were compared and conflicts were resolved by consensus or by contacting the last author. Afterwards, the first author bundled all the results per personal influencing factor on PPT and strengths of recommendations were made, divided into different categories based on the CEBM guideline (Table 3)

(Ackley, 2008).

2.6. Statistical synthesis methods and effect measures

Studies that presented mean and standard deviation for PPT values were combined and presented in different forest plots per influencing factor (grouped by body region) with the software Review Manager (RevMan) 5.4.1 (Review Manager Web, 2020), as subgroup analyses is possible with this software. For studies that presented correlation coefficients the software Jamovi 1.6.23 (The jamovi project, 2021) was used, as RevMan does not provide this correlation meta-analysis function. A Fisher r- to z- transformed correlation coefficient was used in this case. Only studies with full available data were included in the analysis, and authors of the original studies were contacted if data was missing. Analysis went further when the authors did not respond for a period longer than four weeks. Data was pooled through calculating the mean value if multiple categories of the influencing factor were present (e.g., absolute values and correlation coefficients of PPT values [in case of univariate analyses] from women and men were pooled to get a clear view of the influence of the factor age and vice versa, data of different locations was pooled to one data per body region). Standardized mean difference (SMD) was used to compare data, if different units for measuring PPT were used in the included studies. The presence of heterogeneity was assessed with the value I^2 . In case of high heterogeneity ($I^2 > 50\%$), random effects methods were used, and in case of low heterogeneity ($I^2 < 50\%$) fixed effects methods were used. Subgroup analyses per body region were performed if possible. Small-study effects were checked by visual observation of the symmetry of a funnel plot, but could only be checked if more than 10 studies were implemented in the meta-analysis (Debray et al., 2018; Sterne et al., 2011). Afterwards, sensitivity analyses correcting for studies that did not report full eligibility criteria and correcting for the model of meta-analyses (random or fixed effects) were performed as well. An overall p-value of the models was obtained in which significant results meant $p < 0.05$. An effect size with an overall SMD < 0.2 was considered very small, 0.2–0.5 small, 0.5–0.8 medium, and > 0.8 large (Andrade, 2020). An overall correlation coefficient (CC) < 0.2 was considered very weak, 0.2–0.39 weak, 0.4–0.6 moderate, 0.6–0.79 strong, and 0.8–1.0 very strong (11. Correlation and regression, 2021).

3. Results

3.1. Study selection and characteristics

The study selection process is illustrated in the PRISMA flowchart (Page et al., 2021) (Fig. 1). Our search strategy resulted in 32 eligible studies (Alfieri et al., 2017; Alves et al., 2017; Andrzejewski et al., 2010; Azevedo et al., 2008; Campbell et al., 2010; Cimino et al., 2000; Dawson and List, 2009; De Rui et al., 2015; Fedders et al., 2019; Garcia et al., 2007; Girotti et al., 2019; Hastie et al., 2005; Holmgaard et al., 2017; Isselée et al., 2001; Jones et al., 2016; Karmann et al., 2018; Kocur et al.,

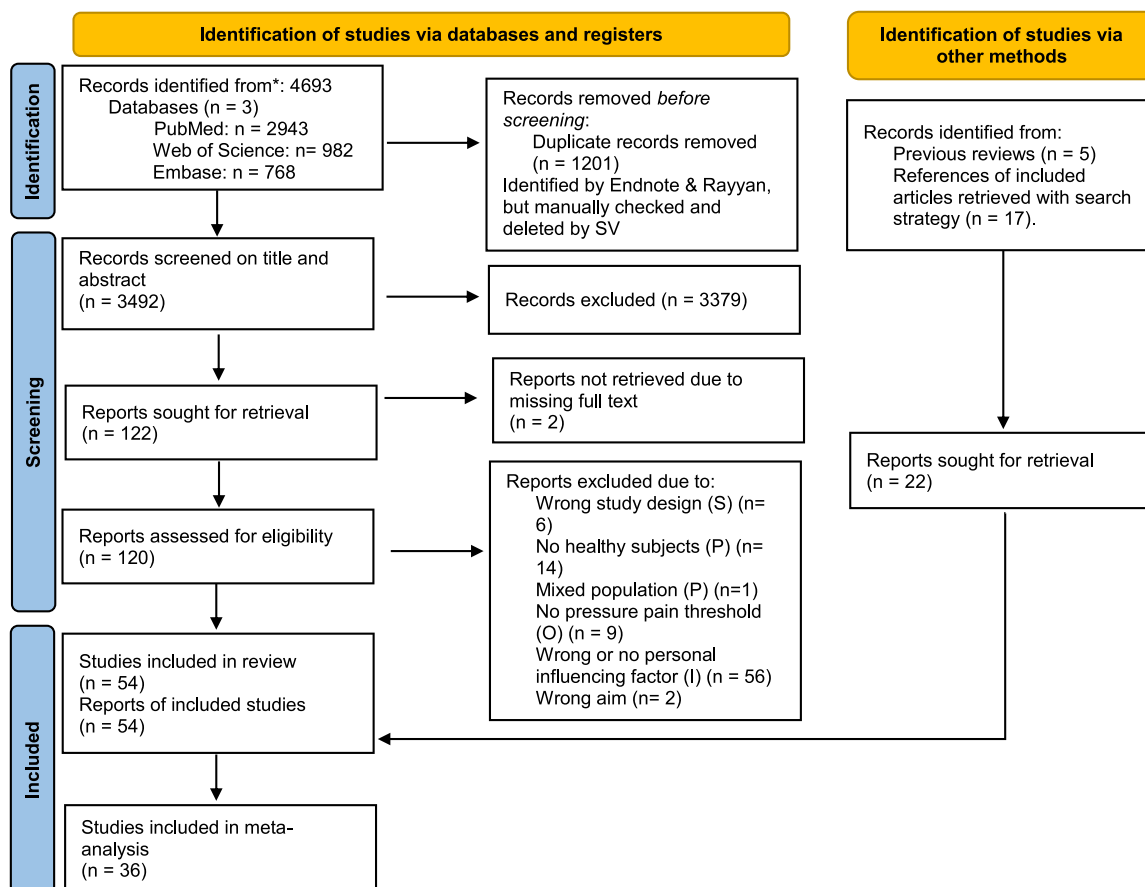


Fig. 1. PRISMA flowchart: overview of in- and exclusion process. Abbreviations: n, number.

2019; Kuppens et al., 2018; Lautenbacher et al., 2005; Lee et al., 2015; Manning and Fillingim, 2002; Moore et al., 2013; Pickering et al., 2002; Shiro et al., 2017; Sibille et al., 2012; Teepker et al., 2010; Yang et al., 2013, 2014; You et al., 2020; Zhang et al., 2013; Shah and Luximon, 2021; Ozasa et al., 2022), and additionally, hand search yielded 22 more eligible studies (Bajaj et al., 2001; Cole et al., 2010; Edwards and Fillingim, 2001; Otto and Dougher, 1985; Rao et al., 2022; Amodei and Nelson-Gray, 1989; Chesterton et al., 2003; Komiyama and De Laat, 2005; Komiyama et al., 2007; Kröner-Herwig et al., 2012; Lee et al., 1994; Lemming et al., 2015; Matos et al., 2011; McKendall and Haier, 1983; Petersen et al., 1992; Petrini et al., 2015; Price et al., 2013; da Silva et al., 2014; Tashani et al., 2017; Vatine et al., 1993; Donat et al., 2005; Martínez-Jauand et al., 2013). Finally, 54 studies (24 non-randomised controlled cohort (Andrzejewski et al., 2010; Dawson and List, 2009; De Rui et al., 2015; Girotti et al., 2019; Holmgaard et al., 2017; Manning and Fillingim, 2002; Pickering et al., 2002; Yang et al., 2013; Shah and Luximon, 2021; Cole et al., 2010; Edwards and Fillingim, 2001; Otto and Dougher, 1985; Rao et al., 2022; Chesterton et al., 2003; Komiyama and De Laat, 2005; Komiyama et al., 2007; Lee et al., 1994; Lemming et al., 2015; Matos et al., 2011; Petersen et al., 1992; Petrini et al., 2015; da Silva et al., 2014; Vatine et al., 1993; Donat et al., 2005), 14 case-control (Azevedo et al., 2008; Campbell et al., 2010; Fedders et al., 2019; Kocur et al., 2019; Kuppens et al., 2018; Lautenbacher et al., 2005; Lee et al., 2015; Yang et al., 2014; You et al., 2020; Ozasa et al., 2022; McKendall and Haier, 1983; Price et al., 2013; Tashani et al., 2017; Martínez-Jauand et al., 2013), nine prospective cohort (Alves et al., 2017; Cimino et al., 2000; Garcia et al., 2007; Isselée et al., 2001; Karmann et al., 2018; Teepker et al., 2010; Zhang et al., 2013; Bajaj et al., 2001; Amodei and Nelson-Gray, 1989), and seven cross-sectional studies (Alfieri et al., 2017; Hastie et al., 2005; Jones et al., 2016; Moore et al., 2013; Shiro et al., 2017; Sibille et al., 2012;

Kröner-Herwig et al., 2012) were eligible for inclusion in this review. In case of comparative studies only data of healthy groups were used. Of these 54 studies, 36 studies were eligible for a meta-analytic approach.

Main reasons for excluding studies were the inclusion of the wrong population (no separate analysis for the healthy group) or the use of an experimentally induced setting and as such no study on personal influencing factors. Although addressing all our recourses and contacting the authors, two studies (Granges and Littlejohn, 1993; Kerem et al., 2002) were further excluded, because no full text could be found. For the screening on title and abstract, there was an agreement of 96.1% (or 3363 studies) between both reviewers, of which the remaining conflicts (3.9% or 138 studies) were resolved by consensus. An agreement of 83.2% (or 99 studies) was found between both reviewers after screening on full text. The remaining conflicts (16.8% or 21 studies) were solved by consensus (60% or 12 studies) and by contacting the last author (40% or 9 studies). Study characteristics are presented in Table 4.

3.2. Risk of bias assessment

Five (Alfieri et al., 2017; Campbell et al., 2010; Fedders et al., 2019; Girotti et al., 2019; Yang et al., 2013), nine (Azevedo et al., 2008; Dawson and List, 2009; Jones et al., 2016; Lautenbacher et al., 2005; Shiro et al., 2017; Yang et al., 2014; Petrini et al., 2015; Price et al., 2013; Tashani et al., 2017), and 40 studies (Alves et al., 2017; Andrzejewski et al., 2010; Cimino et al., 2000; De Rui et al., 2015; Garcia et al., 2007; Hastie et al., 2005; Holmgaard et al., 2017; Isselée et al., 2001; Karmann et al., 2018; Kocur et al., 2019; Kuppens et al., 2018; Lee et al., 2015; Manning and Fillingim, 2002; Moore et al., 2013; Pickering et al., 2002; Sibille et al., 2012; Teepker et al., 2010; You et al., 2020; Zhang et al., 2013; Shah and Luximon, 2021; Ozasa et al., 2022; Bajaj et al., 2001; Cole et al., 2010; Edwards and Fillingim, 2001; Otto and Dougher,

Table 4
Evidence table.

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|--|----------------------------------|--|--|--|--|---|---|---|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| (Alfieri et al., 2017) Brazil | Cross-sectional | N = 75 66.8 y (4.6) ♀ = 75 (100%) | - 60y-75y - Female gender - Absence of psychiatric disorders - Body pain < 4 in VAS - No chronic use of analgesic or anti-inflammatory drugs - Not participating in physical therapy sessions | Not reported | D: algometer (J Tech) S: 1 kg/s RS: pain or discomfort A: not reported P: dorsal/ventral decubitus, or sitting (depending on PPT location) | Bilateral insertion and mid-belly of following muscles: • Biceps brachii • Flexor capri ulnaris/radialis • Vastus medialis/lateralis • Gluteus maximus | - Functional capacity (6MWT) - Handgrip strength (dynamometer) - Lower limb strength (CS) | No correlation between all factors and PPT (p > 0.05). |
| (Alves et al., 2017) Brazil | Prospective cohort | N = 39 28.38 y (7.88) ♀ = 39 (100%) | - Women 18y-47y (fertile age) - Healthy - Normal arterial blood pressure - Regular menstrual cycles (25–30 days) | - Irregular menstrual cycles (<25 or >30 days) - Women at menopause - Use of hormonal contraceptive in last 6 m - Use of pain medication - Use of opioids, antidepressants or ansiolitics in last 6 m - Pregnancy or attempt of pregnancy in last 6 m - Breastfeeding - CV, neuroendocrine, psychiatric or gynaecologic diseases - Chronic or acute pain in last 6 m - Central or peripheral neuropathy - Physical exercises 1 h before evaluations - Smoking | D: electronic pressure algometer (Somedic) S: 50 kPa/s RS: pain A: not reported P: sitting | Right body side: • Maxillary branch of the trigeminal nerve area • Forearm region | - Menstrual cycle | PPT decreased during the phases of the menstrual cycle (p < 0.001). |
| (Amodei and Nelson-Gray, 1989) North Carolina | Prospective cohort | N = 12 18.42 y (SD not reported) ♀ = 12 (100%) | - Menstruating for at least 2 years - Menstrual cycle 20–40 days | - Menstrual discomfort secondary to gynecological disorder of organic origin - Oral contraceptive use < 2 m prior to study participation | D: strain-gauge pain stimulator S: not reported (standard weight 225 g, in s) RS: first pain A: not reported P: sitting | Dominant side: • Middle phalanx of index finger | - Menstrual cycle | No effect on PPT (p > 0.05). |
| (Andrzejewski et al., 2010) Poland | Non-randomized controlled cohort | N = 76 (concerning age influence) Younger age group (38 or 50%) 22 y (SD not reported) Older age group: (38 or 50%) 65 y (SD not reported) | Not reported | Not reported | D: algometer with shut-off and reset button S: 100 g/s RS: pain or discomfort A: 3 trials P: side lying | Bilateral insertion and latent trigger points of following muscles: • Superior fibular retinaculum • Peroneus longus • Biceps femoris • Gluteus maximus/medius • Tensor fascia latae • Latissimus dorsi | - Age - Level of physical activity (self-developed questionnaire) | Younger age resulted in higher PPT (p < 0.05): on both sides at the insertion of: • Peroneus longus, • Biceps femoris, • Gluteus maximus, • Adductor magnus On left side at the insertion of: • Flexor capri ulnaris/radialis, On both sides at trigger points in: <i>(continued on next page)</i> |

Table 4 (continued)

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|----------------------------------|--------------|---|---|--|---|--|--|--|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| | | reported) ♀ = ? N = 22 (concerning physical activity influence) Vigorous physical activity group (16 or 73%) Moderate physical activity group (6 or 27%) Mean age not reported ♀ = ? | | | | <ul style="list-style-type: none"> • Erector spinae • Infraspinatus • Levator scapulare • Pectoralis major/minor • Flexor carpi ulnaris/radialis • Adductor magnus | <ul style="list-style-type: none"> • Flexor carpi radialis • Adductor magnus <p>On right side at trigger points in:</p> <ul style="list-style-type: none"> • Peroneus longus, • Infraspinatus, <p>More physical activity resulted in higher PPT (p < 0.05):</p> <p>On both sides at the insertion of:</p> <ul style="list-style-type: none"> • Superior fibular retinaculum • Peroneus longus • Biceps femoris • Gluteus maximus/medius • Tensor fascia latae • Infraspinatus • Pectoralis major/minor • Adductor magnus <p>On the left side at the insertion:</p> <ul style="list-style-type: none"> • Erector spinae <p>On the right side at the insertion:</p> <ul style="list-style-type: none"> • Levator scapulare • Latissimus dorsi • Flexor carpi ulnaris/radialis <p>On both sides at trigger points in:</p> <ul style="list-style-type: none"> • Superior fibular retinaculum • Peroneus longus • Biceps femoris • Gluteus maximus/medius • Latissimus dorsi • Erector spinae • Infraspinatus • Levator scapulare • Pectoralis major/minor • Flexor carpi ulnaris/radialis • Adductor magnus <p>On left side at trigger point in:</p> <ul style="list-style-type: none"> • Tensor fascia latae <p>Other results were non-significant (p > 0.05)</p> | |
| (Azevedo et al., 2008) Brazil | Case-control | N = 52 Normal scapular group (26 or 50%): 22.2 y (1.2) ♀ = 20 Depressed scapular group (26 or 50%): 21.8 y (1.3) ♀ = 20 | - No history of orthopaedic, neurological or dermatological conditions on the cervical spine and upper limbs for the last 12 m - No use of anti-depressive medication or analgesic and anti-inflammatory drugs for the last 5 days | after posture assessment: -Different combination of position of the anatomic landmarks | D: electronic pressure algometer (J tech) S: 3 Newton/s RS: sensation of pressure changed to pain A: 1 trial P: sitting | M. Trapezius pars descendens dominant side | -Posture (scapular position) | A depressed scapular position resulted in lower PPT (p = 0.008). |

Bilateral at:

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Table 4 (continued)

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|---|----------------------------------|---|--|--|--|---|---|--|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| (Bajaj et al., 2001) Denmark | Prospective cohort | N = 35 ♀ 28 y (1.9) ♂ 30 y (1.4) ♀ = 15 (43%) | - Healthy - Normal menstrual cycle | - Dysmenorrhoea - Oral contraceptives | D: electronic algometer (Somedic) S: 30 kPa/s RS: pain or discomfort A: 3 trials P: lying | • Abdomen (T10-T12) • Lower back (S2-S4) • Upper arm (C7-C8) • Mid-thigh (L2) | - Menstrual cycle - Gender | Being in the ovulatory phase resulted in lower PPT measured at the lower back as compared to the other phases ($p < 0.0002$). Women presented lower PPTs at the lower back compared with men ($p < 0.01$). Other results were non-significant ($p > 0.05$). |
| (Campbell et al., 2015) United Kingdom | Case-control | N = 84 34 y (14.59) ♀ = 38.8% | -No pain condition or medical disorder | - Active alcohol or drug abuse problem - Use of narcotics, antidepressants, anticonvulsant, or muscle relaxants | D: algometer (Somedic) S: 30 kPa/s RS: pain A: 2 trials (both sides together) P: not reported | Bilateral: • M. Trapezius pars descendens | - Depression (BDI, BSI) - Catastrophizing (PCS, SCQ) | No significant correlation ($p > 0.05$). No significant correlation between PCS and PPT ($p > 0.05$) -A correlation between PPT and SCQ ($p < 0.01$, $r = -0.38$) was found. -SCQ predicted PPT after controlling for gender, age, ethnicity, depression and the PCS ($p < 0.01$, $R^2 = 0.32$). -SCQ was a better predictor than PCS ($p < 0.05$). -Women reported lower PPT than men ($p < 0.0005$) |
| (Chesterton et al., 2003) United Kingdom | Non-randomized controlled cohort | N = 240 Women 25 y (Jaber et al., 2018) ♀ = 120 (50%) | -Healthy | - Peripheral neuropathy - Pain symptoms - History of trauma or surgery to the dominant hand - Current medication - Diabetes - Pregnancy - Reporting moderate or severe pain symptoms | D: pressure algometer (Salter Abbey Weighing Machines) S: 5 Newton/s RS: pain distinct from pressure or discomfort A: 2 trials P: not reported | Non-dominant m. interosseoous dorsalis 1 | -Gender | - Women reported lower PPT than men ($p < 0.0005$) |
| (Cimino et al., 2000) Italy | Prospective cohort | N = 24 25.1 y (3.6) ♀ = 24 (100%) | -Regular menstrual cycle (28 ± 2 days) | - TMD and/or orofacial pain diagnosed according to the Research Diagnostic Criteria - Intake of oral contraceptives - Wearing of intrauterine contraceptive devices - Consumption of NSAID or any other medication < 1 m prior to participation - Migraine - Neurological disorders | D: algometer (Somedic) S: 20 kPa/s RS: sensation of pressure changed to pain A: last 3 trials P: sitting | Right body side (2 places): • M. Masseter (M1 and M2) • M. Temporalis pars anterior (T1 and T2) | Menstrual cycle | Being in the preovulatory phase resulted in lower PPT at M1 compared to the other phases ($p < 0.05$), and at T1 compared to the luteal phase ($p < 0.05$). Other results were non-significant ($p > 0.05$). |
| (Cole et al., 2010) Australia | Non-randomized controlled cohort | N = 30 Younger group (15 of 50%): 26 y (Blyth et al., 2019) ♀ = 8 (53%) Older group (15 of 50%): 79 y (Yam | - Not reporting pre-existing pain - Not taking any medication during testing - Additional for older group: ≥ 25 on MMSE | - Peripheral neuropathy - Diabetes - Stroke - Hypertension - Psychiatric disorders | D: hydraulically driven device composed of a circular rubber probe S: 0.25 kg/cm ² /s RS: participants had to rate with a 20-point scale the JNP A: mean of 4 stimulus | Thumb nail | Age | Younger age resulted in higher PPT ($p < 0.05$). |

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Table 4 (continued)

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|--|----------------------------------|---|--|--|--|---|--|---|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| | | et al., 2018) ♀ = 6 (40%) | | | magnitudes that elicited alternating reports of no pain sensation (0/20) and faint pain (1/20). P: not reported | | | |
| (Dawson and List, 2009) Sweden | Non-randomized controlled cohort | N (total) = 64 Middle Easterners (32 or 50%): ♀ 24.1 y (2.3) ♂ 25.2 y (3.6) ♀ = 16 (50%) Swedes (32 or 50%): ♀ 23.3 y (3.3) ♂ 24.8 y (3.5) ♀ = 16 (50%) | Inclusion Middle Easterners: - Participant + parents born in Iraq, Iran, Lebanon, Syria, or Palestine - Spoke first language at home Inclusion Swedish: - Born and raised in Sweden for the last two generations - Spoke Swedish at home -> 65 y -Independence in all activities of daily living, with possible exception of continence -A normal cognitive performance or mild cognitive impairment(>5/10 on SPMSQ) | - Chronic pain - Trauma and/or surgery to the hands - Cardiac disease - Analgesics or other medication that would influence pain perception - Pregnancy | D: algometer S: 30 kPa/s RS: pressure that felt like pain A: not reported P: not reported | Not reported | -Gender -Ethnicity | No difference in PPT between genders (p > 0.05) after pooling for cultures. No difference in PPT between Middle Easterners and Swedes (p > 0.05) after pooling for gender. |
| (De Rui et al., 2015) Italy | Non-randomized controlled cohort | N = 97 ♀ 71.7 y (0.6) ♂ 73.1 y (0.9) ♀ = 63 (65%) | -> 65 y -Independence in all activities of daily living, with possible exception of continence -A normal cognitive performance or mild cognitive impairment(>5/10 on SPMSQ) | - Nursing home residents - Taking NSAID drugs/analgesics in previous month - Chronically treated with antidepressants or membrane-stabilizing drugs - Having type 1 diabetes, systematic rheumatic diseases, tension-type headache, odontogenic pain, TMD, myopathies or fibromyalgia | D: algometer (Fischer) S: 100 g/s RS: pain A: not reported P: not reported | Bilateral: • M. Temporalis (pars anterior, medialis and posterior) • M. Masseter • M. Sternocleidomastoideus • M. Occipitalis • M. Splenius Capitis • M. Hypothenar | -Gender -Age -Educational level (years of education) | Women reported lower PPT compared to men for all muscles (p < 0.05). No difference in PPT (p > 0.05). No difference in PPT (p > 0.05). |
| (Donat et al., 2005) (91) Turkey | Non-randomized controlled cohort | N (total) = 128 60–69 y age group (23 or 18%): ♀ = 16 (70%) 70–79 y age group (62 or 48%): ♀ = 38 (61%) > 80 y age group (43 or 34%): ♀ = 26 (60%) | Not reported | -History of recent upper extremity injury -Any kind of orthopaedic, neurologic, or systemic pathology causing function deficiency or pain | D: dolorimeter (Wagner) S: 1 kg/s RS: pain or discomfort A: mean of 3 trials P: not reported | Bilateral: • Second finger • Fifth finger • Hand | -Age | No significant results (p > 0.05) |
| (Edwards and Fillingim, 2001) Alabama | Non-randomized controlled cohort | N (total) = 68 Younger group (34 or 50%): 22.4 y (2.2) ♀ = 21 (62%) Older group (34 or 50%): 62.2 y (3.4) ♀ = 21 (62%) | Not reported | Not explicitly reported, but participants were screened for: -Ongoing pain problems -Hypertension -Circulatory disorders -Cardiac problems -Metabolic disease -Other significant health | D: algometer (Somedic) S: 30 kPa/s RS: pain A: not reported P: not reported | Left body side: • M. Trapezius pars descendens • M. Masseter | -Age -CV activity (measuring of SBP and MAP in resting state) | No significant differences between age groups (p > 0.05) PPT correlated with, measured at m. Masseter: 1. SBP (p = 0.002, r = 0.50) 2. MAP (p = 0.005, r = 0.46) In younger participants 1. SBP (p = 0.04, r = 0.35) |

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Table 4 (continued)

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|-----------------------------------|--------------------|--|---|---|--|---|--|---|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| (Fedders et al., 2019) Denmark | Case-control | N (total) = 40 Normal BMI group (20 or 50%): 23.30 y (1.81) ♀ = 10 (50%) High BMI group (20 or 50%): 27.05 y (8.53) ♀ = 10 (50%) | - Healthy men and women of 18–65 y - Non-smokers - Caucasian - BMI ≥ 18.5 kg/cm ² | - Pregnant or breastfeeding - Pacemaker - Full-grown board - Lacked the ability to cooperate - Performed extreme athletic activities - Neurological, CV, MSK, or psychological illness - Craniofacial pain, migraine, chronic TTH, new persistent headache or TMD. - Dermatological skin conditions, wounds, scars or skin sensation alteration in facial region - Chronic pain < 3 m or acute pain on day of study - Flu or fever < 2w - Addicted to drugs - Consummation of alcohol < 24 h before study - Use of medication with impact on immune system or pain for the last 24 h - Use supplements or medication that affect body weight | D: handheld pressure algometer (Somedic) S: 30 kPa/s RS: sensation of pressure changed to pain A: 1 trial before CPT P: not reported | Bilateral: • M. Temporalis • M. Masseter • M. Deltoideus | -BMI (weight with SilverCrest Diagnostic Scale, Height with non-elastic measuring tape) -Gender | In older participants PPT correlated with, measured at m. Trapezius: 1. SBP (p = 0.03, r = 0.37) 2. MAP (p = 0.04, r = 0.37) In younger participants 1. SBP (p = 0.03, r = 0.37) In older participants Other results were non-significant (p > 0.05). No significant difference in PPT between the BMI groups or gender (irrespective of BMI) (p > 0.05). |
| (Garcia et al., 2007) Spain | Prospective cohort | N = 30 40.94 y (14.42) ♀ = 18 | -Not suffering from chronic or acute pain just before or during the study | - Chronic MSK disorder - Frequent pain - Analgesic medication in a non-sporadic manner - Traumatic injury - Surgery or suffered pain < 6 m - Psychological disorder - Medical incident < 3 days before measurement (taking analgesic medication, apparition of | D: algometer (DEP) S: 1 kg/s RS: pressure that felt like pain A: mean of 3 trials P: not reported Patients were measured in three sessions (baseline, 15 min post, and 7 days post) | Bilateral tender points of following muscles: • Trapezius pars descendens • Supraspinatus • Gluteus pars anterior Bilateral tender points of: • Occiput • Low cervical • Greater trochanter • Medial fat pad knee • Second rib • Lateral epicondyle | Gender | Woman showed lower mean PPT values than men measured at 'total' of tender points at session 3 (p < 0.05, ES: 0.84). Only in the first trial of session 3, woman showed lower PPT than men measured at 'total' of tender points (p < 0.05, ES: 0.84) Women showed lower PPT than men for the 'total' of control points (p < 0.05, ES: 0.85) Woman showed lower mean PPT values than men measured at control |

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Table 4 (continued)

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|-------------------------------------|----------------------------------|---|--|---|---|---|---|---|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| | | | | medical complications or invasive techniques) | | Bilateral control points: • Hypothenar eminence • Medial tibia • Medial ulna | points at session 1 (p < 0.05, ES: 0.91), 2 (p < 0.05, ES: 0.74) and 3 (p < 0.01, ES: 0.81). Other results are non-significant (p > 0.05) | |
| (Girotti et al., 2019) Italy | Non-randomized controlled cohort | N (total) = 355 Younger group (195 or 55%): 20–45 y (mean and SD not reported) φ = 120 (62%) Middle aged group (75 or 21%): 46–64 y (mean and SD not reported) φ = 35 (47%) Older group (85 or 24%): 65–95 y (mean and SD not reported) φ = 51 (60%) | Not reported | - MSK, skin or joint disease at site of PPT testing - Presence of any pain syndrome or symptomatology at the time of assessment - Use of pain killers - Severe cognitive impairments or neurological diseases that might affect the ability to discriminate between and define painful stimuli | D: algometer (Fisher) S: not reported (Newton/cm ²) RS: pressure became painful (difference) or mean of last 2 trials (regression) P: not reported | Bilateral: • Carpal joint | -Age -Gender -Older group -BMI -Manual work -Educational level (years of education) -Depression (GDS-sf) -Cognitive impairment (SPMQS) -Complex functions in which fully self-sufficient (IADL) -Comorbidities (CIRS-CI) -Poly-pharmacy | -PPT significantly decreased in both men and women from younger age to older age (p < 0.0001). -Adjustment of BMI: negative association between age and PPT in men and woman (p < 0.0001). -Women had lower PPT than men in all age groups, but the difference was more attenuated with advancing age (young group: p = 0.001, middle-aged group: p = 0.02, older group: p = 0.003). Gender and age influenced PPT (p = 0.03) No difference in PPT (p > 0.05). Non-manual work resulted in lower PPT in men (p = 0.03) No difference in PPT (p > 0.05). No difference in PPT (p > 0.05). Cognitive impairment resulted in lower PPT in men (p = 0.04) No difference in PPT (p > 0.05). Higher CIRS-CI resulted in lower PPT in men (p = 0.02). No difference in PPT (p > 0.05). No association with PPT (p > 0.05). Association between the KRS and PPT (p < 0.01, r = 0.254). Association between the CSQ-subscale active factor and PPT (p < 0.05, r = -0.154). |
| (Hastie et al., 2012) USA | Cross-sectional | N = 188 24.14 y (5.47) φ = 110 (59%) | -Healthy participants | - Chronic pain, systemic medical condition - Use of prescription medication | D: handheld pressure algometer (Pain Diagnostics and Therapeutics) S: 1 kg/s RS: Not reported A: mean of 3 trials P: not reported | Right body side: • M. Trapezius pars descendens • M. Masseter • Ulna | -Affective status (PANAS) -Hyper-vigilance (KRS) -Pain coping (CSQ) | No difference in PPT (p > 0.05). No association with PPT (p > 0.05). Association between the KRS and PPT (p < 0.01, r = 0.254). Association between the CSQ-subscale active factor and PPT (p < 0.05, r = -0.154). |
| (Holmgaard et al., 2017) Denmark | Non-randomized controlled cohort | N = 60 22 y (2.30) φ = ? | - No history of persistent pain - Phenotypic features for dark eye and dark hair colour or light eye and light hair colour. | - Red hair - History of neurophysiological or mental illnesses - Ongoing pain treatment - Drug or alcohol abuse - Use of nicotine (<30days) - Chronic headache (>2x week) - Pregnancy or nursing | D: handheld electronic pressure algometer (SENSEbox, Somic) S: 25 kPa/s RS: Pain A: 1 trial (before CPT) P: not reported | • M. Tibialis anterior • M. Temporalis | -Phenotypic features for dark/light eye and hair -Gender | No difference in PPT (p > 0.05) A gender difference for PPT measured at m. Temporalis (p = 0.015). Other results were non-significant (p > 0.05) |
| (Isselée et al., 2001) Belgium | Prospective cohort | N = 30 Group taking oral contraceptives (10 or 33%): 26 y (SD not | Not reported | - History of medical problems (diabetes, neurological or metabolic) - Dysmenorrhea or gynecological problems | D: algometer (Somic Type III) S: 40 kPa/s RS: sensation of pressure changed to pain | Bilateral: • M. Temporalis • M. Masseter • Thumb | -Menstrual cycle -Gender -Taking oral contraceptives | All data together: PPT was different between gender-hormonal phases of all measurements in all muscles, except for the first measurement of the m. Masseter. |

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Table 4 (continued)

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|-----------------------------------|-----------------|--|---|-------------------------------------|---|---|---|--|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| | | reported) ♀ = 10 (100%) Group without contraceptives (10 or 33%): 29 y (SD not reported) ♀ = 10 (100%) Men (10 or 33%): 31 y (SD not reported) ♀ = 0 (0%) | | - Cycle length < 26days or > 33days | A: not reported P: not reported -Women were assessed according to their menstrual cycle during 4 sessions [2 sessions in mid-to-late follicular phase, and two in the mid-to-late follicular phase] and 10 consecutive cycles -Men were assessed weekly for 2 months and every 2 weeks thereafter for 10 months. | | | For women without contraceptives PPT measured at following muscle and location: • Temporalis was different between the menstrual and follicular phases (p = 0.0001, p = 0.0009, and p = 0.0198 measurement 1,2 and 3, respectively), and between the menstrual an luteal phases (p = 0.0256), p = 0.0124 for measurement 1 and 2, respectively). • thumb was different between the menstrual and the follicular phase (p = 0.0179, measurement 1) For women taking oral contraceptives PPT measured at following locations: • M. Masseter (p = 0.0001, p = 0.0014, and p = 0.0038 for measurement 2,3 and 4, respectively) • M; Temporalis (p = 0.0001, p = 0.0001, and p = 0.0011 for measurement 2,3 and 4, respectively) • thumb (p = 0.0008, measurement 2) was different between the menstrual phase and follicular phase compared to men. • M. Masseter (p = 0.0001, p = 0.0014, and p = 0.0033, measurement 2,3, and 4, respectively) • M. Temporalis (p = 0.0001, p = 0.0001, and p = 0.0101, for measurement 2,3, and 4, respectively) • thumb (measurement 2) was different between the menstrual and luteal phase compared to men. No difference in PPT between women and men (p > 0.05). No difference in PPT between women taking contraceptives and women not taking medication (p > 0.05). Association between lower body PPT and VO2peak in men (p = 0.03, r = -0.58). Ischemic pain tolerance |
| (Jones et al., 2016) Australia | Cross-sectional | N = 53 ♀ 24.4 y (3.6) | - Apparently healthy with no history of chronic pain or | Not reported | D: handheld algometer (Wagner) S: 1 kg/s | Right body side: • M. Trapezius • M. Biceps brachii | -Peak aerobic capacity -Gender | (continued on next page) |

Table 4 (continued)

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|--|----------------------------------|---|---|---|--|--|---|---|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| | | ♂ 27.83 y (0.42) ♀ = 17 (32%) | chronic disease - 18y-50y - Absence of a current diagnosis of depression | | RS: sensation of pressure changed to pain A: mean of 3 trials P: not reported | <ul style="list-style-type: none"> • M. Rectus femoris • M. Tibialis anterior | -Ischemic pain tolerance (ischemic tourniquet test) | and VO ₂ peak were predictors for this association (p = 0.01 and p = 0.045, respectively). No association with PPT (p > 0.05). No association with PPT (p > 0.05). Other results were non-significant (p > 0.05). |
| (Karmann et al., 2018) Germany | Prospective cohort | N = 40 38.8 y (13.5) ♀ = 20 (50%) | Not reported | - Acute and chronic pain - Psychological disorders or medical diseases (e.g. sleep disorders) - Taking psychotropic drugs or analgesics | D: computer controlled pressure algometer (Noxitest Biomedical) S: 50 kPa/s RS: slightly painful A: mean of 5 trials P: not reported | Left body side: <ul style="list-style-type: none"> • Fingertip of the middle finger • Fingertip of the index finger | -Overnight changes (1st vs. 2nd night) -Total sleep time, efficiency, and latency -N and period of awakenings -Durations of non-REM stage & slow-wave, and REM sleep (polysomnography) -Subjective sleep quality (morning and evening DGSM) | None of the factors predicted PPT (p > 0.05). |
| (Kocur et al., 2019) Poland | Case-control | N = 50 Normal head posture group (25 or 50%): 39.6 y (8.1) ♀ = 25 (83%) Forward head posture group (25 or 50%): 40.7 y (6.8) ♀ = 25 (83%) | - Healthy individuals without any acute or chronic headaches or neck pain < 6 m - Level of physical activity in their leisure time as average or low - 24–55 y - BMI 18.5–30 kg/m ² - VAS < 5 - NDI < 14 - Weekly working time in a sitting position of at least 35 h - Lack of orthopedic and neurological comorbidities | - Participants with extreme values of anthropometric characteristics - After surgery within the thoracic and cervical spine, and, shoulder girdle region. | D: algometer (Wagner) S: not reported (Newton/cm ²) RS: pain complaint A: not reported P: not reported | <ul style="list-style-type: none"> • M. Trapezius pars descendens • M. Splenius Capitis • M. Sternocleidomastoideus | Forward head posture (photometric method) | No effect on PPT (p > 0.05). |
| (Komiya and De Laet, 2005) Belgium Japan | Non-randomized controlled cohort | N = 32 ♀ 25.3 (5.5) ♂ 25.4 (4.6) ♀ = 16 (50%) | -Caucasian | - Pain in head or neck region (jaw dysfunction and headaches, subjective pain or soreness of the masticatory muscles) - Currently taking medication or received other treatment - General health problems or periodontal disease - History of drug abuse - Recent facial or cervical trauma - Being in menstrual phase - Smoker | D: pressure algometer (Somedic) S: 30 kPa/s RS: pain A: 3 trials P: not reported | Bilateral: <ul style="list-style-type: none"> • M. Masseter • Thenar | -Age -BMI (measurement method not reported) -Gender | No effect on PPT (p = 0.648) No effect on PPT (p = 0.665) Women reported lower PPT on all locations (p < 0.001). |

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Table 4 (continued)

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|---|----------------------------------|---|---|---|--|---|--|---|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| (Komiya et al., 2007) Belgium Japan | Non-randomized controlled cohort | N = 88 Japanese (44 or 50%): ♀ 25.0 (3.6) ♂ 24.7 (3.6) ♀ = 22 (50%) Belgium (44 or 50%): ♀ 23.9 (3.6) ♂ 24.4 (3.1) ♀ = 22 (50%) | - Belgian Caucasian subjects or Japanese subjects | - Pain in head or neck region (jaw dysfunction and headaches, subjective pain or soreness of the masticatory muscles) - Currently taking medication or received other treatment - General health problems or periodontal disease - History of drug abuse - Recent facial or cervical trauma - Being in menstrual phase - Smoker | D: pressure algometer (Somedic) S: 30 kPa/s RS: pain A: 3 trials P: not reported | Bilateral: • M. Masseter • Thenar | -Ethnicity -Age -Gender -Height (measurement method not reported) -Weight (measurement method not reported) | No effect on PPT (p > 0.05). No effect on PPT (p > 0.05). Women reported lower PPT on all locations (p = 0.002) No effect on PPT (p > 0.05). No effect on PPT (p > 0.05). |
| (Kröner-Herwig et al., 2012) Germany | Cross-sectional | N = 74 23.1 y (2.5) ♀ = 35 (47%) | -Speaking German language | - Acute pain at the time of testing and/or persistent pain - Consumption of alcohol on the day of the experiment - Pain medication < 48 h before testing - Pregnancy - Bruises or injuries at the site of the pain application | D: algometer (Fischer) S: 1 kg/s RS: pain A: 5 trials P: not reported | Inner forearm | -Gender -Gender role (masculinity/femininity BSRI) -Pain catastrophizing (PCS) -Fear of Pain (FBQ-III and PASS) -Depression (BDI) -SBP (tourniquet) -Menstrual phase | -Women reported lower PPT than men (p = 0.001) -Gender correlated with PPT (p ≤ 0.05, r = -0.39) No effect on PPT (p > 0.05) No correlation with PPT (p > 0.05) No correlation with PPT (p > 0.05) No correlation with PPT (p > 0.05) No correlation with PPT (p > 0.05). |
| (Kuppens et al., 2018) Belgium | Case-control | N = 25 26.12 y (8.29) ♀ = 13 (52%) | - Pain-free and healthy subjects - No history of shoulder or neck pain requiring medical treatment | Not reported | D: digital algometer (Wagner) S: 1 kg/s RS: pain A: not reported P: not reported | Bilateral: • M. Trapezius pars descendens • dorsal side of middle finger Right body side: • m. Gastrocnemius | - Pain Vigilance and Awareness (PVAQ) - Pain catastrophizing (PCS) - Sports participation (participation in sport whether or not) | No correlation with PPT for all factors (p > 0.05). |
| (Lautenbacher et al., 2005) Germany | Case-control | N = 40 Younger group (20 or 50%): 27.1 y (3.5) ♀ = 10 (50%) Older group (20 or 50%): 71.6 y (5.9) ♀ = 10 (50%) | -Pain-free | - Conditions that could affect pain perception and report such as diabetes, hypertension, peripheral and central neuropathy, neuropsychological and psychiatric disorders. - Analgesic or sedative medication < 48 h prior to test session | D: computer-controlled pneumatic pressure algometer S + RS: steps of 200 kPa until participant reported first pain or discomfort, then decreased in steps of 100 kPa until 'no pain' was reported, followed by steps of 50 kPa until 3 upward turning points were reached. A: median value of 3 upward turning points P: not reported | Bilateral: • Middle finger • Ring finger | -Age -Gender | Younger age resulted in higher PPT (p = 0.003). No effect on PPT (p > 0.05). |
| (Lee et al., 1994) Korea | Non-randomized controlled cohort | N = 167 20–59 y (no info about mean age or SD) ♀ = 83 (50%) | - Free of pain in head and neck region at the time of the interview - No tenderness to | - Difficulty and/or pain opening mouth - Sometimes stuck or locked jaw - Noises in jaw joints | D: pressure algometer (Somedic) S: 40 kPa/s RS: pain | Following muscles: • Temporalis pars anterior, medius and posterior • Masseter pars inferior, superior and profunda | -Age -Gender | Younger age resulted in lower PPT in women measured at following muscles: • Temporalis pars anterior, medius and posterior |

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Table 4 (continued)

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|-------------------------|--------------|---------------------------------------|-------------------------------|--|--|--|--|--|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| | | | digital palpation at any site | <ul style="list-style-type: none"> - Pain in face, cheeks, jaws, throat or temples - Uncomfortable or unusual feeling of bite - Frequent headache, neck and/or shoulder pain - Previously treated for jaw joint problem - Jaw symptoms or headache in the morning | A: 2 trials P: not reported | <ul style="list-style-type: none"> • Pterygoideus medialis • Digastricus posterior • Sternocleidomastoideus pars medialis and superficialis • Splenius capitis • Trapezius insertion • Trapezius pars descendens | <ul style="list-style-type: none"> • Masseter pars profunda • Pterygoideus medialis • Digastricus posterior • Sternocleidomastoideus pars superficialis • Splenius capitis • Trapezius insertion • Trapezius pars descendens <p>Younger age resulted in lower PPT in men measured at following muscles:</p> <ul style="list-style-type: none"> • Pterygoideus medialis • Digastricus posterior • Splenius capitis • Trapezius insertion • Trapezius pars descendens <p>Women in their 20ies reported lower PPT than men in their 20ies measured at following muscles:</p> <ul style="list-style-type: none"> • Temporalis pars anterior, medius and posterior • Masseter pars inferior, superior and profunda • Digastricus posterior • Sternocleidomastoideus pars medialis and superficialis • Splenius capitis • Trapezius insertion • Trapezius pars descendens <p>Women in their 30ies reported lower PPT than men in their 30ies measured at following muscles:</p> <ul style="list-style-type: none"> • Masseter pars inferior, superior and profunda • Pterygoideus medialis • Digastricus posterior • Sternocleidomastoideus pars medialis and superficialis • Splenius capitis • Trapezius insertion <p>Women in their 40ies reported lower PPT than men in their 40ies measured at following muscles:</p> <ul style="list-style-type: none"> • Masseter pars inferior, superior and profunda • Pterygoideus medialis • Digastricus posterior <p>Women in their 50ies reported lower PPT than men in their 50ies measured at following muscles:</p> <ul style="list-style-type: none"> • M. masseter pars anterior • Digastricus posterior | |

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Table 4 (continued)

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|--------------------------------------|--------------------------------------|--|--|---|--|--|--|---|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| (Lee et al., 2015) Taiwan | Case-control | N (total)= 20 Depressed scapular group (8 or 40%): 21.7 y (0.7) ♀ = 3 (38%) Normal scapular group (12 or 60%): 22.2 y (0.4) ♀ = 7 (58%) | Not reported | - History of orthopedic, neurological, or dermatological conditions of the cervical spine - History of orthopedic conditions of upper limbs - Antidepressants or any analgesics < 3 m - Anti-inflammatory drugs < 5days - Body-implanted electronic devices - Pain in m. Trapezi - Current or previous presence of pain (through brief medical history) | D: electronic pressure algometer (Wagner) S: not reported (kgf/cm ²) RS: sensation of pressure changed to pain A: mean of 3 trials P: sitting | Bilateral: • M. Trapezius pars descendens • M. Trapezius pars transversa | Scapular position (posture assessment) | • Sternocleidomastoideus pars medialis and superficialis Depressed scapular position resulted in a lower PPT compared to normal scapular position on all locations (right m. Upper trapezius: p = 0.021, left m. Upper trapezius: p = 0.011, right m. Middle trapezius: p = 0.030, and left m. Middle trapezius: p = 0.027). |
| (Lemming et al., 2015) Denmark | Non-randomized controlled cohortches | N = 98 Highly active men (22 or 22%): 30.6 y (1.9) ♀ = 0 (0%) Normally active men (26 or 27%): 36 y (2.4) ♀ = 0 (0%) Highly active women (27 or 28%): 34.8 y (1.8) ♀ = 27 (100%) Normally active women (23 or 23%): 35.7 y (2.5) ♀ = 23 (100%) | - 20–65 y - Pain-free | | D: manual pressure algometer (Somedic) S: 30 kPa/s RS: pain A: 1 trial P: not reported | Dominant side: • M. Tibialis anterior | -Gender -Physical activity level (GLTEQ) | Women reported lower PPT than men (p = 0.019) Highly active participants had higher PPT than normally active participants (p = 0.049) |
| (Manning and Fillingim, 2002) USA | Non-randomized controlled cohort | N = 24 20y-24y (no info about mean age and SD) ♀ = 12 (50%) | Athlete group: - Soccer, gymnastics, football, tennis, fencing, crew, and wrestling sports Non-athlete group: -Not participating athletics on an intercollegiate level, but being physically active and participating in ≥ 3 h exercise per week. | Not reported | D: pressure algometer S: 1 kg/s RS: sensation of pressure changed to pain A: mean of all trials (Mäntyselkä et al., 2001; Blyth et al., 2019; Yam et al., 2018; Backonja et al., 2009)P: not reported | Following muscles: • Biceps brachii • Pectoralis • Quadriceps • Deltoideus | -Athletic status (competition team or not) -Gender -Locus of control (RIELCS) -Ability to dissociate (DES) -Gender role attitudes (BSRI) -Coping strategies (CSQ) -Mood states (POMS and STAI) -Physical activity (questionnaire) -Number of injury experience | No overall effect of athletic status on PPT (p > 0.05). No overall effect of gender on PPT (p > 0.05), but non-athletic women had lower PPT at the m. Deltoid (p = 0.013), m. Pectoralis (p = 0.013), and m. Quadriceps (p = 0.028) than non-athletic men. (ES: 0.23–0.37) No effect on PPT (p > 0.05). No effect on PPT (p > 0.05). No effect on PPT (p > 0.05). No effect on PPT (p > 0.05). No effect on PPT (p > 0.05). No effect on PPT (p > 0.05). No effect on PPT (p > 0.05). |

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| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|---|----------------------------------|--|--|---|---|--|---|--|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| (Martínez-Jauand et al., 2013) Argentina | Case-control | N = 32 57.0 y (1.1) ♀ = 32 (100%) Early menopause (17 or 53%) Late menopause (15 or 47%) | -Postmenopausal women -Last menstrual period > 1 y | -Pregnancy -Neurologic disease | D: digital dynamometer (Wagner) S: not reported RS: pain A: not reported P: not reported | Not reported | -Pain-related self-efficacy (own design) Menopause | No difference in PPT between early and late menopause (p > 0.05) |
| (Matos et al., 2011) Denmark | Non-randomized controlled cohort | N = 30 18–25 y (no info about mean age and SD) ♀ = 15 (50%) | - Healthy | - Signs or symptoms of pain, hyperalgesia or allodynia in head, neck, and face region (jaw dysfunction and headaches, subjective pain or soreness of the masticatory muscles) | D: pressure algometer (Somedic) S: 30 kPa/s RS: pain A: mean of 3 trials P: not reported | Bilateral: • Infraorbital foramen • Mental foramen | -Gender | Women reported lower PPT than men (p = 0.006). |
| (McKendall and Haier, 1983) Netherlands | Case-control | N = 60 ♀ 43.78 y (11.22) ♂ 42.92 y (14.67) ♀ = 40 (67%) | Not reported | - < 20 y or > 67 y | D: pressure device with constant and equal pressure of 3 pounds S: not reported (in pounds/s) RS: time to first pain A: mean of 2 trials P: not reported | Dominant side: • First joint of index finger | -Obesity (< or > than 130% of IBW) | The obese group reached sooner the PPT compared to the non-obese group (p < 0.01). If mid-weight participants were excluded (obese > 180% of IBW, and non-obese < 125% of IBW), obese women reported lower PPT than non-obese woman (p < 0.05). Other results were non-significant (p > 0.05). |
| (Moore et al., 2013) UK | Cross-sectional | N = 189 23.65 y (6.15) ♀ = 119 (63%) | Not explicitly reported, but: Patients reported that they were not currently in pain, had no existing chronic pain condition, and were not taking analgesic medication | Not reported | D: pressure pain algometer (Somedic) S: 50 kPa/s RS: first pain A: mean of 5 trials P: not reported | Dominant side: • Back of the hand | -Gender -Pain-related fear and anxiety (PASS) -Anxiety-related symptoms (ASI-3) -Fear of different causes of pain (FPQ-III) -Pain catastrophizing (PCS) -Depression, anxiety, and stress experiences (DASS-21) | Women had lower PPT than men (p < 0.01) (t-test), gender predicted PPT (p < 0.001, R ² = 0.07) No effect on PPT (p > 0.05). No effect on PPT (p > 0.05). No effect on PPT (p > 0.05). No effect on PPT (p > 0.05). |
| (Otto and Dougher, 1985) Mexico | Non-randomized controlled cohort | N = 80 ♀ 22.2 y (SD not reported) ♂ 24.9 y (SD not reported) ♀ = 40 (50%) | Not reported | Not reported | D: focal pain stimulator S: not reported (gradually increase 640 gm) RS: participant reported a 5 on a 7-point Likert scale (slight pain) A: not reported P: not reported | Second phalanx of finger | -Gender -Masculinity /femininity (>50 BSRI) | Women reported lower PPT (p < 0.05). Masculinity-Femininity influenced PPT significantly (p < 0.01) A significant interaction between masculinity-femininity scores and gender for PPT (p < 0.05). |
| (Ozasa et al., 2022) China | Case-control | N = 42 Premenopausal (21 or 50%) 45.2 y (2.4) Early | -Healthy | Not reported | D: not reported S: not reported RS: not reported A: not reported P: not reported | Tip of the tongue | Menopause | None of the results were significant (p > 0.05) |

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| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|------------------------------------|----------------------------------|---|---|--|--|--|---|--|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| (Petersen et al., 1992) Denmark | Non-randomized controlled cohort | postmenopausal (10 or 24%) 55.6 (2.8) Late postmenopausal (11 or 26%) 64.9 (10.8) ♀ = 42 (100%) N = 40 24.2 y (4.1) ♀ = 20 (50%) | - Headache free - Not taken analgesic or psychotropic drugs < 24 h before the test | Not reported | D: pressure algometer (Somedic) S: 1.1 Newton/s RS: lowest pressure that gives a sensation of pain A: 2 trials P: supine | Bilateral: • M. Temporalis with myofascial tissue • M. Temporalis without myofascial tissue • Middle phalanx of second finger | -Gender -Hand dominance | Women reported lower PPT than men at all locations: • Temporalis with myofascial tissue (p = 0.09) • Temporalis without myofascial tissue (p = 0.03) • Second finger (p < 0.05) PPT was higher on the right finger, compared to the left finger in right-handed participants (p = 0.07). Other results were non-significant (p > 0.05). |
| (Petri et al., 2015) Denmark | Non-randomized controlled cohort | N = 40 Younger group (20 or 50%): 24.6 y (3.6) ♀ 10 (50%) Older group (20 or 50%): 73.6 y (6.6) ♀ = 10 (50%) | - Cognitive intact capabilities (MMSE score 28–30) - Pain-free | - Conditions that could affect pain perception and pain report - Presence of severe ongoing pain - Neuropsychological and psychiatric disorders - Diabetes - Signs of rheumatic or arthritic disease especially on hand/fingers and neck/shoulders - Taken any analgesic or sedative < 48 h prior to test | D: electronic hand-held pressure algometer (Somedic) S: 30 kPa/s RS: pain A: mean of 4 trials P: not reported | Bilateral: • Index finger • M. Trapezius | -Age -Gender | Elderly men reported lower PPT compared to young men (p < 0.001). Young women reported lower PPT compared to young men (p < 0.001). Other results were non-significant (p > 0.05). |
| (Pickering et al., 2002) France | Non-randomized controlled cohort | N = 42 Younger group: ♀ 22 y (Raja et al., 2020) ♂ 22 y (Mäntyselkä et al., 2001) Older group: ♀ 74 y (Blyth et al., 2019) ♂ 74 y (Yam et al., 2018) Total of ♀ = 21 (50%) | Inclusion: - 18y-25y (young group) or > 70 y (older group) - Living in the community - Physically and psychologically autonomous - No overt history of cardiovascular Disease - No medication, especially no analgesics - Limited consumption | - Any disorder likely to affect sensory function, neurological and psychiatric antecedents - Cutaneous illness of upper limbs - Alcohol and street drug consumption | D: electronic pressure algometer (Somedic) S: 1.1 Newton/s RS: pain A: mean of 4 trials P: not reported | • Second finger • Third finger • Fourth finger • Fifth finger | -Age -Gender -Cognitive capacities (MMSE) -Psychomotor performance (CRT) | Younger age in men resulted in higher PPT in men (p < 0.001). No effect on PPT (p > 0.05). No effect on PPT (p > 0.05). Correlation between PPT and CRT (p = 0.01, r = -0.52) |

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| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|--------------------------------|----------------------------------|--|--|---|--|---|--|--|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| (Price et al., 2013) Canada | Case-control | N = 40 Obese group (20 or 50%): 26.3 (7.1) ♀ = 10 (50%) Non-obese group (20 or 50%): 26.5 y (7.4) ♀ = 10 (50%) | of tobacco, tea or coffee Extra inclusion (older group): - No decreased finger mobility - No sign of rheumatic or arthritic disease - No pain or uncomfortable sensation on passive and active hand and finger movements - Obesity (BMI \geq 30 kg/cm ²) (obese group) - Non-obesity (control group) | - < 18 y or > 45 y - Habitual use of recreational drugs, tobacco or alcohol - Regular or frequent night shift work - Presence or history of psychiatric or neurological disorder - Diabetes - Hypertension - Chronic pain - Any other severe medical condition as these conditions may be associated with altered pain sensitivity | D: hand-held pressure gauge (Wagner) S: 0.5 kg/s RS: pain A: mean of 3 trials P: not reported | Non-dominant side: • Thenar eminence • Thenar thumbnail | -Obesity (measurement method not reported) | No effect on PPT (p > 0.1). |
| (Rao et al., 2022) Bhopal | Non-randomized controlled cohort | N = 95 Group 1 (25 or 26%): 18y-21y (no info about mean age and SD) ♀ = 25 (100%) Group 2 (20 or 21%): 30y-40y (no info about mean age and SD) ♀ = 20 (100%) Group 3 (25 or 26%): 25y-41y (no info about mean age and SD) ♀ = 25 (100%) Group 4 (25 or 26%): 20y-22y (no info | - Physically and mentally healthy Group 1: studying medical laboratory technology Group 2: housewives and working women Group 3: family planning center and taking oral contraceptives Group 4: medical students | - Consumption of analgesic, antidepressant, anxiolytic drug or hormones | D: metallic aerated water bottle cap and a sphygmomanometer S: 4 mm/Hg RS: pricking pain A: mean of 3 trials (group 1–3), mean of 9 trials (group 4) P: not reported | Flexor surface forearm | Menstrual cycle | PPT varied related to age and menstrual cycle in women. PPT was higher in phase I and II of menstruation in women taking oral contraceptives, while PPT was high only at phase II of the menstrual cycle in women taking no oral contraceptives (p < 0.001). |

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| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|-----------------------------------|----------------------------------|---|---|---|--|---|--|---|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| Shah and Luximon (2021) China | Non-randomized controlled cohort | about mean age and SD) ♀ = 0 (0%) N = 218 ♀ 27.79 y (11.55) ♂ 26.36 y (9.24) ♀ = 109 (50%) | Healthy | -Facial soft tissue or bone deformities | D: a hand-held ultrasound indentation device S: less than 2 mm/s RS: pain A: mean of 3 trials P: not reported | <ul style="list-style-type: none"> • 23 landmarks on head- and forehead region • 13 landmarks on frontal part of the face • 16 landmarks on both sides of the face • 8 landmarks on the neck region | -Age -Gender -BMI | Age correlated with 27 landmarks of the face region in women (p < 0.05). Women reported lower PPT in 67 out of 76 landmarks compared to men (p < 0.05). BMI correlated with 12 landmarks of the face region in men (p < 0.05). Other results were non-significant (p > 0.05). Women had lower PPT than men (p = 0.019). No effect on PPT (p > 0.05). BMR was a predictor of PPT in the overall study population (p = 0.018, r ² = 0.054), but not if accounted for gender (p > 0.05). No effect on PPT (p > 0.05). |
| (Shiro et al., 2017) Japan | Cross-sectional | N = 86 20.9 y (0.8) ♀ = 43 (50%) | - 20y-29y - No ongoing pain problems | -History of chronic pain conditions and serious health conditions such as neurological diseases or diabetes -Use of sedatives, analgesics, or other medications. | D: mechanical pressure algometer (Digital Force Gage) S: 5 Newton/s RS: pain because of pressure A: not reported P: sitting | Dominant side: <ul style="list-style-type: none"> • M. Extensor carpi radialis brevis | -Gender -BMI (scale) -BMR (formula) -Moderate-to-vigorous physical activity (accelerometer past 7 days) transformed to METs | No significant results (p > 0.05). |
| (Sibille et al., 2012) Florida | Cross-sectional | N = 372 23.7 y (SD not reported) ♀ = 205 | - 18y-45y - No report of clinical pain - No psychiatric disturbance or substance disorder - No use of tobacco products or centrally acting medications | Not reported | D: handheld algometer (Pain Diagnostics and Therapeutics) S: 1 kg/s RS: pain because of pressure A: mean of 3 trials P: semi-lying | Right body side: <ul style="list-style-type: none"> • M. Trapezius pars descendens • M. Masseter pars superficialis • ulna | Affect balance style (PANAS) | No significant results (p > 0.05). |
| (da Silva et al., 2014) Brazil | Non-randomized controlled cohort | N = 126 49.4 (23.7) ♀ = 65 (52%) | - Healthy | - Previous trauma or surgery to the face or skull - Orofacial and/or generalized pain - Neuropathic conditions - Neurodegenerative diseases - Neuroendocrine or rheumatological diseases - Neural infections - Chronic use of medication - Nasal obstructions - Allergies or other upper respiratory, gustative abnormalities -Issues before the tests that might interfere with the results | D: electronic pressure algometer (Somedic) S: 50 kPa/s RS: pain A: not reported P: sitting | Bilateral: <ul style="list-style-type: none"> • Front • Cheek • Chin • Anterior tibia skin | -Age -Gender | Participants between 61 and 75 y reported higher PPT compared to participants between 18 and 30 y and between 45 and 60 y (p < 0.001). Women reported higher PPT compared to men (p < 0.001). |
| (Tashani et al., 2017) UK | Case-control | N = 74 Normal BMI (25 or 33%): 28.3 y (9.3) | Not reported | -Pre-existing medical condition - Currently seeking medical care | D: handheld algometer (Somedic) S: 10 kPa/s RS: pain | Non-dominant side: <ul style="list-style-type: none"> • Thenar eminence | BMI (scale) | The obese group had lower PPT compared to the overweight group (p = 0.005) and the normal range group (p = 0.001). |

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Table 4 (continued)

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|---|----------------------------------|---|---|--|--|--|---|--|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| | | Overweight BMI (24 or 33%): 32.7 y (9.1) Obese BMI (25 or 33%): 36.3 (7.5) Total of ♀ = 37 (50%) | | - Taking medication - Experienced pain < 6 m - Previously diagnosed with a chronic pain condition - Experiencing disturbances in skin sensation - Dermatological condition - Pregnant - Regularly undertake vigorous exercise | A: mean of last 3 trials P: not reported | | | Obese and normal BMI women reported lower PPT compared to overweight women (p = 0.002). Higher BMI predicted lower PPT (p = 0.019, r ² = 0.074) Other results were non-significant (p > 0.05). |
| (Teepker et al., 2010) Germany | Prospective cohort | N = 32 27.3 y (6.1) ♀ = 32 (100%) | - Regular menstrual cycle (28 ± 1 day) - Examined by a neurologist and psychologist - Not taking any drugs or oral contraceptives on a regular basis - No use of analgesics and sedatives < 24 h before testing - Right-hand dominant | - Pregnancy - Hypertension - Acute and chronic pain - Endocrine, gynecological, or psychiatric disorders - Peripheral and central neuropathy - Dermatitis at the test side | D: pressure algometer (Somedic) S: 10 kPa/s RS: slight pain A: mean of last 3 trials P: not reported | Left body side: • Forearm | Menstrual cycle | PPT was higher on the 22nd day compared to the 1st day of menstrual cycle (p = 0.004, Bonferroni: p = 0.015) Other results were non-significant (p > 0.05). |
| (Vatine et al., 1993) Israel | Non-randomized controlled cohort | N = 24 ♀ = 14 (58%) Mean age not reported | - Right-hand dominant | - Systemic disease or pain syndrome | D: pressure algometer S: 1 kg/s RS: pain A: not reported P: not reported | Bilateral: • Mastoid processes • External malleolus • Sternum (2 locations) | Gender | No significant differences at all locations (p > 0.05). |
| (Yang et al., 2013) Denmark China | Non-randomized controlled cohort | N = 58 Danish group (29 or 50%): 27.0 y (5.0) ♀ = 15 (50%) Chinese group (29 or 50%): 28.2 y (4.0) ♀ = 15 (50%) | - No experience with similar tests - Born and raised in their home country without migration - ≥ 3 y of university education | - Ongoing pain or reports of chronic pain < 6 m - Serious systemic diseases - Previous radiotherapy or chemotherapy - Intake of medicine affecting the central nervous system - Fibromyalgia - Self-reported bruxism or psychogenic illnesses | D: computerized pressure algometer S: 30 kPa/s RS: first pain A: not reported P: not reported | Bilateral: • M. Masseter • Mandibula | - Ethnicity - Gender | Chinese participants showed lower total (both PPT locations summed) PPT than Danes (p < 0.001, ES: 0.227). Women showed lower total PPT than men (p < 0.001, ES 0.184) |
| (Yang et al., 2014) Denmark | Case-control | N = 70 42.3 y (12.5) ♀ = 36 (51%) | - Healthy | - Participated in any kind of clinical test similar to the present one - Ongoing pain or chronic pain < 6 m - Systemic diseases or previous radio or chemotherapy - Taken any medicine < 1 week that affects the nervous system - Physical or mental disorders | D: computerized pressure algometer S: 30 kPa/s RS: first pain A: not reported P: not reported | Bilateral: • M. Masseter • M. Temporalis • Thenar | - Age - Gender | None of the results were significant (p > 0.05). |

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| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|----------------------------|------------------------|--|--|--|--|---|---|--|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| (You et al., 2020) USA | Case-control | N = 177 Group 1 (43 or 24%): 18.7 y (1.2) ♀ = 23 (53%) Group 2 (23 or 13%): 20.3 y (2.0) ♀ = 6 (26%) Group 3 (50 or 28%): 20.1 y (2.5) ♀ = 25 (50%) Group 4 (25 or 14%): 19.6 y (2.3) ♀ = 11 (44%) Group 5 (36 or 20%): 19.8 y (1.8) ♀ = 21 (58%) | -Healthy adults 18y-30y Group 1: abstainers Group 2: moderate drinkers with recent drinking episode Group 3: moderate drinkers without recent drinking episode Group 4: binge drinkers with a recent drinking episode Group 5: binge drinkers without recent drinking | - Women: being in their menstrual period - Any chronic physical and mental health issues - Prescription medication use (except contraceptives and vitamins) - Needle phobia - Injury or skin condition on the feet (pain testing site) | D: handheld algometer (Wagner) S: Not explicitly reported (according to Rolke et al.: 30 kPa/s) RS: not reported A: mean of 3 trials P: Not reported | Non-dominant side: • Dorsum foot | -Drinking history -Standard drinks and hours spent drinking for a typical week (DDQ) | PPT was different between groups (p < 0.001). Group 5 had lower PPT compared to group 3 (p = 0.013). Moderate drinking was associated with an increase, binge drinking was associated with a decrease in PPT. Group 4 showed reduced PPT compared to all the other groups (p < 0.005). Other results were non-significant (p > 0.05). |
| (Zhang et al., 2013) China | Epidemiological cohort | N = 2517 18y-85y (No info about mean age and SD) ♀ = 0 (0%) | -Men | - History of rheumatoid arthritis, gout, diabetes, or cancer - History of chronic prostatitis - Anti-inflammation medication < 4weeks | D: digital pressure algometer (Wagner) S: 1 kg/cm2/s RS: unpleasant pain sensation A: mean of both sides (1 trial) P: not reported | Bilateral: • M. Triceps • Inguinal line | -Age -BMI (scale and stadiometer) -Waist circumference -SBP and DBP (sphygmomanometer) -Education (interview) -Manual occupation (interview) -Leisure time physical exercise (interview) -Smoking (interview) -Drinking (interview) -Obesity within age groups | Younger age resulted in lower PPT (p < 0.001) on both locations. -Lower BMI resulted in higher PPT (p < 0.001) at m. Triceps. -Correlation between BMI and PPT at m. Triceps (p < 0.001, r = -0.119) -Smaller waist circumference resulted in higher PPT on both locations (p < 0.001) -Correlation between waist circumference and PPT at m. Triceps (p < 0.001, r = -0.150). -The PPT at m. Triceps had a negative association with waist -Lower PPT at m. Triceps was found in men with waist circumference ≥ 90 cm in all age groups (p < 0.05) (95%CI= -0.122 to -0.038). -A SBP (p = 0.005) and DPB (p = 0.048) difference between participants with a lower, middle or higher PPT at inguinal line. -Correlation between DBP and PPT at m. Triceps (p = 0.041, r = -0.041). -Higher level of education resulted in lower PPT on both locations (p < 0.001) |

(continued on next page)

Table 4 (continued)

| Author, year and origin | Study Design | Participants | | | Device, speed, and analysis of PPT Reported signal and position of patient | Location of PPT | Influencing factor (measurement method) | Results (p value + ES or correlation coefficient [r] if significant and if reported) |
|-------------------------|--------------|---------------------------------------|--------------------|-----------|--|-----------------|--|--|
| | | Group composition and characteristics | Inclusion criteria | Exclusion | | | | |
| | | | | | | | <ul style="list-style-type: none"> - Higher level of education resulted in lower PPT on both locations (p < 0.001) after age and BMI adjustment. -Non-manual occupation resulted in lower PPT on both locations (p < 0.001), also after age and BMI adjustment (p < 0.001). -Moderate or high leisure time physical exercise resulted in lower PPT (p < 0.001 for m. Triceps, p = 0.006 for Inguinal line), also after age and BMI adjustment on both locations (p < 0.001). No effect on PPT (p > 0.05). -Drinking more alcohol resulted in higher PPT at m. Triceps (p < 0.001 or age and BMI adjusted: p = 0.005) and inguinal line (p = 0.008). -Central obesity resulted in lower PPT on both locations (p < 0.001 at m. Triceps, p = 0.001 at inguinal line) after age and BMI adjustment. -Lower PPT at inguinal line in central obesity men in age group 40–50 y (p = 0.03) -Lower PPT at m. Triceps in total obesity men only in age group ≥ 40 y. | |

Abbreviations: 6MWT, 6-minute walk-test; A, analysis; ASI-3, Anxiety Sensitivity Index; BDI, Beck Depression Index; BMI, body mass index; BMI, Body Mass Index; BMI, Body Mass Index; BMR, Basal Metabolic Rate; BSI, Brief Symptom Inventory; BSRI, Bem Gender Role Inventory; CIRS-CI, Cumulative Illness Rating Scale – Comorbidity Index; cm, centimetre; CPT, Cold Pressure Test; CRT, choice reaction time; CS, 30 s Chair-to-stand-test; CSQ, Coping Strategies Questionnaire; CV, cardiovascular; D, device; DASS-21, Depression Anxiety Stress Questionnaire-21; DBP, diastolic blood pressure; DDQ, Daily Drinking Questionnaire; DES, Dissociative Experiences Scale; DGSM, German Sleep Society; DGSM, German Sleep Society; ES, effect size; FPQ-III, Fear of Pain Questionnaire; FPT, filament pin-prick pain threshold; g, gram; GDS-sf, Geriatric Depression Scale-short form; GLTEQ, Godin Leisure-Time Exercise Questionnaire; h, hour; IADL, Instrumental Activities of Daily Living; IBW, Ideal Body Weight; JNP, Just Noticeable Pain; kg, kilogram; kPa, kilopascal; KRS, Kohn Reactivity Scale; m., muscle; MAP, mean arterial blood pressure; METs, Metabolic Equivalents; MMSE, Mini-mental test; MSK, musculoskeletal; N, Newton; N, sample size; NDI, Neck Disability Index; NDI, Neck Disability Index; NSAID, Non-steroidal anti-inflammatory agents; P, position; PANAS, Positive and Negative Affect Scale; PANAS, Positive and Negative Affect Scale; PASS, Pain Anxiety Symptoms Scale; PCS, Pain Catastrophizing Scale; PMS, Profile of Moods States; PPT, pressure pain threshold; PPT, Pressure Pain Threshold; PVAQ, Pain Vigilance and Awareness Questionnaire; REM, rapid-eye movement; RIELCS, Rotter Internal-External Locus of Control Scale; RS, reported signal; s, second; S, speed (increase in force); SBP, systolic blood pressure; SBP, systolic blood pressure; SCQ, Situational Catastrophizing Questionnaire; SD, Standard Deviation; SES, Schmerzempfindungsskala; SPMSQ, Short Portable Mental Status Questionnaire; STAI, State Trait Anxiety Inventory; TDT, tactile detection threshold; TMD, Temporomandibular Disorder; TTH, tension type headache; VAS, Visual Analogue Scale; y, years of age

1985; Rao et al., 2022; Amodei and Nelson-Gray, 1989; Chesterton et al., 2003; Komiyama and De Laat, 2005; Komiyama et al., 2007; Kröner-Herwig et al., 2012; Lee et al., 1994; Lemming et al., 2015; Matos et al., 2011; McKendall and Haier, 1983; Petersen et al., 1992; da Silva et al., 2014; Vatine et al., 1993; Donat et al., 2005; Martínez-Jauand et al., 2013) received a low, moderate and high RoB score, respectively. After scoring, reviewers agreed on 57.1% of the domains (Kappa value: 0.34) and 67.8% of the sub-domains (Kappa value: 0.41), but a full agreement was achieved after discussion. In most studies the domain “Study attrition” and “Study confounding” were not applicable due to the study design, and therefore not considered for the judgement of overall RoB score. Limited reporting of study attrition in prospective studies and limited reporting of study participation in cross-sectional and

case-control studies were the main reasons for attaining a higher RoB score (Table 5). Regarding the LoE, four studies received a LoE 3 (Dawson and List, 2009; Girotti et al., 2019; Yang et al., 2013; Petrini et al., 2015), 39 studies a LoE 4 (Alfieri et al., 2017; Alves et al., 2017; Andrzejewski et al., 2010; Azevedo et al., 2008; Campbell et al., 2010; Cimino et al., 2000; De Rui et al., 2015; Fedders et al., 2019; Garcia et al., 2007; Holmgaard et al., 2017; Isselée et al., 2001; Jones et al., 2016; Karmann et al., 2018; Lautenbacher et al., 2005; Manning and Fillingim, 2002; Pickering et al., 2002; Shiro et al., 2017; Teepker et al., 2010; Yang et al., 2014; Zhang et al., 2013; Shah and Luximon, 2021; Bajaj et al., 2001; Cole et al., 2010; Edwards and Fillingim, 2001; Otto and Dougher, 1985; Rao et al., 2022; Amodei and Nelson-Gray, 1989; Chesterton et al., 2003; Komiyama and De Laat, 2005; Komiyama et al.,

Table 5
Quality assessment.

| Study | 1 | 2 | 3 | 4 | 5 | 6 | Overall RoB | LoE |
|--------------------------------|----------|----------|----------|----------|------|----------|-----------------|-----|
| (Alfieri et al., 2017) | Low | N/A | Low | Moderate | N/A | Low | Low | 4 |
| (Alves et al., 2017) | High | High | Low | Moderate | High | Low | High | 4 |
| (Amodei and Nelson-Gray, 1989) | High | High | Moderate | Moderate | N/A | Moderate | High | 4 |
| (Andrzejewski et al., 2010) | High | N/A | Moderate | Moderate | N/A | Moderate | High | 4 |
| (Azevedo et al., 2008) | Moderate | N/A | Low | Moderate | N/A | Low | Moderate | 4 |
| (Bajaj et al., 2001) | High | High | Moderate | Moderate | N/A | High | High | 4 |
| (Campbell et al., 2015) | Moderate | N/A | Low | Low | N/A | Low | Low | 4 |
| (Chesterton et al., 2003) | High | N/A | Low | Moderate | N/A | Low | High | 4 |
| (Cimino et al., 2000) | High | High | Moderate | Low | High | Moderate | High | 4 |
| (Cole et al., 2010) | High | N/A | Low | Moderate | N/A | Moderate | High | 4 |
| (Dawson and List, 2009) | Low | N/A | Low | Moderate | N/A | Moderate | Moderate | 3 |
| (De Rui et al., 2015) | Moderate | N/A | Low | Moderate | N/A | Moderate | High | 4 |
| (Donat et al., 2005) | Moderate | N/A | Low | Moderate | N/A | Moderate | High | 4 |
| (Edwards and Fillingim, 2001) | High | N/A | Low | Moderate | N/A | Moderate | High | 4 |
| (Fedders et al., 2019) | Low | N/A | Low | Moderate | N/A | Low | Low | 4 |
| (Garcia et al., 2007) | High | High | Moderate | Low | High | Low | High | 4 |
| (Girotti et al., 2019) | Moderate | N/A | Low | Low | N/A | Low | Low | 3 |
| (Hastie et al., 2012) | Moderate | N/A | Moderate | Moderate | N/A | Low | High | 5 |
| (Holmgaard et al., 2017) | High | N/A | Low | Moderate | N/A | Moderate | High | 4 |
| (Isselée et al., 2001) | High | High | High | Moderate | High | Low | High | 4 |
| (Jones et al., 2016) | Low | N/A | Moderate | Moderate | N/A | Low | Moderate | 4 |
| (Karmann et al., 2018) | High | High | Low | Moderate | N/A | Low | High | 4 |
| (Kocur et al., 2019) | High | N/A | Moderate | Moderate | N/A | Low | High | 5 |
| (Komiyama and De Laat, 2005) | High | N/A | Low | Moderate | N/A | Moderate | High | 4 |
| (Komiyama et al., 2007) | High | N/A | Low | Moderate | N/A | Low | High | 4 |
| (Kröner-Herwig et al., 2012) | High | N/A | Low | Moderate | N/A | Low | High | 5 |
| (Kuppens et al., 2018) | High | N/A | Moderate | Moderate | N/A | Moderate | High | 5 |
| (Lautenbacher et al., 2005) | Moderate | N/A | Low | Moderate | N/A | Low | Moderate | 4 |
| (Lee et al., 1994) | High | N/A | Low | Moderate | N/A | Moderate | High | 4 |
| (Lee et al., 2015) | Moderate | N/A | Moderate | Moderate | N/A | Low | High | 5 |
| (Lemming et al., 2015) | Moderate | N/A | Moderate | Moderate | N/A | Moderate | High | 4 |
| (Manning and Fillingim, 2002) | High | N/A | Moderate | Moderate | N/A | Moderate | High | 4 |
| (Martínez-Jauand et al., 2013) | High | N/A | Moderate | Moderate | N/A | Moderate | High | 5 |
| (Matos et al., 2011) | High | N/A | Low | Moderate | N/A | Low | High | 4 |
| (McKendall and Haier, 1983) | High | N/A | Moderate | High | N/A | Moderate | High | 5 |
| (Moore et al., 2020) | High | N/A | Low | Moderate | N/A | Low | High | 5 |
| (Otto and Dougher, 1985) | High | N/A | Moderate | Moderate | N/A | Moderate | High | 4 |
| (Ozasa et al., 2022) | High | N/A | Moderate | High | N/A | Low | High | 5 |
| (Petersen et al., 1992) | High | N/A | Moderate | Moderate | N/A | Low | High | 4 |
| (Petrini et al., 2015) | Moderate | N/A | Low | Moderate | N/A | Low | Moderate | 3 |
| (Pickering et al., 2020) | High | N/A | Moderate | Moderate | N/A | Low | High | 4 |
| (Price et al., 2013) | Low | N/A | Moderate | Moderate | N/A | Low | Moderate | 4 |
| (Rao et al., 2022) | High | High | High | Moderate | High | Moderate | High | 4 |
| (Shah and Luximon, 2021) | High | N/A | Low | Moderate | N/A | Low | High | 4 |
| (Shiro et al., 2017) | Moderate | N/A | Low | Moderate | N/A | Low | Moderate | 4 |
| (Sibille et al., 2012) | High | N/A | Low | Moderate | N/A | Moderate | High | 5 |
| (da Silva et al., 2014) | High | N/A | Low | High | N/A | Low | High | 4 |
| (Tashani et al., 2017) | Moderate | N/A | Low | Moderate | N/A | Low | Moderate | 4 |
| (Teepker et al., 2010) | Moderate | Moderate | Low | Moderate | N/A | Moderate | High | 4 |
| (Vatine et al., 1993) | High | N/A | Low | Moderate | N/A | Moderate | High | 4 |
| (Yang et al., 2013) | Low | N/A | Low | Moderate | N/A | Low | Low | 3 |
| (Yang et al., 2014) | Low | N/A | Low | Moderate | N/A | Moderate | Moderate | 4 |
| (You et al., 2020) | High | N/A | Moderate | High | N/A | Moderate | High | 5 |
| (Zhang et al., 2013) | Low | High | Moderate | Moderate | N/A | Low | High | 4 |

Abbreviations: LoE= Level of Evidence, N/A= not applicable

Bias due to 1 = Study Participation, 2 = Study attrition, 3 = Prognostic factor measurement, 4 = Outcome measurement, 5 = Study Confounding, 6 = Statistical Analysis and Reporting

2007; Lee et al., 1994; Lemming et al., 2015; Matos et al., 2011; Petersen et al., 1992; Price et al., 2013; da Silva et al., 2014; Tashani et al., 2017; Vatine et al., 1993; Donat et al., 2005), and 11 studies a LoE 5 (Hastie et al., 2005; Kocur et al., 2019; Kuppens et al., 2018; Lee et al., 2015; Moore et al., 2013; Sibille et al., 2012; You et al., 2020; Ozasa et al., 2022; Kröner-Herwig et al., 2012; McKendall and Haier, 1983; Martínez-Jauand et al., 2013). None of the prospective cohort studies scored LoE 3, because their overall RoB was high.

3.3. PPT measurement & locations

Forty-six studies (Alfieri et al., 2017; Alves et al., 2017; Andrzejewski et al., 2010; Azevedo et al., 2008; Campbell et al., 2010; Cimino et al., 2000; Dawson and List, 2009; De Rui et al., 2015; Fedders et al., 2019; Garcia et al., 2007; Girotti et al., 2019; Hastie et al., 2005; Holmgaard et al., 2017; Isselée et al., 2001; Jones et al., 2016; Karmann et al., 2018; Kocur et al., 2019; Kuppens et al., 2018; Lautenbacher et al., 2005; Lee et al., 2015; Manning and Fillingim, 2002; Moore et al., 2013; Pickering et al., 2002; Shiro et al., 2017; Sibille et al., 2012; Teepker et al., 2010; Yang et al., 2013, 2014; You et al., 2020; Zhang et al., 2013; Bajaj et al., 2001; Edwards and Fillingim, 2001; Chesterton et al., 2003; Komiyama and De Laat, 2005; Komiyama et al., 2007; Kröner-Herwig et al., 2012; Lee et al., 1994; Lemming et al., 2015; Matos et al., 2011; Petersen et al., 1992; Petrini et al., 2015; Price et al., 2013; Tashani et al., 2017; Vatine et al., 1993) used an algometer as device to determine PPT (Alves et al., 2017; Campbell et al., 2010; Cimino et al., 2000; Fedders et al., 2019; Holmgaard et al., 2017; Isselée et al., 2001; Moore et al., 2013; Pickering et al., 2002; Teepker et al., 2010; Bajaj et al., 2001; Edwards and Fillingim, 2001; Komiyama and De Laat, 2005; Komiyama et al., 2007; Lee et al., 1994; Lemming et al., 2015; Matos et al., 2011; Petersen et al., 1992; Petrini et al., 2015; Tashani et al., 2017). A strain-gauge pain stimulator (Amodei and Nelson-Gray, 1989), a focal pain stimulator (Otto and Dougher, 1985), a digital dynamometer (Martínez-Jauand et al., 2013), a dolorimeter (Donat et al., 2005), a hand-held ultrasound indentation device (Shah and Luximon, 2021), a hydraulically driven device (Cole et al., 2010) and a water bottle cap and sphygmomanometer (Rao et al., 2022) were used in the other studies. Kilopascal (kPa) served as the most prevalent unit (Alves et al., 2017; Campbell et al., 2010; Cimino et al., 2000; Dawson and List, 2009; Fedders et al., 2019; Holmgaard et al., 2017; Isselée et al., 2001; Karmann et al., 2018; Lautenbacher et al., 2005; Moore et al., 2013; Teepker et al., 2010; Yang et al., 2013, 2014; You et al., 2020; Bajaj et al., 2001; Edwards and Fillingim, 2001; Komiyama and De Laat, 2005; Komiyama et al., 2007; Lee et al., 1994; Lemming et al., 2015; Matos et al., 2011; Petrini et al., 2015; da Silva et al., 2014; Tashani et al., 2017), followed by kilogram force (kgf) (Alfieri et al., 2017; Andrzejewski et al., 2010; De Rui et al., 2015; Garcia et al., 2007; Hastie et al., 2005; Jones et al., 2016; Kuppens et al., 2018; Lee et al., 2015; Sibille et al., 2012; Zhang et al., 2013; Cole et al., 2010; Otto and Dougher, 1985; Amodei and Nelson-Gray, 1989; Kröner-Herwig et al., 2012; Price et al., 2013; Vatine et al., 1993; Donat et al., 2005), Newton (N) (Azevedo et al., 2008; Girotti et al., 2019; Kocur et al., 2019; Pickering et al., 2002; Shiro et al., 2017; Chesterton et al., 2003; Petersen et al., 1992), millimetres of mercury (mmHg) (Rao et al., 2022), pounds (McKendall and Haier, 1983) and millimetres (mm) (Shah and Luximon, 2021). Speed of pressure administration differed between 20 kPa/s (Cimino et al., 2000) and 50 kPa/s (Alves et al., 2017; Karmann et al., 2018; Moore et al., 2013; da Silva et al., 2014), between 0.1 kg/s (Andrzejewski et al., 2010; De Rui et al., 2015) and 1 kg/s (Alfieri et al., 2017; Garcia et al., 2007; Hastie et al., 2005; Jones et al., 2016; Kuppens et al., 2018; Manning and Fillingim, 2002; Sibille et al., 2012; Zhang et al., 2013; Kröner-Herwig et al., 2012; Vatine et al., 1993; Donat et al., 2005), between 1.1 N/s (Pickering et al., 2002; Petersen et al., 1992) and 5 N/s (Shiro et al., 2017; Chesterton et al., 2003), 4 mmHg/s (Rao et al., 2022), less than 2 mm/s (Shah and Luximon, 2021), or was not given (Girotti et al., 2019; Kocur et al., 2019; Lee et al., 2015; Amodei and Nelson-Gray,

1989; McKendall and Haier, 1983; Martínez-Jauand et al., 2013). There was a wide variety in locations assessed, but locations could be pooled into different body regions: lower arm/hand region (Alfieri et al., 2017; Alves et al., 2017; Andrzejewski et al., 2010; Girotti et al., 2019; Hastie et al., 2005; Isselée et al., 2001; Karmann et al., 2018; Kuppens et al., 2018; Lautenbacher et al., 2005; Moore et al., 2013; Pickering et al., 2002; Shiro et al., 2017; Teepker et al., 2010; Yang et al., 2014; Cole et al., 2010; Rao et al., 2022; Amodei and Nelson-Gray, 1989; Chesterton et al., 2003; Komiyama and De Laat, 2005; Komiyama et al., 2007; Kröner-Herwig et al., 2012; McKendall and Haier, 1983; Petersen et al., 1992; Petrini et al., 2015, 2015; Price et al., 2013; Tashani et al., 2017; Donat et al., 2005), shoulder girdle/upper arm region (Alfieri et al., 2017; Andrzejewski et al., 2010; Campbell et al., 2010; De Rui et al., 2015; Fedders et al., 2019; Jones et al., 2016; Kocur et al., 2019; Kuppens et al., 2018; Manning and Fillingim, 2002; Zhang et al., 2013; Bajaj et al., 2001; Lee et al., 1994; Petrini et al., 2015; Vatine et al., 1993), neck region (Azevedo et al., 2008; Campbell et al., 2010; De Rui et al., 2015; Hastie et al., 2005, 2005; Kocur et al., 2019; Kuppens et al., 2018; Lee et al., 2015; Sibille et al., 2012; Edwards and Fillingim, 2001; Lee et al., 1994; Petrini et al., 2015), leg region (Alfieri et al., 2017; Andrzejewski et al., 2010; Holmgaard et al., 2017; Jones et al., 2016; Kuppens et al., 2018; Manning and Fillingim, 2002; Zhang et al., 2013; Bajaj et al., 2001; Lemming et al., 2015; Vatine et al., 1993), face region (Alves et al., 2017; Cimino et al., 2000; De Rui et al., 2015; Fedders et al., 2019; Hastie et al., 2005; Holmgaard et al., 2017; Isselée et al., 2001; Yang et al., 2013, 2014; Shah and Luximon, 2021; Edwards and Fillingim, 2001; Komiyama and De Laat, 2005; Komiyama et al., 2007; Lee et al., 1994; Matos et al., 2011; Petersen et al., 1992; Vatine et al., 1993) or other (e.g. tongue (Ozasa et al., 2022), head (Shah and Luximon, 2021), or different body regions pooled by the authors of the included studies or if only one study examined a specific body region (Garcia et al., 2007); da Silva et al., 2014). Calculation and reported signal to stop the measurement was comparable between studies, but details can be found in Table 4.

3.4. (Possible) influencing factors

Activities of daily living (ADL) (Girotti et al., 2019), age (Andrzejewski et al., 2010; De Rui et al., 2015; Girotti et al., 2019; Lautenbacher et al., 2005; Pickering et al., 2002; Yang et al., 2014; Zhang et al., 2013; Shah and Luximon, 2021; Cole et al., 2010; Edwards and Fillingim, 2001; Komiyama and De Laat, 2005; Komiyama et al., 2007; Lee et al., 1994; Petrini et al., 2015; da Silva et al., 2014; Donat et al., 2005); alcohol consumption (You et al., 2020; Zhang et al., 2013), blood pressure (Zhang et al., 2013; Edwards and Fillingim, 2001; Kröner-Herwig et al., 2012), body mass index (BMI) (Fedders et al., 2019; Girotti et al., 2019; Shiro et al., 2017; Zhang et al., 2013; Shah and Luximon, 2021; Komiyama and De Laat, 2005; McKendall and Haier, 1983; Price et al., 2013; Tashani et al., 2017), cognitive factors (depression (Campbell et al., 2010; Manning and Fillingim, 2002; Moore et al., 2013; Kröner-Herwig et al., 2012), pain catastrophizing (Campbell et al., 2010; Hastie et al., 2005; Kuppens et al., 2018; Moore et al., 2013; Kröner-Herwig et al., 2012), pain vigilance (Hastie et al., 2005; Kuppens et al., 2018; Kröner-Herwig et al., 2012), affect (Hastie et al., 2005; Sibille et al., 2012), cognitive capacities (Girotti et al., 2019; Manning and Fillingim, 2002; Pickering et al., 2002), fear (Moore et al., 2013), self-efficacy (Manning and Fillingim, 2002), and ability to dissociate and locus of control (Manning and Fillingim, 2002)), comorbidity (Girotti et al., 2019; Manning and Fillingim, 2002), contraceptives (Isselée et al., 2001), hair colour (Holmgaard et al., 2017), education (De Rui et al., 2015; Girotti et al., 2019; Zhang et al., 2013), ethnicity (Dawson and List, 2009; Yang et al., 2014; Komiyama et al., 2007), forward head posture (Kocur et al., 2019), function (Alfieri et al., 2017), gender (Dawson and List, 2009; De Rui et al., 2015; Fedders et al., 2019; Garcia et al., 2007; Girotti et al., 2019; Holmgaard et al., 2017; Isselée et al., 2001; Jones et al., 2016; Lautenbacher et al., 2005; Manning and

Table 6
Strength of Recommendation table (qualitative approach).

| Influencing factor | Study | Location of PPT measurement | Influence (+) or not (-) | Direction of influence | Level of evidence | Subgroup SoR (if possible) | Overall SoR |
|----------------------------|------------------------------|-----------------------------------|---|--|-----------------------|-----------------------------|----------------------------------|
| Age | Andrzejewski, 2010 (41) | Lower arm/hand region | + | Younger = higher PPT | 4 | } Conflicting | } Conflicting |
| | Cole, 2010 (72) | | + | Younger = higher PPT | 4 | | |
| | Girotti, 2019 (49) | | + | Younger = higher PPT | 4 | | |
| | Lautenbacher, 2005 (57) | | + | Younger = higher PPT | 4 | | |
| | Petrini, 2015 (86) | | + | Younger = higher PPT | 3 | | |
| | Pickering, 2002 (61) | | + | Younger = higher PPT | 4 | | |
| | Donat, 2005 (91) | | - | | 4 | | |
| | Komiyama, 2005 (78) | | - | | 4 | | |
| | Komiyama, 2007 (79) | | - | | 4 | | |
| | Yang, 2014 (66) | | - | | 4 | | |
| | Lee, 1994 (81) | Shoulder girdle/arm region* | + | Older = higher PPT | 4 | } Conflicting | |
| | Zhang, 2013 (68) | | + | Older = higher PPT | 4 | | |
| | Andrzejewski, 2010 (41) | | + | Younger = higher PPT | 4 | | |
| | Lee, 1994 (81) | Neck region | + | Older = higher PPT | 4 | } Conflicting | |
| | Petrini, 2015 (86) | | + | Younger = higher PPT | 3 | | |
| | De Rui, 2015 (46) | | - | | 4 | | |
| | Edwards, 2001 (73) | Face region | - | | 4 | } Conflicting | |
| | Shah, 2021 (69) | | - | | 4 | | |
| | Lee, 1994 (81) | | + | Older = higher PPT | 4 | | |
| | Shah, 2021 (69) | | +/- | Older = higher PPT (only in women) | 4 | | |
| | De Rui, 2015 (46) | | - | | 4 | | |
| | Edwards, 2001 (73) | | - | | 4 | | |
| | Komiyama, 2005 (78) | | - | | 4 | | |
| Komiyama, 2007 (79) | - | | | 4 | | | |
| Yang, 2014 (66) | - | | | 4 | | | |
| Zhang, 2013 (68) | Leg region | | + | Older = higher PPT | 4 | | } Conflicting |
| Andrzejewski, 2010 (41) | | + | Younger = higher PPT | 4 | | | |
| Shah, 2021 (69) | Head region | - | | 4 | | | |
| Da Silva, 2014 (88) | Face region + Tibia | + | Older = higher PPT | 4 | | | |
| Alcohol Consumption | You, 2020 (67) | Foot | + | More alcohol = lower PPT | 5 | } Conflicting | |
| | Zhang, 2013 (68) | Upper arm, inguinal line | + | More alcohol = higher PPT | 4 | | |
| Blood pressure* | Zhang, 2013 (68) | Shoulder girdle/upper arm region | + | Association PPT and SBP, not DBP | 4 | } Conflicting | } Conflicting |
| | Kröner-Herwig, 2012 (80) | | - | | 5 | | |
| | Edwards, 2001 (73) | Neck, face region | + | Higher SBP and MAP = higher PPT | 4 | | |
| | Zhang, 2013 (68) | Inguinal line | + | Higher SBP and DBP = higher PPT | 4 | | |
| BMI* | McKendall, 1982 (84) | Lower arm/hand region | + | Lower BMI = higher PPT | 5 | } Conflicting | } Conflicting |
| | Tashani, 2017 (89) | | + | Lower BMI = higher PPT | 4 | | |
| | Price, 2013 (87) | | - | | 4 | | |
| | Shiro, 2013 (62) | - | | 4 | | | |
| | Girotti, 2019 (49) | - | | 3 | | | |
| | Komiyama, 2005 (78) | - | | 4 | | | |
| | Zhang, 2013 (68) | Shoulder girdle/upper arm region* | + | Lower BMI = higher PPT | 4 | } Conflicting | |
| | Fedders, 2019 (47) | | + | | 4 | | |
| | Shah, 2021 (69) | Face region | +/- | | 4 | } Weak SoR for no influence | |
| | Komiyama, 2005 (78) | | - | | 4 | | |
| | Fedders, 2019 (47) | - | | 4 | | | |
| Shah, 2021 (69) | Neck region | - | | 4 | | | |
| Shah, 2021 (69) | Head region | - | | 4 | | | |
| Zhang, 2013 (68) | Inguinal line | - | | 4 | | | |
| Cognitive factor | Ability to dissociate | Manning, 2002 (59) | Shoulder girdle/upper arm region, thigh | - | 4 | | Preliminary SoR for no influence |
| | | Affect | Sibille, 2012 (63) | Shoulder, neck, face, lower arm region | - | 5 | } Very weak SoR for no influence |
| Hastie, 2005 (97) | - | | 5 | | | | |
| Catastrophizing | Campbell, 2010 (43) | Shoulder girdle, neck region | +/- | Only CSQ predicted PPT | 4 | } Conflicting | |
| | | | Hastie, 2005 (97) | + | Association CSQ – PPT | | 5 |
| | Kuppens, 2018 (56) | - | | 5 | | | |
| | Hastie, 2005 (97) | Lower arm/hand | + | Association CSQ – PPT | 5 | | |

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Table 6 (continued)

| | | | | | | | |
|-----------------------------|--------------------------|---|----------------------|------------------------------------|---|---|---------------------------------|
| Cognitive impairment | Moore, 2013 (60) | region | - | | 5 | } Conflicting | } Conflicting |
| | Kröner-Herwig, 2012 (80) | | - | | 5 | | |
| | Kuppens, 2018 (56) | | - | | 5 | | |
| | Hastie, 2005 (97) | Face region | + | Association CSQ – PPT | 5 | | |
| | Kuppens, 2018 (56) | Lower leg | - | | 5 | | |
| Depression | Girotti, 2019 (49) | Hand region | + | Cognitive impairment = lower PPT | 3 | } Conflicting | } Conflicting |
| | Pickering, 2002 (61) | | - | | 4 | | |
| Fear | Manning, 2002 (59) | Shoulder girdle/upper arm region, thigh | - | | 4 | } Weak SoR for no influence } Very weak SoR for no influence | } Moderate SoR for no influence |
| | Campbell, 2010 (43) | Shoulder girdle/upper arm region | - | | 4 | | |
| | Manning, 2002 (59) | | - | | 4 | | |
| | Kröner-Herwig, 2012 (80) | Lower arm/hand region | - | | 5 | | |
| | Moore, 2013 (60) | Leg region | - | | 5 | | |
| Locus of control | Moore, 2013 (60) | Hand | - | | 5 | } Preliminary SoR for no influence | |
| | Manning, 2002 (59) | Shoulder girdle/upper arm region, thigh | - | | 4 | | |
| Pain vigilance* | Hastie, 2005 (97) | Shoulder, neck, face, lower arm region | + | Higher hypervigilance = higher PPT | 5 | } Conflicting | |
| | Kuppens, 2018 (56) | Shoulder, neck, hand, lower leg region | - | | 5 | | |
| Self-efficacy | Kröner-Herwig, 2012 (80) | Forearm | - | | 5 | } Preliminary SoR for no influence | |
| | Manning, 2002 (59) | Shoulder girdle/upper arm region, thigh | - | | 4 | | |
| Comorbidity | Girotti, 2019 (49) | Wrist | + | More comorbidities = lower PPT | 3 | } Conflicting | |
| | Manning, 2002 (59) | Shoulder girdle/upper arm region, thigh | - | | 4 | | |
| Education | Zhang, 2013 (68) | Upper arm, inguinal line | + | Higher education = lower PPT | 4 | } Conflicting | |
| | De Rui, 2015 (46) | Face, neck, hand | - | | 4 | | |
| | Girotti, 2019 (49) | Wrist | - | | 3 | | |
| Ethnicity | Yang, 2013 (65) | Face | + | Chinese = lower PPT than Danes | 4 | } Conflicting | |
| | Dawson, 2009 (45) | ? | - | | 3 | | |
| | Komiyama, 2007 (79) | Lower arm/hand | - | | 4 | | |
| Gender* | Chesterton, 2003 (77) | Lower arm/hand region* | + | Women = lower PPT | 4 | } Conflicting } See following page } Conflicting | |
| | Girotti, 2019 (49) | | + | Women = lower PPT | 3 | | |
| | Komiyama, 2005 (78) | | + | Women = lower PPT | 4 | | |
| | Komiyama, 2007 (79) | | + | Women = lower PPT | 4 | | |
| | Kröner-Herwig, 2012 (80) | | + | Women = lower PPT | 5 | | |
| | Moore, 2013 (60) | | + | Women = lower PPT | 5 | | |
| | Otto, 1985 (74) | | + | Women = lower PPT | 4 | | |
| | Petersen, 1992 (85) | | + | Women = lower PPT | 4 | | |
| | Petrini, 2015 (86) | | + | Women = lower PPT | 3 | | |
| | Shiro, 2017 (62) | | + | Women = lower PPT | 4 | | |
| | Isselée, 2001 (52) | | - | | 4 | | |
| | Lautenbacher, 2005 (57) | | - | | 4 | | |
| | Pickering, 2002 (61) | | - | | 4 | | |
| | Yang, 2014 (66) | | - | | 4 | | |
| | De Rui, 2015 (46) | Shoulder girdle/upper arm region | + | Women = lower PPT | 4 | | |
| | Lee, 1994 (81) | | + | Women = lower PPT | 4 | | |
| | Manning, 2002 (59) | | + | Non athletic women = lower PPT | 4 | | |
| | Petrini, 2015 (86) | | + | Women = lower PPT | 3 | | |
| | Bajaj, 2001 (71) | | - | | 4 | | |
| | Fedders, 2019 (47) | | - | | 4 | | |
| | Jones, 2016 (53) | | - | | 4 | | |
| | Vatine, 1993 (90) | | - | | 4 | | |
| Lemming, 2014 (82) | Leg region* | + | Women = lower PPT | 5 | | | |
| Manning, 2002 (59) | | + | Non athletic women = | 4 | | | |

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Table 6 (continued)

| | | | | | | | | | |
|-----------------------------------|----------------------------|---|-----|--|---|----------------------------------|----------------------|--|--|
| | | | | lower PPT | 4 | Conflicting | | | |
| | Holmgaard, 2017 (51) | | - | | 4 | | | | |
| | Bajaj, 2001 (71) | | - | | 4 | | | | |
| | Jones, 2016 (53) | | - | | 4 | | | | |
| | Vatine, 1993 (90) | | - | | 4 | | | | |
| | De Rui, 2015 (46) | Face region* | + | Women = lower PPT | 4 | } Conflicting | } Conflicting | | |
| | Holmgaard, 2017 (51) | | + | Women = lower PPT | 4 | | | | |
| | Komiyama, 2005 (78) | | + | Women = lower PPT | 4 | | | | |
| | Komiyama, 2007 (79) | | + | Women = lower PPT | 4 | | | | |
| | Lee, 1994 (81) | | + | Women = lower PPT | 4 | | | | |
| | Matos, 2011 (83) | | + | Women = lower PPT | 4 | | | | |
| | Petersen, 1992 (85) | | + | Women = lower PPT | 4 | | | | |
| | Shah, 2021 (69) | | + | Women = lower PPT | 4 | | | | |
| | Yang, 2013 (65) | | + | Women = lower PPT | 3 | | | | |
| | Fedders, 2019 (47) | | - | | 4 | | | | |
| | Isselée, 2001 (52) | | - | | 4 | | | | |
| | Vatine, 1993 (90) | | - | | 4 | | | | |
| | Yang, 2014 (66) | | - | | 4 | | | | |
| | Shah, 2021 (69) | Head region | + | Women = lower PPT | 4 | | | | |
| | Shah, 2021 (69) | Neck region | + | Women = lower PPT | 4 | | | | |
| | Garcia, 2007 (48) | Shoulder, neck, upper leg region, knee, elbow, lower leg, ribs pooled | + | Women = lower PPT | 4 | | | | |
| | Da Silva, 2014 (88) | Face, lower leg pooled | + | Women = higher PPT | 4 | | | | |
| | Bajaj, 2001 (71) | Abdomen, lower back | +/- | (only at lower back, women = lower PPT) | 4 | | | | |
| | Dawson, 2009 (45) | ? | - | | 4 | | | | |
| Gender Role | Otto, 1985 (74) | Finger | + | Influence on PPT | 4 | } Conflicting | | | |
| | Manning, 2002 (59) | Arm, shoulder, thigh | - | / | 4 | | | | |
| | Kröner-herwig, 2012 (80) | Forearm | - | / | 5 | | | | |
| Level of physical activity | Andrzejewski, 2010 (41) | Leg region | + | Higher PA = higher PPT | 4 | } Conflicting | } Conflicting | | |
| | Zhang, 2013 (68) | | + | Higher PA= lower PPT | 4 | | | | |
| | Lemming, 2014 (82) | | + | Higher PA = higher PPT | 5 | | | | |
| | Jones, 2016 (53) | | + | Higher VO2peak = lower PPT in men | 4 | | | | |
| | Kuppens, 2018 (56) | | - | | 5 | | | | |
| | Manning, 2002 (59) | | - | | 4 | | | | |
| | Andrzejewski, 2010 (41) | Shoulder girdle/upper arm region | + | Higher PA = higher PPT | 4 | | | | |
| | Zhang, 2013 (68) | | + | Higher PA = lower PPT | 4 | | | | |
| | Jones, 2016 (53) | | - | | 4 | | | | |
| | Manning, 2002 (59) | | - | | 4 | | | | |
| | Kuppens, 2018 (56) | | - | | 5 | | | | |
| | Shiro, 2017 (62) | Lower arm/hand region | +/- | / (only BMR predicted PPT) | 4 | | | | |
| | Andrzejewski, 2010 (41) | | + | Higher PA = higher PPT | 4 | | | | |
| | Kuppens, 2018 (56) | | - | | 5 | | | | |
| | Andrzejewski, 2010 (41) | Back | + | Higher PA= higher PPT | 4 | | | | |
| Menopause | Martinez-Jauand, 2013 (92) | ? | - | | 5 | } Very weak SoR for no influence | | | |
| | Ozasa, 2022 (70) | Tongue | - | | 5 | | | | |
| Menstrual cycle | Alves, 2017 (40) | Face region | + | PPT decreased during the menstrual cycle | 4 | } Conflicting | } See following page | | |
| | Isselée, 2001 (52) | | + | PPT decreased during the menstrual cycle | 4 | | | | |
| | Cimino, 2000 (44) | | + | Being in preovulatory phase = lower PPT | 4 | | | | |
| | Isselée, 2001 (52) | Lower arm/hand region | + | PPT decreased during the menstrual cycle | 4 | | | | |
| | Alves, 2017 (40) | | + | PPT decreased during the menstrual cycle | 4 | | | | |
| | Rao, 1987 (75) | | + | First phases of menstrual cycle = higher PPT | 4 | | | | |
| | Teepker, 2010 (64) | | + | PPT increased during the menstrual cycle | 4 | | | | |
| | Amodei, 1988 (76) | | - | / | 4 | | | | |
| | Bajaj, 2001 (71) | Abdomen, lower back, upper arm, thigh | + | Being in ovulatory phase = lower PPT | 4 | | | | |
| | | | | | | | | | |
| Scapular position* | Azevedo, 2008 (42) | Neck, shoulder region, | + | Depressed scapular = | 4 | | | | |

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Table 6 (continued)

| | | | | | | |
|---|----------------------|--|---|--|---|--|
| | Lee, 2015 (58) | upper back Neck, shoulder region, upper back | + | lower PPT Depressed scapular = lower PPT | 5 | } Weak SoR for influence |
| Hand dominance | Petersen, 1992 (85) | Face, finger | + | Right handed = higher PPT on right side | 4 | |
| Psychomotor performance | Pickering, 2002 (61) | Finger | + | Better psychomotor performance = lower PPT | 4 | Preliminary SoR for influence |
| Manual work | Zhang, 2013 (68) | Upper arm, inguinal line | + | Non-manual work = lower PPT | 4 | Preliminary SoR for influence |
| ADL | Girotti, 2019 (49) | Wrist | - | | 3 | Preliminary SoR for no influence |
| Forward head posture | Kocur, 2019 (55) | Neck, shoulder region | - | / | 5 | Preliminary SoR for no influence |
| Contraceptives | Isselée, 2001 (52) | Face, thumb | - | / | 4 | Preliminary SoR for no influence |
| Hair colour | Holmgaard, 2017 (51) | Face, lower leg | - | / | 4 | Preliminary SoR for no influence |
| Functional capacity/strength | Alfieri, 2017 (39) | Upper and lower arm, Upper leg | - | / | 4 | Preliminary SoR for no influence |
| Sleep | Karmann, 2018 (54) | Finger | - | / | 4 | Preliminary SoR for no influence |
| Polypharmacy | Girotti, 2019 (49) | Wrist | - | / | 3 | Preliminary SoR for no influence |
| Smoking | Zhang, 2013 (68) | Upper arm, inguinal line | - | / | 4 | Preliminary SoR for no influence |

Studies in **bold** could be included in the meta-analyses. * = meta-analysis is dominant over qualitative analysis.

Abbreviations: SoR, Strength of Recommendation; PPT, pressure pain threshold; ADL, activities of daily living; BMI, Body Mass Index; CSQ, Coping Strategies Questionnaire; PCS, pain catastrophizing scale; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PA, physical activity

Filligim, 2002; Moore et al., 2013; Pickering et al., 2002; Shiro et al., 2017; Yang et al., 2013, 2014; Shah and Luximon, 2021; Bajaj et al., 2001; Otto and Dougher, 1985; Chesterton et al., 2003; Komiyama and De Laet, 2005; Komiyama et al., 2007; Kröner-Herwig et al., 2012; Lee et al., 1994; Lemming et al., 2015; Matos et al., 2011; Petersen et al., 1992; Petrini et al., 2015; da Silva et al., 2014; Vatine et al., 1993), gender role (the gender that one associates with, not biologically related) (Manning and Filligim, 2002; Otto and Dougher, 1985; Kröner-Herwig et al., 2012), hand-dominance (Petersen et al., 1992), level of physical activity (Andrzejewski et al., 2010; Jones et al., 2016; Kuppens et al., 2018; Manning and Filligim, 2002; Shiro et al., 2017; Zhang et al., 2013; Lemming et al., 2015), menopause (Ozasa et al., 2022; Martínez-Jauand et al., 2013), menstrual cycle phase (Alves et al., 2017; Cimino et al., 2000; Isselée et al., 2001; Teeper et al., 2010; Bajaj et al., 2001; Rao et al., 2022; Amodei and Nelson-Gray, 1989), polypharmacy (Girotti et al., 2019), psychomotor performance (Pickering et al., 2002), scapular position (Azevedo et al., 2008; Lee et al., 2015), sleep (Karmann et al., 2018), smoking (Zhang et al., 2013), and manual work (Zhang et al., 2013) were examined in the included studies as possible personal influencing factors for PPT.

Most factors were only examined in univariate analysis, except for some studies investigating the influence of age (controlled for gender and measurement site (Lautenbacher et al., 2005), gender and BMI (Girotti et al., 2019), and gender and site (Yang et al., 2014)), alcohol consumption (controlled for age and BMI (Zhang et al., 2013)), cognitive factors (controlled for gender, age, and/or ethnicity (Campbell et al., 2010); Girotti et al., 2019; Moore et al., 2013; Pickering et al., 2002), comorbidity, (controlled for gender (Girotti et al., 2019)), education (controlled for gender and/or BMI (Girotti et al., 2019); Zhang et al.,

2013), ethnicity (controlled for gender (Yang et al., 2013); Komiyama et al., 2007), gender (controlled for ethnicity, site, age, measurement site and gender role (Lautenbacher et al., 2005); Yang et al., 2013, 2014; Komiyama et al., 2007; Kröner-Herwig et al., 2012), gender role (controlled for gender (Otto and Dougher, 1985); Kröner-Herwig et al., 2012), level of physical activity (controlled for gender (Lemming et al., 2015)), psychomotor performance (controlled for age and cognitive impairment (Pickering et al., 2002)), manual work and smoking (controlled for age and BMI (Zhang et al., 2013)), ADL (which controlled for gender (Girotti et al., 2019)) and sleep (controlled for measurement trial (Karmann et al., 2018)).

3.5. Meta-analytic and qualitative analysis of influencing factors

All clinically measurable personal influencing factors are summarized in a strength of recommendation table (Table 6). In addition, forest plots of the meta-analyses are added and studies were included if sufficient data was present (Figs. 2–14). Results of univariate analysis were used to make conclusions in both the meta-analytic and qualitative approach, in order to create an overview per personal factor. Only for the study of Campbell et al (Campbell et al., 2010). the multivariate analysis was used (no reporting of univariate analysis). For the meta-analytic approach, the 95% confidence interval (CI) in Zhang et al (Zhang et al., 2013). and standard error of mean in Rao et al (Rao et al., 2022). was recalculated as standard deviation according to the method described in the handbook of Cochrane (7.7.3.2 Obtaining standard deviations from standard errors, 2021).

If at least 2/3 of the studies could be included in the (subgroup) meta-analysis, the meta-analysis was dominant and the studies not

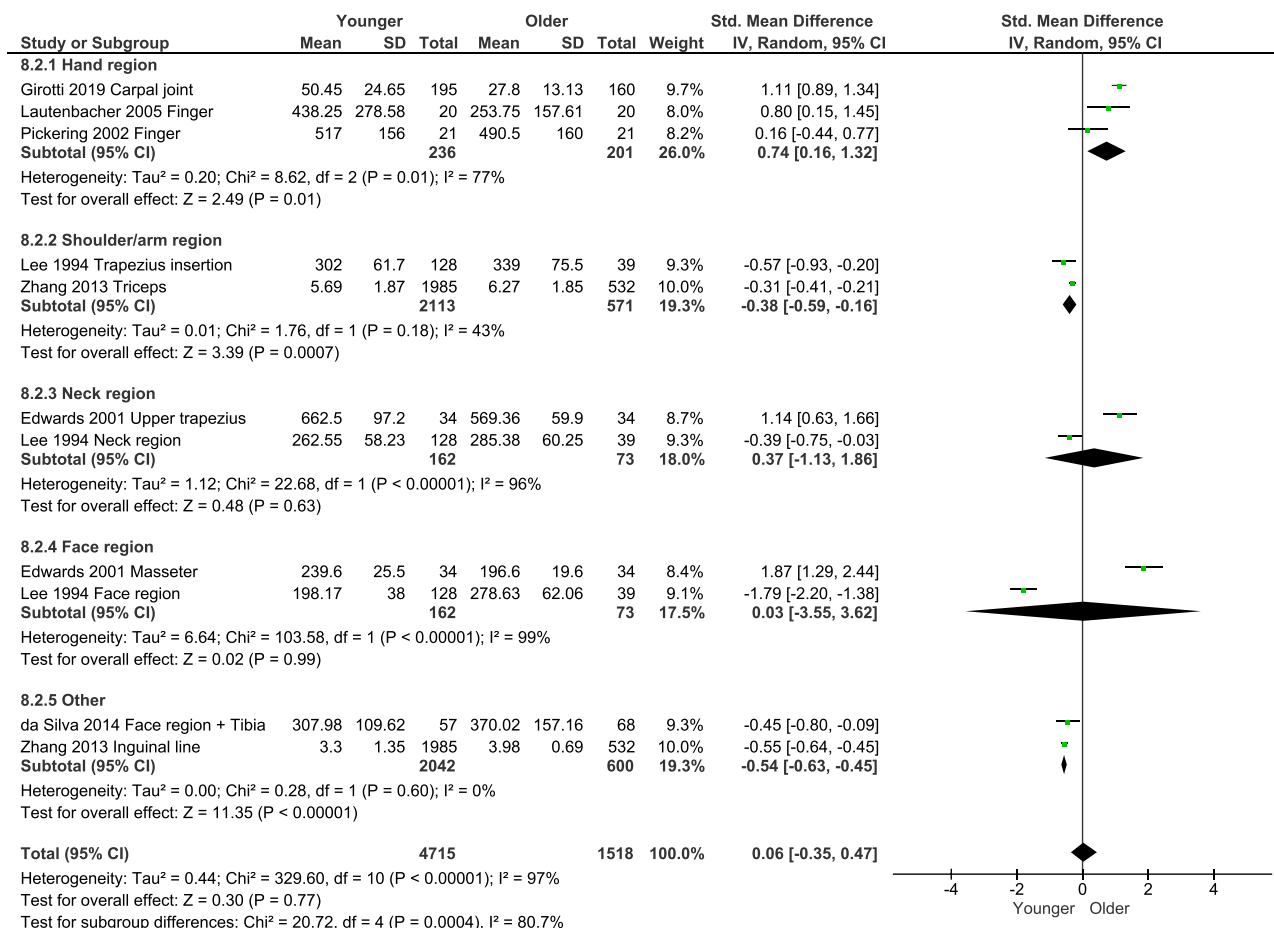


Fig. 2. Meta-analysis for the influence of age (mean differences + standard deviation). Abbreviations: CI, confidence interval; SD, standard deviation; Random, random effect methods; Std., standard.

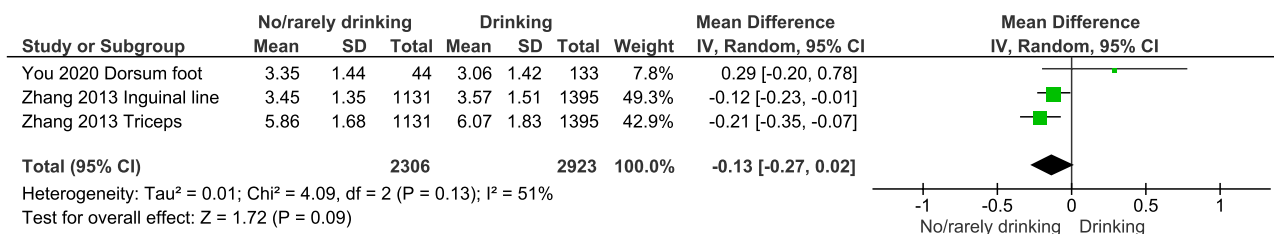


Fig. 3. Meta-analysis for the influence of alcohol consumption (mean difference + standard deviation). Abbreviations: CI, confidence interval; SD, standard deviation; Random, random effect methods; Std., standard.

included in the meta-analysis are described separately. Otherwise, both the findings of the meta-analytic and the qualitative approach are described (all articles included in both approaches). If subgroup analyses per body region were possible, the result is given, otherwise only an overall result (not taken into account the body region of the PPT measurement) is presented.

Results are described following the methods described in Santesso et al (Santesso et al., 2020).

3.6. Age

Influencing factor: PPT measured at shoulder girdle/upper arm region. Three studies evaluated the influence of age on PPT measured at the shoulder/arm region, Fig. 2 shows the results of the meta-analysis of two studies (Zhang et al., 2013; Lee et al., 1994) and displays that older age

may result in a slight higher PPT measured at the shoulder girdle/upper arm region compared to younger age (SMD: -0.38, 95%CI: -0.59; -0.16). A third study could not be implemented in the meta-analysis, but also reported an influence, however in the opposite direction (Andrzejewski et al., 2010) (Table 6).

Conflicting results: overall PPT and PPT measured in all body region subgroups, except shoulder girdle/upper arm region. Sixteen studies investigated the influence of age on PPTs (Andrzejewski et al., 2010; De Rui et al., 2015; Girotti et al., 2019; Lautenbacher et al., 2005; Pickering et al., 2002; Yang et al., 2014; Zhang et al., 2013; Shah and Luximon, 2021; Cole et al., 2010; Edwards and Fillingim, 2001; Komiyama and De Laet, 2005; Komiyama et al., 2007; Lee et al., 1994; Petrini et al., 2015; da Silva et al., 2014; Donat et al., 2005). Fig. 2 presents the meta-analysis of seven studies (Girotti et al., 2019; Lautenbacher et al., 2005; Pickering et al., 2002; Zhang et al., 2013; Edwards and Fillingim,

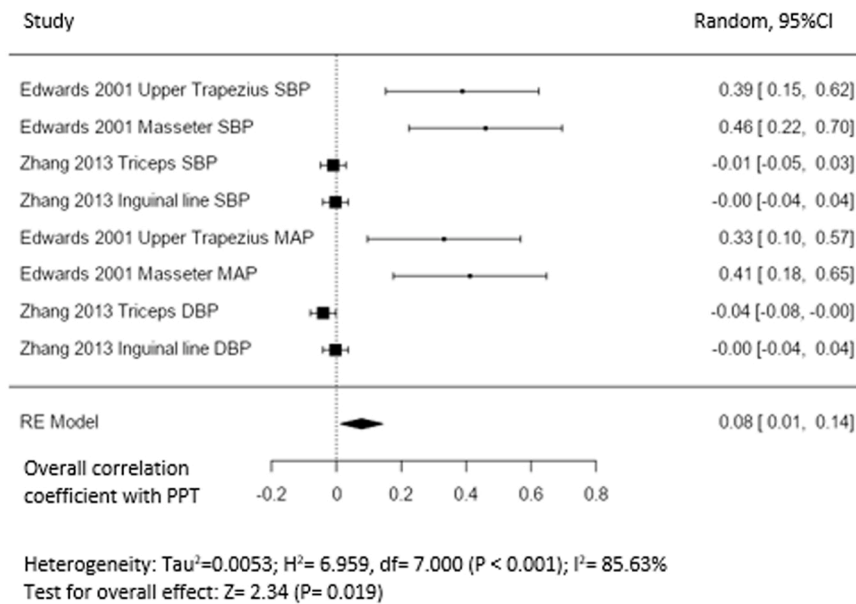


Fig. 4. Meta-analysis for the influence of blood pressure (correlation coefficients). Abbreviations: RE, random effects; PPT, pressure pain threshold; SBP, systolic blood pressure; MAP, mean arterial blood pressure, DBP, diastolic blood pressure.

2001; Lee et al., 1994; da Silva et al., 2014) and showed probably no overall influence of age on PPT (SMD: 0.06; 95%CI: -0.35; 0.47). However, subgroup analyses revealed that being of older age may result in having a lower PPT in the lower arm/hand region (SMD: 0.74; 95%CI: 0.16; 1.32) (Girotti et al., 2019; Lautenbacher et al., 2005; Pickering et al., 2002). More than half of the studies could not be integrated in the meta-analysis, and as such, also qualitative description including all 16 studies was necessary and showed an overall and subgroup-related conflicting strength of recommendation or conclusion (Table 6).

3.7. Alcohol consumption

Non-influencing factor. Two studies examined the influence of alcohol consumption on PPT, Fig. 3 shows the meta-analysis (You et al., 2020; Zhang et al., 2013). The frequency of alcohol consumption may have no influence on PPT (SMD: -0.13, 95%CI: -0.27; 0.02) (Fig. 3).

3.8. Blood pressure

Influencing factor. Three studies examined the effect of systolic (Zhang et al., 2013; Edwards and Fillingim, 2001; Kröner-Herwig et al., 2012), diastolic (Edwards and Fillingim, 2001) and mean arterial blood pressure (Zhang et al., 2013) on PPT, Fig. 4 shows the results of the meta-analysis, including two studies (Zhang et al., 2013; Edwards and Fillingim, 2001). Having higher blood pressure values may be associated with a slight higher PPT (CC= 0.08, 95%CI: 0.01; 0.14). The remaining study reported no influence (Kröner-Herwig et al., 2012). However, this study was of the lowest evidence (level 5) (Table 6).

3.9. BMI

Non-influencing factor. Nine studies investigated the influence of higher BMI on PPT (Fedders et al., 2019; Girotti et al., 2019; Shiro et al., 2017; Zhang et al., 2013; Shah and Luximon, 2021; Komiya and De Laat, 2005; McKendall and Haier, 1983; Price et al., 2013; Tashani et al., 2017), of which six had sufficient data to perform a meta-analysis (Fedders et al., 2019; Zhang et al., 2013; Shah and Luximon, 2021; McKendall and Haier, 1983; Price et al., 2013; Tashani et al., 2017). Having a higher BMI probably result in no difference in PPT compared to normal BMI regarding mean differences and standard deviations

(Fedders et al., 2019; Zhang et al., 2013; McKendall and Haier, 1983; Price et al., 2013; Tashani et al., 2017) (Fig. 5, SMD: -0.20, 95%CI: -0.46; 0.05) and regarding correlation coefficients (Fedders et al., 2019; Zhang et al., 2013; Shah and Luximon, 2021) (Fig. 6, CC: -0.00, 95%CI: -0.08; 0.08) (Fig. 6). Also subgroup meta-analyses (lower arm/hand region [SMD: -0.56, 95%CI: -1.17, 0.04] and shoulder girdle/upper arm region [SMD: -0.15, 95%CI: -0.53; 0.22]) likely showed no influence. The three remaining studies (Girotti et al., 2019; Shiro et al., 2017; Komiya and De Laat, 2005) also reported no influence at the lower arm/hand and face region (Table 6).

3.10. Cognitive factors

Non-influencing factor: pain vigilance, affect, depression, fear, self-efficacy, ability to dissociate and locus of control. Three studies evaluated the influence of pain vigilance on PPT, and two studies (Kröner-Herwig et al., 2012; Hastie et al., 2012) were included in the meta-analysis (Fig. 7). According to the meta-analysis, pain vigilance may not be associated with PPT (CC: 0.02, 95%CI: -0.26; 0.30), however the evidence is very uncertain. The third study also showed no influence on PPT (Kuppens et al., 2019) (Table 6). Two studies examined the influence of affect on PPT at different body regions (Hastie et al., 2005; Sibille et al., 2012). This qualitative analysis suggests no influence (Table 6). Four studies evaluated the influence of depression on PPT (Manning and Fillingim, 2002; Moore et al., 2013; Kröner-Herwig et al., 2012; Campbell et al., 2015). This analysis probably resulted in no overall influence. Also subgrouping revealed no influence (Table 6). Furthermore, the results of the qualitative analysis about fear (Moore et al., 2013), self-efficacy (Manning and Fillingim, 2002), ability to dissociate (Manning and Fillingim, 2002) and locus of control (Manning and Fillingim, 2002) showed no influence on PPT, but is preliminary, because the conclusion is based on only one study per personal factor (Table 6).

Conflicting results: pain catastrophizing and cognitive impairment. Five studies included pain catastrophizing as possible influencing factor for PPT (Campbell et al., 2010; Kröner-Herwig et al., 2012; Hastie et al., 2012; Kuppens et al., 2019; Moore et al., 2020). Meta-analysis, including three studies (Campbell et al., 2010; Kröner-Herwig et al., 2012; Hastie et al., 2012), revealed that pain catastrophizing may have no overall influence on PPT measured at different body regions (Fig. 8, CC: -0.11,

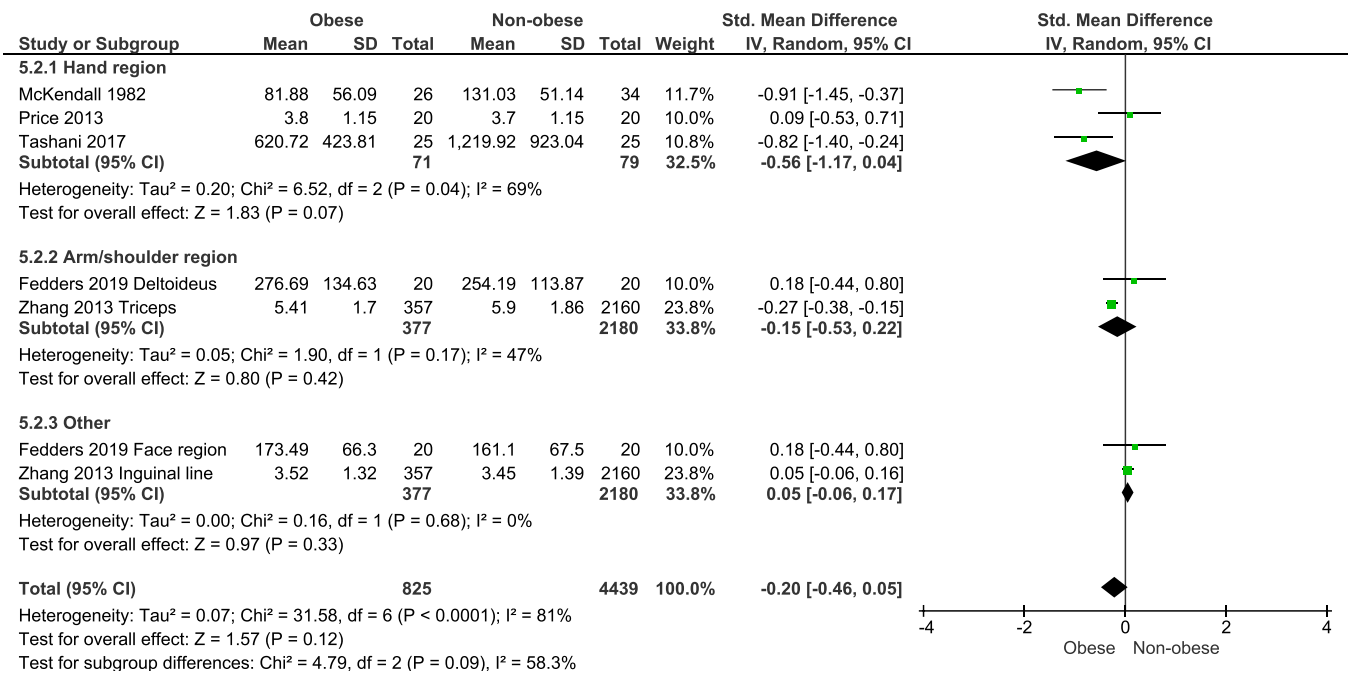


Fig. 5. Meta-analysis for the influence of body mass index (mean differences + standard deviation). Abbreviations: CI, confidence interval; SD, standard deviation; Random, random effect methods; Std., standard.

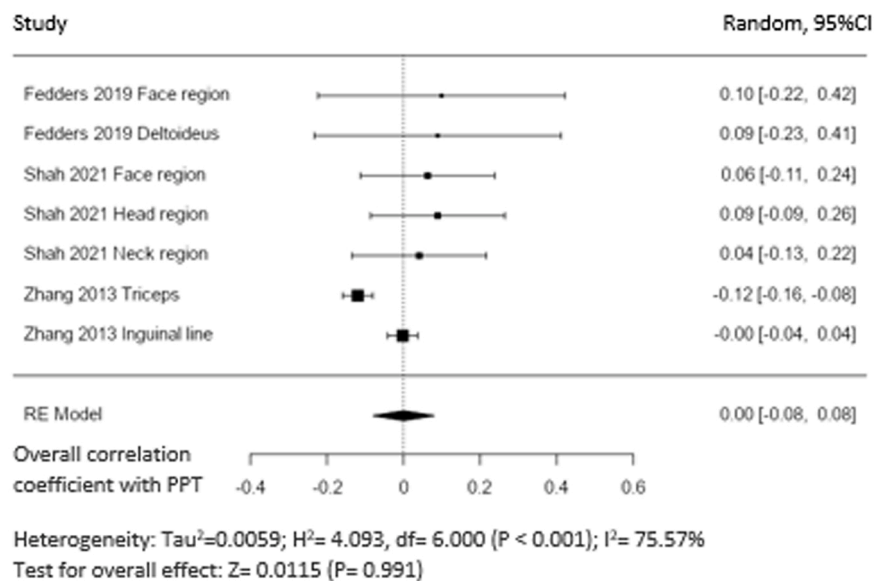


Fig. 6. Meta-analysis for the influence of body mass index (correlation coefficients). Abbreviations: RE, random effects; PPT, pressure pain threshold.

95%CI: -0.32; 0.10). However, two other studies were not included in the meta-analysis, and as a result, qualitative analysis of all five studies reported overall and subgroup-related conflicting results (Table 6). Three studies examined if cognitive impairment influenced PPT. One study showed that having cognitive impairment may result in lower PPT (Girotti et al., 2019), while two other studies (Manning and Fillingim, 2002; Pickering et al., 2020) found no difference (Table 6).

3.11. Comorbidity

Conflicting results. Two studies investigated the effect of comorbidities (Girotti et al., 2019) or previous pain injuries (Manning and Fillingim, 2002) on PPT, and conflicting influence was found (Table 6).

Having more comorbidities resulted in a lower PPT (Girotti et al., 2019), but having previous pain injuries resulted in no influence (Manning and Fillingim, 2002).

3.12. Education

Conflicting results. Three studies investigated the effect of education level on PPT, of which one study found that higher education resulted in lower PPT (Zhang et al., 2013), while the other two found no effect (De Rui et al., 2015; Girotti et al., 2019) (Table 6).

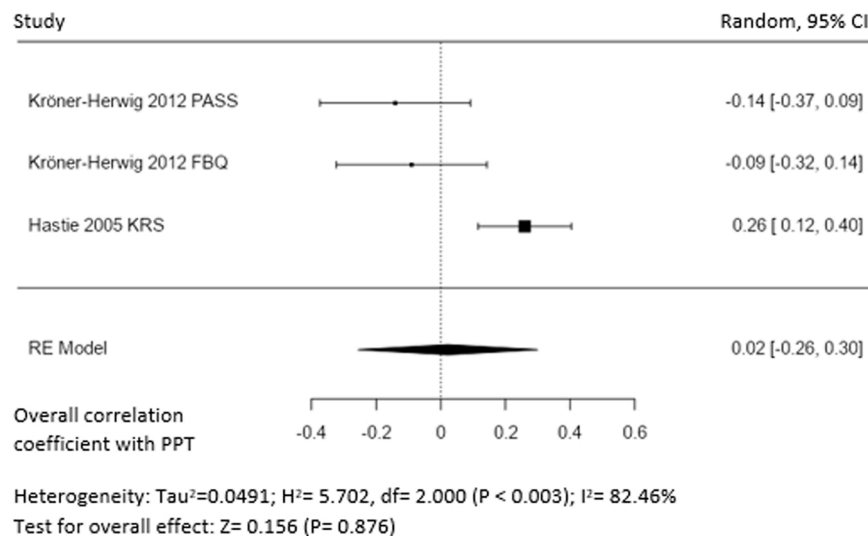


Fig. 7. Meta-analysis for the Influence of pain vigilance (correlation coefficients). Abbreviations: RE, random effects; PPT, pressure pain threshold.

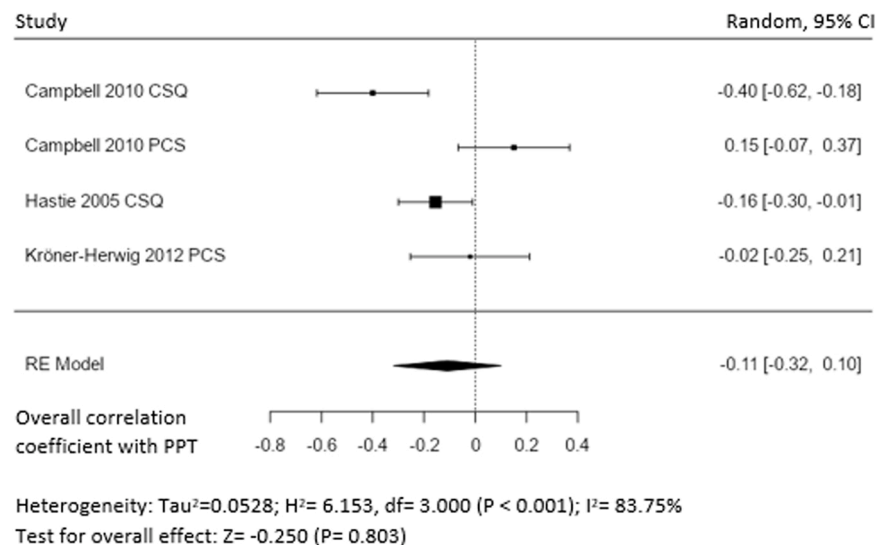


Fig. 8. Meta-analysis for the influence of pain catastrophizing (correlation coefficients). Abbreviations: RE, random effects; PPT, pressure pain threshold.

3.13. Ethnicity

Conflicting results. One study reported a difference between two ethnicities (Yang et al., 2013) regarding PPT and two other studies did not (Dawson and List, 2009; Komiyama et al., 2007). However, different ethnicities were included in the three studies (Table 6).

3.14. Gender

Influencing factor. Twenty-eight studies examined the influence of gender on PPT, Fig. 9 shows the meta-analysis, including 19 studies (Garcia et al., 2007; Girotti et al., 2019; Jones et al., 2016; Lautenbacher et al., 2005; Manning and Fillingim, 2002; Moore et al., 2013; Pickering et al., 2002; Shiro et al., 2017; Otto and Dougher, 1985; Chesterton et al., 2003; Komiyama and De Laat, 2005; Komiyama et al., 2007; Lee et al., 1994; Lemming et al., 2015; Matos et al., 2011; Petersen et al., 1992; da Silva et al., 2014; Vatine et al., 1993). Being a woman probably results in having a lower PPT compared to men (SMD: 0.57, 95%CI: 0.39; 0.75). Subgroup analyses of lower arm/hand region (Girotti et al., 2019; Lautenbacher et al., 2005; Moore et al., 2013; Pickering et al., 2002; Shiro et al., 2017; Otto and Dougher, 1985; Chesterton et al.,

2003; Komiyama and De Laat, 2005; Komiyama et al., 2007; Petersen et al., 1992), and face region (Komiyama and De Laat, 2005; Komiyama et al., 2007; Lee et al., 1994; Matos et al., 2011; Petersen et al., 1992; Vatine et al., 1993) also revealed a similar influence of gender (Fig. 9, SMD: 0.68, 95%CI: 0.52; 0.84; and SMD: 0.58, 95%CI: 0.36; 0.79, respectively). Fig. 10 shows the funnel plot with a symmetrical shape, meaning the chance for small study effects is low (Sterne et al., 2011). Of the nine remaining studies, four also reported that being a women resulted in having a lower PPT (De Rui et al., 2015; Kröner-Herwig et al., 2012; Lee et al., 1994; Petrini et al., 2015), but five reported no influence (Dawson and List, 2009; Isselée et al., 2001; Yang et al., 2013, 2014; Bajaj et al., 2001), as such conflicting results regarding qualitative analysis of these nine remaining studies were found (Table 6).

Non-influencing factor: PPT measured at the leg region. Six studies examined the influence of gender on PPT measured at the leg region, Fig. 9 shows the meta-analysis of five studies (Holmgaard et al., 2017; Jones et al., 2016; Manning and Fillingim, 2002; Lemming et al., 2015; Vatine et al., 1993). Gender may have no influence on PPT measured at the leg region (SMD 0.71, 95%CI: -0.22; 1.65). The remaining study also revealed no influence on PPT (Bajaj et al., 2001) (Table 6).

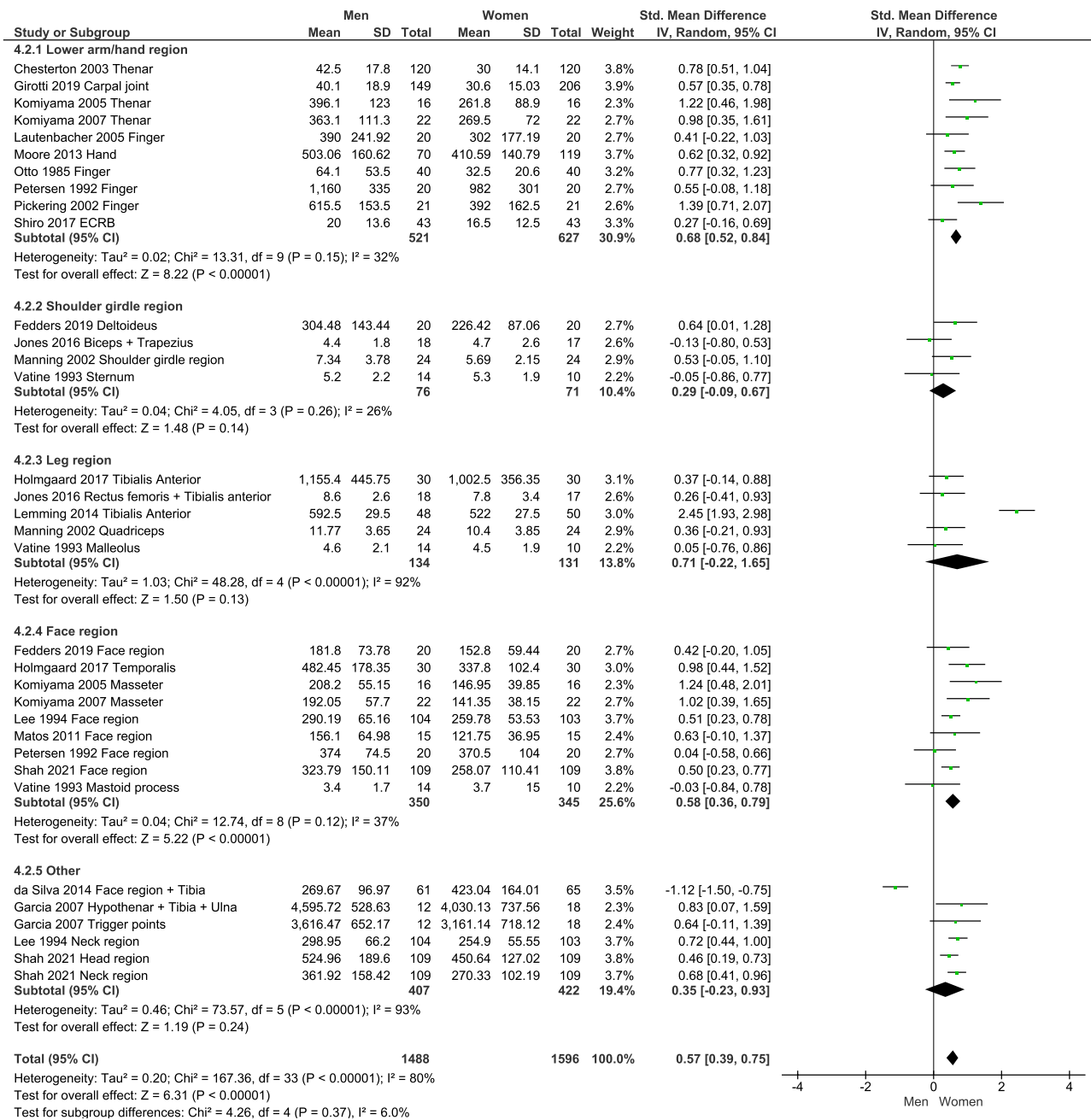


Fig. 9. Meta-analysis for the influence of gender (mean difference + standard deviation). Abbreviations: CI, confidence interval; SD, standard deviation; Random, random effect methods; ECRB, musculus Extensor carpi radialis brevis; Std., standard.

3.15. Gender role

Conflicting results. One study revealed that gender role influenced PPT (Otto and Dougher, 1985), while the other two studies did not (Manning and Fillingim, 2002; Kröner-Herwig et al., 2012) (Table 6).

3.16. Level of physical activity

Conflicting results. Seven studies investigated if the level of physical activity influenced PPT (Andrzejewski et al., 2010; Jones et al., 2016; Manning and Fillingim, 2002; Shiro et al., 2017; Zhang et al., 2013; Lemming et al., 2015; Kuppens et al., 2019). Fig. 11 displays the meta-analysis of three studies (Manning and Fillingim, 2002; Zhang et al., 2013; Lemming et al., 2015) indicating that the level of physical activity may have no overall influence on PPT (SMD: 0.41, 95%CI:

-0.00; 0.83), but may have an influence on PPT measured at the shoulder girdle/upper arm region (SMD: -0.18, 95%CI: -0.27; -0.09). However, as four studies could not be included in the meta-analysis, also interpretation of the qualitative analysis with all studies was necessary: overall, and subgroup-related conflicting results were found (Table 6).

3.17. Menopause

Non-influencing factor. Two studies (Ozasa et al., 2022; Martinez-Jauand et al., 2013) investigated the influence of being in the menopause, and age of onset of menopause on PPT, but qualitative analysis showed that this factor may not influence PPT (Table 6).

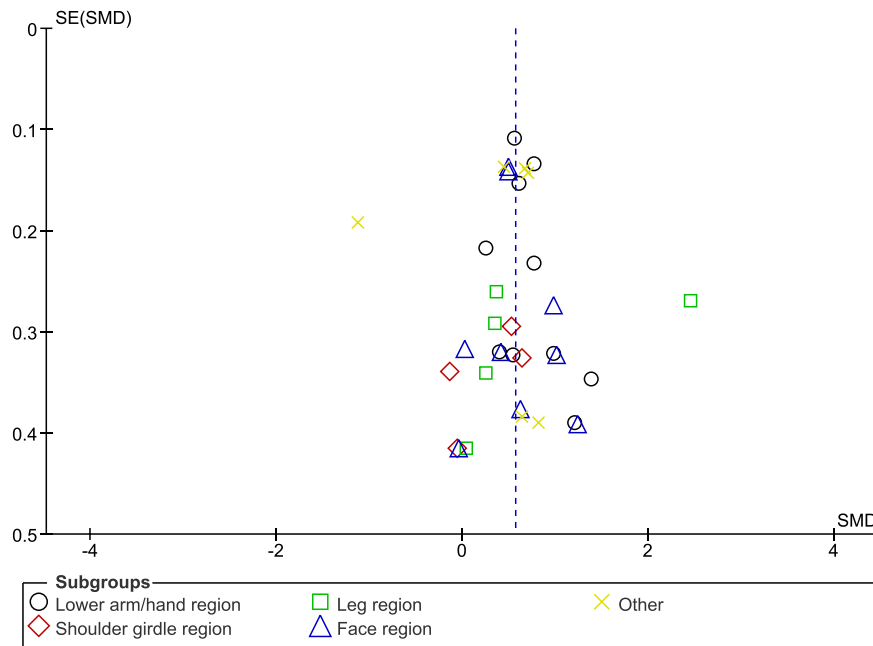


Fig. 10. Funnel plot of gender meta-analysis. Abbreviations: SE, standard error; SMD, standard mean difference.

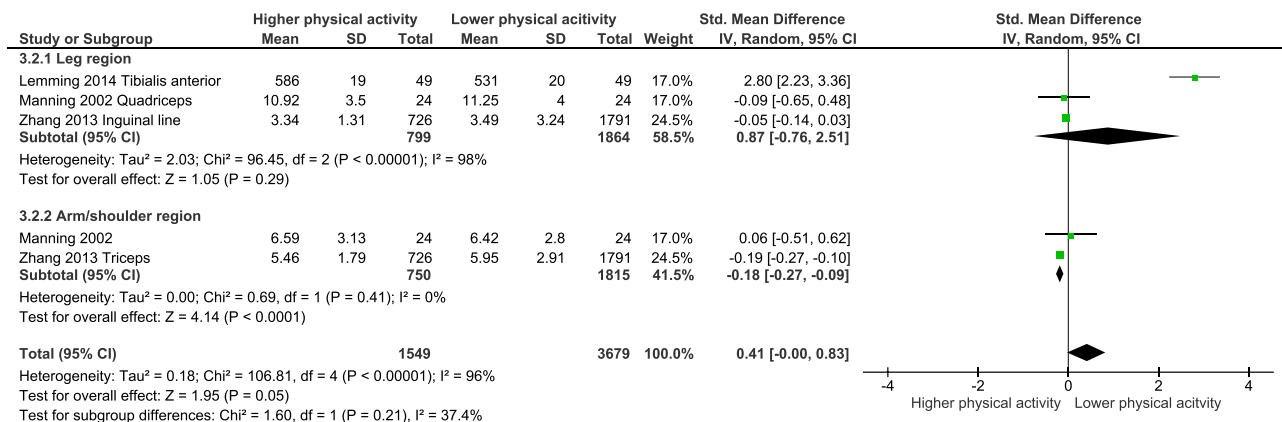


Fig. 11. Meta-analysis for the influence of physical activity (mean difference + standard deviation). Abbreviations: CI, confidence interval; SD, standard deviation; Random, random effect methods; Std., standard.

3.18. Menstrual cycle

Conflicting results. Seven studies investigated the influence of the menstrual cycle on PPT (Alves et al., 2017; Cimino et al., 2000; Isselée et al., 2001; Teepker et al., 2010; Bajaj et al., 2001; Rao et al., 2022; Amodei and Nelson-Gray, 1989), Figs. 12–14 show the meta-analysis of three studies (Teepker et al., 2010; Rao et al., 2022; Amodei and Nelson-Gray, 1989). None of the phases showed differences compared to the other phases of the menstrual cycle regarding PPT (intermenstrual

phase vs. other phases [Fig. 12]: SMD: 1.42, 95%CI: -0.80; 3.63; menstrual phase vs. other phases [Fig. 13]: SMD: -1.01; 95%CI: -2.72, 0.70; premenstrual phase vs. other phases [Fig. 14]: SMD: -0.50, 95% CI: -1.47; 0.47). Regarding the qualitative analysis of all studies, six out of seven studies found an influence of menstrual cycle on PPT, meaning that differences in PPT were found throughout the menstrual cycle. However, the direction differed between studies. As such, the overall and subgroup-related results were conflicting (Table 6).

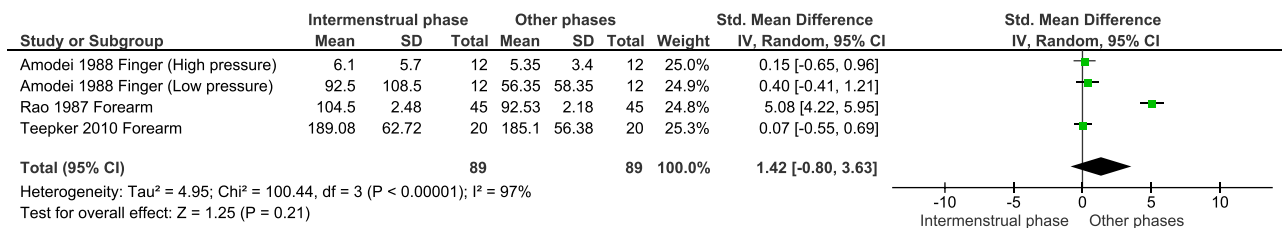


Fig. 12. Meta-analysis for the influence of intermenstrual phase compared to other phases (mean difference + standard deviation). Abbreviations: CI, confidence interval; SD, standard deviation; Random, random effect methods; Std., standard.

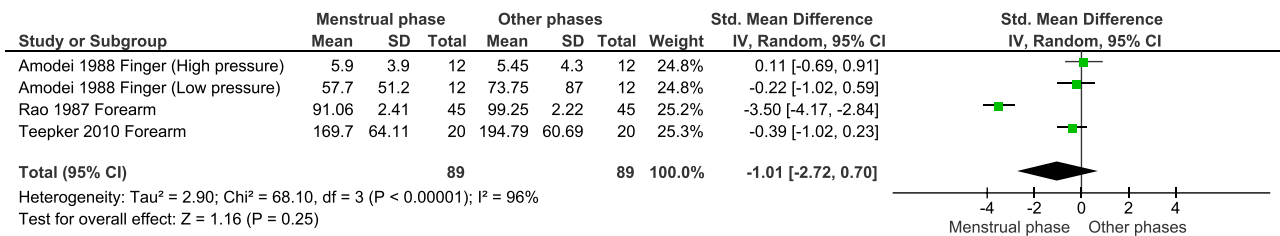


Fig. 13. Meta-analysis for the influence of menstrual phase compared to other phases (mean difference + standard deviation). Abbreviations: CI, confidence interval; SD, standard deviation; Random, random effect methods; Std., standard.

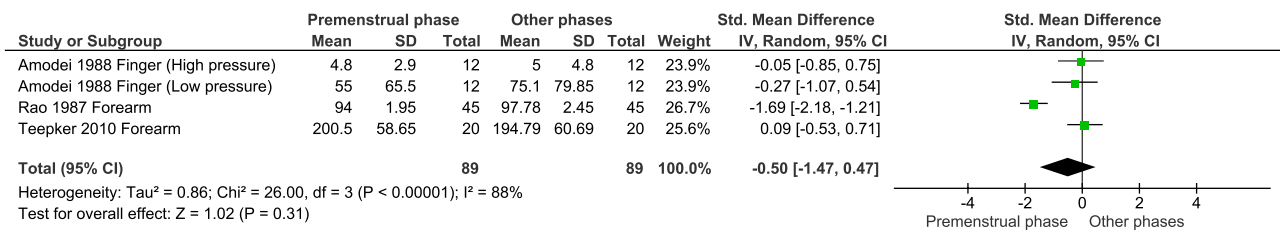


Fig. 14. Meta-analysis for the influence of premenstrual phase compared to other phases (mean difference + standard deviation). Abbreviations: CI, confidence interval; SD, standard deviation; Random, random effect methods; Std., standard.

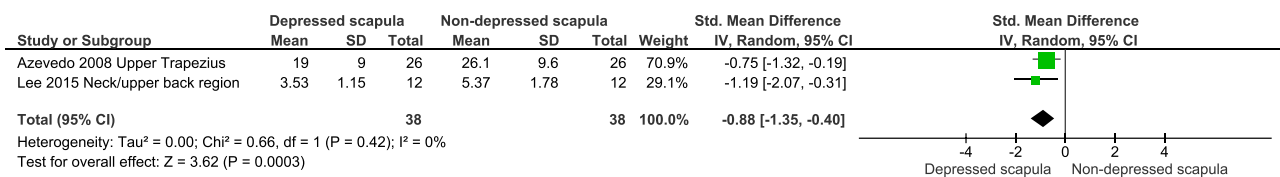


Fig. 15. Meta-analysis for the influence of scapular position (mean difference + standard deviation). Abbreviations: CI, confidence interval; SD, standard deviation; Random, random effect methods; Std., standard.

3.19. Scapular position

Influencing factor. Two studies evaluated the influence of a depressed scapular position on PPT, with Fig. 15 showing the meta-analysis of those two studies (Azevedo et al., 2008; Lee et al., 2015). Having a depressed scapular position does result in having lower PPT values compared to having a normal scapular position in the neck/shoulder region (SMD: -0.88, 95%CI: -1.35; -0.40).

3.20. Other personal factors - preliminary evidence

Influencing factors. Hand dominance, psychomotor performance, and manual work were each measured by only one study. Therefore, qualitative analysis is preliminary, but may suggest that having a right hand dominance (Petersen et al., 1992) resulted in a higher PPT on the right side, and that having a better psychomotor performance (Pickering et al., 2002), and performing non-manual work (Zhang et al., 2013) resulted in lower PPT (Table 6).

Non-influencing factors. A preliminary qualitative analysis (evidence based on only one study) may show no influence of ADL (Girotti et al., 2019), forward head posture (Kocur et al., 2019), the use of contraceptives (Isselée et al., 2001), hair colour (Holmgaard et al., 2017), functional capacity (Alfieri et al., 2017), sleep (Karmann et al., 2018), polypharmacy (Girotti et al., 2019) and smoking (Zhang et al., 2013) on PPT (Table 6).

3.21. Differences univariate – multivariate analyses

In four (Girotti et al., 2019; Karmann et al., 2018; Yang et al., 2014; Campbell et al., 2015) out of 12 studies, the result of the multivariate

analysis was equal to the result of the univariate analysis. However, in eight studies, multivariate analysis differed from univariate analysis: the influence of age (Lautenbacher et al., 2005), alcohol (only one out of two body regions) (Zhang et al., 2013), gender (Pickering et al., 2002; Yang et al., 2013; Komiyama et al., 2007; Kröner-Herwig et al., 2012), ethnicity (Yang et al., 2013; Komiyama et al., 2007), gender role (Otto and Dougher, 1985; Kröner-Herwig et al., 2012) and physical activity (Lemming et al., 2015) did not withstand after correction for different factors (see paragraph ‘(possible) influencing factors’).

3.22. Sensitivity analyses

Sensitivity analyses correcting for studies that did not report full eligibility criteria showed similar results except for the influencing factor age, of which the SMD changed of direction (SMD: 0.06 to -0.45) (Table S2). Sensitivity analyses correcting for meta-analysis model showed no important differences except for the change in SMD direction of the influencing factors age (SMD: 0.06 to -0.29) and level of physical activity (SMD: 0.41 to -0.08), and the amount of SMD change of the influencing factor menstrual cycle (SMD premenstrual phase: -0.50 to -0.75, and SMD intermenstrual phase: 1.21-1.11) (Table S3).

4. Discussion

4.1. Main findings

The goal of this systematic review and meta-analysis was to summarise all studies that had the purpose to explore clinically measurable personal factors which might influence the PPT in healthy people. Only results of univariate analysis (except for the factor ‘sleep’) were used for

interpretation.

Influencing factors for PPT overall were blood pressure (very weak conclusion), gender (moderate conclusion) and scapular position (strong conclusion) and subgroup analyses also revealed an influence of age when PPT was measured at the shoulder girdle/upper arm region (weak conclusion), and of gender when PPT was measured at the lower arm/hand region and face region (moderate conclusion) according to the meta-analytic approach.

Only a *preliminary conclusion of influence* (based on the result of one study) of hand dominance, psychomotor performance and manual work on PPT was found.

Non-influencing factors for PPT were alcohol consumption (weak conclusion), BMI (moderate conclusion) and pain vigilance (very weak conclusion). Subgroup analyses revealed no influence of BMI when PPT was measured at the shoulder girdle/upper arm region, and of gender when PPT was measured at the leg region according to the meta-analytic approach. Depression (moderate conclusion) and menopause (very weak conclusion) and subgroup analysis of BMI when PPT was measured at the face region (weak conclusion) revealed no influence according to the qualitative approach.

Only a *preliminary conclusion of no influence* (based on the result of one study) of affect, fear, ability to dissociate, locus of control ADL, forward head posture, contraceptives, hair colour, function sleep, polypharmacy, and smoking on PPT was found according to the qualitative approach.

Conflicting results were found for all the other personal factors, but further explanation is needed. The overall meta-analytic approach of age, pain catastrophizing, level of physical activity and menstrual cycle showed no influence on PPT, and the subgroup meta-analysis of age measured in the hand region showed influence on PPT (moderate conclusion). However, less than 2/3 of the studies could be implemented in the different meta-analyses and therefore, it seemed also necessary to summarize all studies in a qualitative approach. This resulted in conflicting results (no influence regarding meta-analyses vs. conflicting results regarding qualitative approach).

5. Limitations of the included studies

First, clearly a lot of conflicting results are presented. This can be explained due to the fact that, regarding most influencing factors, meta-analyses were only possible with a subset of the studies. Only a dominant effect according to the meta-analysis of blood pressure, gender, scapular position, alcohol consumption and pain vigilance could be presented. For all the other factors, the qualitative approach or a mix of the qualitative and meta-analytic approach is presented. Second, several limitations can be described regarding the included studies. Many studies did not present sufficient data, which makes inclusion in meta-analysis limited. If more studies could be included in the meta-analyses focusing on the influence of age, BMI, pain catastrophizing, level of physical activity and menstrual phase on PPT, maybe less conflicting results will be found. Gender was also the only factor that was measured in more than 10 studies, and as such the only factor for which small study effects could be checked (Sterne et al., 2011) (which was not present). Next, most (42 out of 54) studies performed univariate analyses and did not compensate for confounders, as such, the described (non-)influencing factors are more 'associated' with PPT instead of 'influencing or predicting' PPT (Varga et al., 2020).

Also, important to mention, is the considerable heterogeneity of most meta-analyses. Only the meta-analysis of scapular position had a low heterogeneity (I^2). A part of the overall considerable heterogeneity could be explained by the body region: when accounting for subgroups based on body region, heterogeneity decreased for age with PPT measured at lower arm/hand- or shoulder girdle/upper arm region, BMI with PPT measured at lower arm/hand- or shoulder girdle/upper arm region, gender with PPT measured at face-, lower arm/hand- and shoulder girdle/upper arm region and physical activity with PPT

measured at shoulder girdle/upper arm region with no to moderate heterogeneity. Another explanation could be the measurement method used for measuring the potentially influencing factors regarding blood pressure (systolic, diastolic or mean arterial pressure), BMI (weight and length measured or part of demographic questions), level of physical activity, pain vigilance and pain catastrophizing (different questionnaires). Especially the use of different questionnaires can lead to slight differences, resulting in higher heterogeneity. The difference in cut-off values for age (e.g. older group from 45 (Girotti et al., 2019; da Silva et al., 2014), 50 (Zhang et al., 2013; Lee et al., 1994), 60 (Lautenbacher et al., 2005; Edwards and Fillingim, 2001) or 70 years old (Pickering et al., 2002)) and menstrual phase (e.g. intermenstrual phase between 12th and 16th day (Amodei and Nelson-Gray, 1989) or 15th and 18th day of menstruation (Rao et al., 2022)) for the different groups could also be an explanation. In addition, sensitivity analyses of age (Table S2 and S3), physical activity and menstrual cycle (Table S3) showed non-robustness of their meta-analysis results, indicating these results are sensitive to relatively small changes. Not all studies examining these influencing factors could be implemented in the meta-analysis, and as such, the results of these meta-analyses were not dominant over the results in the qualitative approach. In this way, a correction for the interpretation was already implemented.

5.1. Relation to other reviews and explanations for findings

The overall conflicting result regarding the influence of age is in line with the review of Tumi et al (Tumi et al., 2017), as they also reported an inconsistent direction of the influence of age. However, in the meta-analysis of Tumi et al (Tumi et al., 2017), tentative lower PPT in older compared to younger people were found. This is in contrast with our meta-analysis, which reported no influence of age on PPT. An important remark is that only four studies were included in their meta-analysis compared to seven studies in ours. The fact that higher PPT was seen in older age when measured in the arm/shoulder region, can be explained by the reduced somatosensory perception due to aging, leading to a loss of nociceptive function and as such reduced sensitivity (Tinnirello et al., 2021). An explanation that this result was only found in the arm/shoulder region could be due to the difference in muscle mass and fat distribution compared to other regions, as previous research indeed showed a difference in PPT at places with extra subcutaneous fat and with little extra fat (Price et al., 2013).

The overall influence of gender is in line with the review of Riley et al (Riley et al., 1998), showing that men had higher PPT compared to women, and with the review of Racine et al (Racine et al., 2012), in which the mediating factors for the influence of gender on PPT were investigated. This difference could be partly explained by hormone differences, as testosterone shows less nociceptive characteristics (Craft, 2007). These hormone differences can also be suggested by findings of six out of seven included studies, in which PPT differences throughout the menstrual cycle were found. However, the direction of influence is inconsistent and therefore the effect is unclear, this is also in line with the conclusions of a previous review (Iacovides et al., 2015). Martin's review (Martin, 2009) found increased pain sensitivity in the intermenstrual phase, but this could not be confirmed for PPT in current review. In addition, Isselée et al (Isselée et al., 2001), found no differences in PPT between women taking contraceptives and women taking no contraceptives. Remarkable, in the leg region, the influence of gender was non-significant. An explanation could be again the difference in muscle mass and fat distribution in the leg, compared to the face or lower arm/hand (Price et al., 2013).

Having a higher blood pressure resulted in higher PPT and could therefore be described as 'blood pressure-related hypoalgesia', which is confirmed by a recent review (Makovac et al., 2020). An explanation for this phenomenon is still unclear, previously it was described that this could be an early sign of a silent asymptomatic myocardial infarct (Ghione, 1996) or that this relation is mediated through endogenous

opioids (McCubbin and Bruehl, 1994). However, according to a more recent review, moderating factors for the link between higher blood pressure and higher PPT seems being a woman, when blood pressure is assessed for 24 h ambulatory, when pain stimuli are provided in the arm/leg or mouth/teeth region and when studies did not adjust for confounders. However, future research should examine the underlying factors for this relation (Makovac et al., 2020).

The influence of scapular position on PPT measured at the trapezius muscles can be explained by the fact that the trapezius muscles and brachial plexus are in a more lengthened position when the scapular is depressed. This lengthened position could lead to increased tension, and as such disrupted sarcomeres within the muscles (Kleinrensink et al., 2000). This again can be the cause of higher mechanical hyperalgesia found with PPT measurements (Azevedo et al., 2008; Lee et al., 2015).

The review of Horn-Hofmann et al (Horn-Hofmann et al., 2015) found an overall damping effect of alcohol on pain threshold, tolerance and intensity; and the review of Alabas et al (Alabas et al., 2012) found that gender role was related to pain threshold and tolerance (no separate analysis of which threshold). However, an effect of these two personal factors could not be revealed for PPT with our meta-analysis and qualitative approach, respectively. However, only one study was included regarding gender role in the current review, so caution for the interpretation of the results is needed. An important remark is that the current review and meta-analysis could make conclusions for the influence on PPT separately (instead of combining different pain threshold modalities), which both other reviews (Horn-Hofmann et al., 2015; Alabas et al., 2012) could not.

6. Clinical implications for future research

The influence of many personal factors (ADL, fear, self-efficacy, ability to dissociate, locus of control, contraceptives, hair colour, forward head posture, function, hand dominance, polypharmacy, psychomotor performance, sleep, smoking and manual work) on PPT was only of preliminary strength of recommendation. Therefore, more research regarding whether there is an influence present or not, in combination with an explanation for that (possible) influence is necessary. Future studies should at least present complete absolute data (mean and standard deviation for each group/factor, or correlation coefficient and sample size) or ideally focus on multiple linear regression analysis as statistical analysis, in which the influencing factors can be determined (Schneider et al., 2010). To date, at least blood pressure, gender (PPT measured in lower arm/hand or face region), scapular position (PPT measured in neck/shoulder region), and age (PPT measured in arm/shoulder region) can be considered in research when determining normative values for PPT. This can be used in clinical practice when interpreting sensitivity to pressure using PPT.

7. Strengths and limitations of the review

The strengths of this review include the double-blinded screening in both phases, the RoB assessment, the data extraction, and the fact that this is the first review in the field of influencing factors for PPT that was not restricted to solely one influencing factor. Thereupon, the performance of various subgroup- and different types of meta-analyses (considering mean differences and correlation values) led to stronger conclusions than based on qualitative analysis alone. Although meta-analysis required two different software programs to analyse both subgroup and correlation results.

The current review and meta-analysis should also be considered in the light of some limitations. First, many included studies were found by hand search screening. Despite the non-specification of the influencing factors in the search strategy, many studies were missed. A possible explanation could be the absence of the P-term 'controls' in the search strategy. However, adding this term would led to an overload (+10 000) of hits to screen. Secondly, our inclusion criteria were restricted to

clinically measurable personal factors. This means that there is a possibility that other factors, such as environmental factors or genetics, can influence PPT. Thirdly, grey literature search was not performed, as such publication bias cannot be fully excluded. Fourthly, the goal of our systematic review was prognostic, and therefore the QUIPS was chosen to score the RoB. However, most studies only performed univariate analyses in a cross-sectional/ case-control design and received as such higher RoB scores, making the QUIPS tool too strict or too difficult for scoring our included studies. This resulted also in a rather low to moderate Kappa value. However, we tried to compensate for this pitfall by not considering the domains "Study attrition" and "Study confounding" for the overall RoB score when a study design was cross-sectional/ case-control. Fifthly, the LoE allocation was performed only by the first author, ideally, a double blind allocation was set up. Finally, our review focused on all personal factors separately and did not focus on the multivariate analyses, despite some factors can be linked to each other and as such be confounding factors (e.g., age after correcting for gender) leading to different results (as seen in eight out of 12 studies that performed multivariate analyses). However, this was the most feasible way to present our findings in order to create a clear overview for the reader.

8. Conclusion

In summary, age (for PPT assessments at shoulder girdle/upper arm region), blood pressure, gender, and scapular position are personal factors that could be considered when determining normative PPT values. Alcohol consumption, BMI, pain vigilance, depression and menopause are personal factors that do not need to be considered. For the influence of other factors there was only preliminary or conflicting evidence, and should be examined further. Caution for interpretation of these results is advised, because of the univariate analysis of most included studies and because many studies were not eligible to include in meta-analyses. Most meta-analyses had considerable heterogeneity, and most conclusions were weak. More research focusing on personal factors, performing adequate statistics and presenting full absolute data is necessary.

Other information

The details of the protocol were prospectively registered at PROSPERO (registration number 275 191).

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Declaration of interest

None

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.neubiorev.2022.104727](https://doi.org/10.1016/j.neubiorev.2022.104727).

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