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Abstract

Objectives: Existing equipment for quantitative sensory testing is generally expensive and not easily applicable in a clinical setting thus simple bed-side devices are warranted. Pressure hyperalgesia is a common finding in patients with musculoskeletal pain and an experimental model is delayed-onset muscle soreness (DOMS). DOMS is characterised by muscle hyperalgesia and some studies report facilitation of temporal summation of pain. This study aimed to detect DOMS induced muscle hyperalgesia and temporal summation of pain using a newly developed bed-side quantitative sensory testing device to deliver standardised pressure.

Methods: Twenty-two healthy participants participated in two sessions with the second session approximately 48 h after baseline. Pressure pain intensities were assessed from the gastrocnemius muscle with four probes calibrated to apply 2, 4, 6 and 8 kg, respectively. Temporal summation of pain (10 stimuli delivered at 0.5 Hz using the 6 kg probe) intensities were assessed from the same location. DOMS was evoked in the gastrocnemius muscle by an eccentric exercise. Sleepiness and physical activity were measured with the Epworth Sleepiness Scale and the Global Physical Activity Questionnaire to investigate if they were associated with the quantitative sensory testing measures.

Results: Pressure pain intensity was significantly increased 48 h after induction of DOMS when compared to baseline for all four probes ($p<0.05$). Temporal summation of pain was not statistically significant affected by DOMS and sleep quality and physical activity did not associate with any of the measures.

Conclusions: This study introduces a simple, bed-side assessment tool for the assessment of pressure pain intensity and hence hyperalgesia and temporal summation of pain.

Keywords: bed-side assessments; delayed onset muscle soreness; hyperalgesia; Pressure pain thresholds; quantitative sensory testing.

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Introduction

The estimated prevalence of chronic pain is 20% [1–3], it accounts for 15–20% of consultations to general practitioners [4, 5] and has negative consequences for the individuals' quality of life [2, 6].

The underlying mechanisms of chronic pain can be explored by mechanistic, quantitative sensory testing (QST) [7, 8]. Several standardised QST protocols exists [9–11] but many are time consuming, expensive and difficult to implement in clinical practice.

Pressure stimuli are among the most widely used QST measures specifically for assessing muscle hyperalgesia in

chronic musculoskeletal pain [7, 12, 13]. Different pressure algometers have been developed [14–16], but most commercially available pressure algometers are generally expensive and are mainly used for research purposes. If a simple, cheap and quick bed-side pressure algometer existed it might be more widely used in clinical settings for monitoring and quantification.

Previous studies have found lowered pressure pain thresholds (PPTs), and facilitated temporal summation of pain (TSP) in patients with e.g., severe osteoarthritis [17, 18], neck pain [19, 20], or chronic low back pain [21] although conflicting evidence exist for e.g., young adults with patellofemoral pain [22–24]. PPTs assessed over a painful area is considered to reflect peripheral sensitisation whereas PPTs assessed outside of a painful area can reflect widespread hyperalgesia [21]. TSP is a phenomenon of increased pain perception evoked by repetitive painful stimulation with fixed intensity, and it is considered to compose the perceptual equivalent of the neuronal wind-up responses in dorsal horn seen in animals, which is an indicator for central sensitisation [21].

A frequently utilised experimental muscle pain model for evoked pressure hyperalgesia, is delayed onset muscle soreness (DOMS) [25–32]. DOMS is evoked by intense and unaccustomed muscle contraction from physical activity and exposes the individual to a sub-clinical pain lasting 5–7 days, with peak intensity 24–72 h after exercise [33]. Studies have demonstrated that PPTs decrease as a consequence of DOMS [25–27, 30, 31] and some studies have found that TSP is facilitated by DOMS [28, 29]. The general level of physical activity for the individual might affect the degree to which DOMS is manifested after exercise [33]. Furthermore, PPTs has been demonstrated to decrease subsequently to 24 h of total sleep deprivation, while TSP was facilitated under the same conditions [34], suggesting that sleep might be another important factor to consider when assessing PPTs and TSP.

The aims of this study were (1) to investigate if a newly developed, bed-side, pressure algometer could quantify pressure pain intensity and TSP in healthy participants following DOMS and (2) if sleep quality and physical activity influenced pressure hyperalgesia and TSP.

Methods

This experimental study was composed of two sessions separated by approximately 48 h.

Session 1 *(baseline):* The participants completed the Epworth Sleepiness Scale (ESS) and the Global Physical Activity Questionnaire (GPAQ) and were assessed for pressure pain intensity using the four probes, followed by assessment of TSP. Session 1 was concluded by having the participant perform an eccentric calf-raise exercise to evoke DOMS in the lower leg. *Session* 2 *(*48 h after induction of delayed onset muscle soreness, DOMS*):* This session was similar to session 1, except for no GPAQ and calf-raise exercise.

Participants

A previous study found an average decrease in PPT from 375 kPa (SD 93) to 325 kPa (SD 128) with DOMS [30]. Consequently, the present sample size calculations (conducted using the G*power version 3.1 software, Kiel University, Germany) were performed with an effect size at 0.55, 0.05 alpha level and 80% power, thus 22 participants were required. A total of 25 participants were recruited to account for potential drop-outs.

Healthy participants aged 18–45 years were recruited through notices on social media and community boards. Exclusion was warranted if they reported any of the following: drug or alcohol addiction; current use of medications, which might affect the trial (e.g., analgesics and anti-inflammatory drugs); previous or current history of chronic musculoskeletal, neurological, pulmonary, cardiac, or chronic pain conditions as well as mental illness; recent or acute pain; consumption of stimulants or painkillers on the morning of the experiment; lack of ability to cooperate.

Participants who reported mild or no perception of DOMS were excluded, where mild DOMS were defined as "Presence of tenderness, but no pain or difficulties associated with movement and daily activities". The study was approved by the North Denmark Region Committee on Health Research Ethics, case number N-20170088, and conducted in accordance with the Helsinki Declaration. All participants signed informed consent prior to participation.

Pressure probe assessments

The probes were composed of a cylinder containing a spring whose tension could be adjusted by a screw thread (Figure 1). A wing nut secured the spring tension level which determined the resulting pressure delivered by the probe.

Each probe (sphere of 15 mm diameter) was tested each day before application and calibrated, if needed, to ensure the delivered pressure matched the intended pressure. The probes were calibrated using a 10 kg Strain Gauge Load Cell force sensor from Adafruit (Adafruit Industries, New York City, New York USA). The sensor measurements were read by an Arduino UNO through an HX711 Load Cell Amplifier and ADC Module (SparkFun Electronics, Niwot, Colorado USA).

The participants lay on their abdomen during the pressure stimuli. The stimuli were applied to the muscle belly of the medial gastrocnemius muscle. The exact point of stimulation was determined through palpation to locate a point of stability. All assessments were performed by the same assessor (Søren Nicolai Frederiksen Hostrup).

Pressure pain was applied sequentially in order of 2, 4, 6, and 8 kg to the calf on the dominant leg. The evoked pain intensity by each pressure probe was rated by the participant on a Visual Analog Scale (VAS) ranging from 0 to 10, where 0 corresponded to no pain and 10 corresponded to worst pain imaginable.

TSP was applied to the dominant calf with the 6 kg probe and similar to previous studies, 10 stimulations were given with approximately 1 s

Figure 1: The four probes utilised in the present study with the respective calibrated pressure. The probes are approximately 0.23 m long. Developed and calibrated by University of Southern Denmark, Odense, Denmark.

duration and 1 s between stimulations [35]. The pain intensities of the initial and final stimulation were rated on the VAS and the difference between the ratings was defined as the TSP score.

DOMS

DOMS was evoked by having the participants performing calf-raises standing on an elevation with the dominant leg, with no additional load to the body weight, similar to previous studies [31, 32]. The toes were at the edge of the elevation whilst the heel was alternately raised and lowered. The participants were asked to do a maximum of 4 × 30 repetitions (30 s break between sets) with full range of motion. The participant was supported in case of fatigue before reaching the maximum repetitions, however, similar to previous methodology [32] the set was concluded if the participant was incapable of performing the exercise with full range motion.

Questionnaires

The ESS [36] assessed sleep quality as daytime sleepiness. The ESS has differentiated between individuals diagnosed with sleep disorders and healthy individuals [36]. The propensity of falling asleep was evaluated in the range of 0–3 in eight everyday scenarios, where 0 corresponded to "would never doze" and 3 corresponded to "high chance of dozing". Thus, total scores range from 0 to 24, with higher scores indicating worse quality of sleep.

The GPAQ is a questionnaire constructed by The World Health Organization designed to assess physical activity [37]. The GPAQ measures physical activity across three domains of everyday life in moderate and vigorous intensity levels, thus providing a wide measure of the individual's activity level [37]. The results of the GPAQ have been found to provide an acceptable valid measure of physical activity levels [37–39]. Each question was posed to the participant, and the questionnaire was answered in continuous dialog between the experimenter and the participant. Each intensity level in each domain was converted to a Metabolic Equivalent (MET)-value as prescribed by the GPAQ guidelines [30]. The sum of MET-values composed the resulting activity level (GPAQ score) of the participant, with higher scores indicating greater physical activity.

Statistical analysis

All statistical analyses were performed with the IBM SPSS Statistics 26 software, with $p<0.05$ considered as a statistically significant finding. All VAS data were analysed with a Shapiro–Wilk test for normality. The data are presented as mean ± standard deviation.

Pressure pain intensity and TSP in session 1 and 2 were compared with paired t-tests and in case of non-gaussian data distribution Wilcoxon Signed Rank Tests were utilised to assess the difference between the measures. To account for the possible impact of physical activity and sleep quality, one-way repeated measures ANCOVAs were applied to the pressure pain intensity and TSP paradigm. Physical activity was denoted as the calculated MET-values and daytime sleepiness was denoted as the difference in ESS score between session 1 and session 2. VAS baseline and VAS DOMS were dependent variables, time were the independent variable and GPAQ score or ESS score were respectively covariate variables in the ANCOVAs.

Results

Twenty-five participants were recruited, 24 completed both sessions and two were excluded from the analysis as the exercise failed to evoke DOMS. DOMS were evoked in the remaining 22 participants that were included for statistical analysis. Table 1 illustrates demographic information about the participants.

Pressure pain intensity and temporal summation of pain

Significant higher pressure pain intensities were found in the presence of DOMS for the 2 kg ($p=0.014$), 4 kg ($p=0.016$), 6 kg ($p=0.031$) and 8 kg ($p=0.002$) probes when compared to baseline (Figure 2).

Table 1: Participant demographics and questionnaire responses.

Characteristic	Values
Age	24.8 ± 1.8
Sex	Male 11; Female 11
BMI	24.1 ± 2.3
Dominant leg	Right 21; Left 1
ESS score	Baseline 5.0 ± 3.2; DOMS 4.8 ± 3.2
GPAQ score	2,763 ± 2,065

Data are reported as mean ± standard deviation. BMI, body mass index; ESS, Epworth Sleepiness Scale; GPAQ, global physical activity questionnaire.

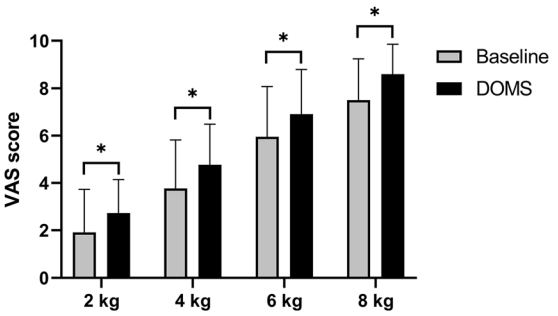

Figure 2: Pressure pain intensity assessed by the visual analog scale (VAS) from the application of different probes comparing session 1 (baseline) with session 2 (48 h after induction of delayed onset muscle soreness, DOMS). *illustrates p<0.05 comparing baseline and DOMS sessions.

Figure 2 shows the pressure pain intensity comparison between session 1 and 2.

No statistically significant difference was found in TSP between baseline 1.32 ± 2.34 and after induction of DOMS 1.50 ± 2.04 (p=0.639).

Sleep and physical activity

Pressure pain intensity measurements and TSP were analysed for differences between baseline and DOMS controlling for covariance of sleep quality (ESS score) and physical activity (GPAQ score) and no statistically significant association was found (Table 2).

Discussion

This study applied a newly developed, bed-side, assessment tool for assessing pressure pain intensity and temporal summation of pain. DOMS was found to significantly increase pressure pain intensity when utilising each of the four calibrated probes. Sleep quality and physical activity levels showed no statistically significant impact on pressure pain intensity and TSP.

Table 2: The column 'Pressure probe' refers to the specific utilised pressure probe and the pain assessment paradigm by which it was applied.

Pressure probe	Time·ESS [P–Value]	Time·GPAQ [P–Value]
2 kg pressure	0.962	0.976
4 kg pressure	0.766	0.817
6 kg pressure	0.618	0.950
8 kg pressure	0.274	0.942
6 kg pressure used for temporal summation of pain	0.229	0.651

The column 'Time·ESS' is the resulting p–values from the ANCOVA with ESS as covariate for baseline-DOMS comparison, the same is shown for the column "Time·GPAQ", though with GPAQ as covariate. ESS, Epworth Sleepiness Scale; GPAQ, global physical activity questionnaire.

Pressure hyperalgesia and temporal summation of pain

Many studies have demonstrated that pressure pain thresholds decreases in the presence of DOMS [25–27, 30, 31] making this a validated experimental muscle pain model. The present assessment tool was capable of assessing muscle hyperalgesia after induction of DOMS and hence may have potential for clinical applications. Future studies are warranted to confirm the reliability of the probes and potentially to assess the importance of e.g., other probe diameters.

TSP has been an experimental proxy for assessment of sensitisation most likely of a central origin [40]. Facilitated TSP has been found in a range of patients with chronic pain including fibromyalgia [41], osteoarthritis [42], low back and neck pain [19], irritable bowel syndrome patients [43] and some neuropathic chronic pain patients [44], and evidence suggest that TSP is predictive for chronic postoperative pain and response to weak analgesics [7, 45–47]. Thus, including TSP in bed-side settings might provide complementary clinical information and have predictive value. Conflicting evidence suggests that TSP is facilitated [28, 29], or unaffected [48, 49] by DOMS. Previous studies have argued that facilitation of TSP require continuous peripheral drive for a long duration (years) [8], such as seen in e.g., severe osteoarthritis [8, 18]. DOMS is a short-lasting pain model at low intensity, which could explain why the current study does not find DOMS to alter the TSP response.

Sleep and physical activity

Impaired sleep quality is associated with many chronic pain conditions [50], with a minimum of 50% chronic pain patients affected by sleep impairments [51]. Additionally, co-occurrence of sleep impairments might enhance chronic pain symptoms [51]. Assessment of pressure pain tolerance thresholds shows that total sleep deprivation induces pressure pain sensitivity [34, 52]. By contrast, the present study showed no evidence of facilitated pain sensitivity in relation to sleep deprivation. However, the participants in this study were not sleep deprived as indicated by ESS scores similar to those seen in healthy

controls [36]. Since DOMS is the product of unaccustomed eccentric exercise, it might be generally associated with physical activity levels [33]. However, the present findings showed no significant relation between DOMS related evoked pain and physical activity levels. Nonetheless, DOMS was successfully induced in all included participants which might explain why physical activity levels did not account for any significant variance in pain measures between baseline and DOMS.

Limitations

DOMS was only reported as present or absent in the current study and the degree of DOMS per se was not quantified. No participants could be categorised as sleep deprived, and the measure for sleep quality simply reflected the difference in self-reported daytime sleepiness between the two sessions, and the measure is not sufficiently sensitive to assess minor changes in sleepiness.

This preliminary study was initiated to assess if the newly developed bed-side pressure algometer could detect pressure hyperalgesia. It is however important to assess reliability of the assessments and to investigate the clinical usefulness prior to implementation.

Conclusions

This study evaluated a newly developed bed-side pressure algometer and confirmed that pressure hyperalgesia can be assessed in healthy individuals following delayed onset muscle soreness. Sleep quality and physical activity levels did not affect pressure pain intensity and temporal summation of pain. Future studies are needed to assess the reliability of the tool.

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Informed consent: Informed consent has been obtained from all individuals included in this study.

Ethical approval: This research, involving human subjects, complied with all relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration (as amended in 2013), and has been approved by the authors and by the North Denmark Region Committee on Health Research Ethics, case number N-20170088.

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