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Pressure and cold pain threshold reference values in a large, young adult, pain-free population

Robert Waller[a,*], Anne Julia Smith[a], Peter Bruce O'Sullivan[a], Helen Slater[a], Michele Sterling[b], Joanne Alexandra McVeigh[a], Leon Melville Straker[a]

[a] School of Physiotherapy and Exercise Science, Curtin University, Perth, Western Australia 6845, Australia
[b] RECOVER Injury Research Centre, NHMRC Centre of Research Excellence in Road Traffic Injury, Menzies Health Institute, Griffith University, QLD 4222, Australia

HIGHLIGHTS

- Provides reference pressure and cold pain threshold data for a 'healthy' young adult population.
- The data represent the most comprehensive and robust data available for young adults aged 21–24.
- Statistically significant, independent correlates of pain sensitivity measures are provided.
- The data enable more accurate interpretation of pain sensitivity in clinical pain disorders.
- Provides insight into the complex associations of pain sensitivity for use in future research.

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ABSTRACT

Background and aims: Currently there is a lack of large population studies that have investigated pain sensitivity distributions in healthy pain free people. The aims of this study were: (1) to provide sex-specific reference values of pressure and cold pain thresholds in young pain-free adults; (2) to examine the association of potential correlates of pain sensitivity with pain threshold values.
Methods: This study investigated sex specific pressure and cold pain threshold estimates for young pain free adults aged 21–24 years. A cross-sectional design was utilised using participants ($n = 617$) from the Western Australian Pregnancy Cohort (Raine) Study at the 22-year follow-up. The association of site, sex, height, weight, smoking, health related quality of life, psychological measures and activity with pain threshold values was examined. Pressure pain threshold (lumbar spine, tibialis anterior, neck and dorsal wrist) and cold pain threshold (dorsal wrist) were assessed using standardised quantitative sensory testing protocols.
Results: Reference values for pressure pain threshold (four body sites) stratified by sex and site, and cold pain threshold (dorsal wrist) stratified by sex are provided. Statistically significant, independent correlates of increased pressure pain sensitivity measures were site (neck, dorsal wrist), sex (female), higher waist-hip ratio and poorer mental health. Statistically significant, independent correlates of increased cold pain sensitivity measures were, sex (female), poorer mental health and smoking.
Conclusions: These data provide the most comprehensive and robust sex specific reference values for pressure pain threshold specific to four body sites and cold pain threshold at the dorsal wrist for young adults aged 21–24 years. Establishing normative values in this young age group is important given that the transition from adolescence to adulthood is a critical temporal period during which trajectories for persistent pain can be established.
Implications: These data will provide an important research resource to enable more accurate profiling and interpretation of pain sensitivity in clinical pain disorders in young adults. The robust and comprehensive data can assist interpretation of future clinical pain studies and provide further insight into the complex associations of pain sensitivity that can be used in future research.

* Corresponding author at: School of Physiotherapy and Exercise Science, Building 408, Level 3, Curtin University, GPO Box U1987, Perth, Western Australia 6845, Australia. Fax: +161 9266 3699.
E-mail address: R.Waller@curtin.edu.au (R. Waller).
URL: http://www.curtin.edu.au (R. Waller).

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1. Introduction

Quantitative sensory testing (QST) as a measure of pain sensitivity, is being increasingly used to generate somatosensory profiles of patients in clinical pain studies [1,2] and to measure outcomes in randomised controlled trials [3,4]. However meaningful interpretation of data from these studies requires appropriate reference values for what is 'normal'. This ideally should be drawn from large population-based samples of 'healthy pain-free participants', adjusted for age, sex, and other potential confounders [5], thereby allowing for generalisability. Currently there is a lack of large population studies that have investigated pain sensitivity distributions in healthy people.

While there are some 'normative' datasets against which to reference clinical QST data [6–12], currently there is no comprehensive reference QST data specific to young adults. As the transition from adolescence to adulthood is a critical time during which trajectories for persistent pain can become established [13–16] there is value in establishing normative data for this young age group. Issues with the utility of current normative datasets for QST include a lack of adherence to recent calls for standardised definitions, and best practice recommendations to adjust for potential confounding variables such as age and sex [17]; datasets that include participants with pain [7,8]; having relatively small numbers in each age and sex range [9–11]; or wide ranging age groups [12]. There is thus a gap in knowledge of normal age-sex specific pain sensitivity distributions.

Further, without large cohort reference values to define 'normal' and an understanding of potential correlates, the interpretation of QST measures in pain studies is severely limited, as is their utility in management of people with pain [5,18]. Potential independent correlates associated with increased pain sensitivity to pressure and cold stimuli include younger age [6], female sex [19], increasing Body Mass Index [6,20], higher psychological symptoms of depression, anxiety, stress and catastrophizing, [2,6,21–23], decreased health related quality of life [6], lower physical activity and increased sedentary behaviour, [21,24,25], and smoking [8,26]. Only one normative study of pain sensitivity has investigated a broad range of potential correlates (demographic, psychological and health-related factors), but this study was limited by a relatively wide age range with small age-specific participant numbers [6].

Clinically, the assessment of an individual's pain sensitivity can inform treatment options [27]. In this context, exploring normative ranges for deep tissue pain sensitivity (pressure pain threshold: PPT) is particularly important given deep tissues are implicated in musculoskeletal conditions [28–32]. With the availability of affordable algometers, there is increasing use of PPT testing in clinical settings to assess and monitor tissue sensitivity levels Cold hypersensitivity (cold pain threshold: CPT) has also demonstrated clinical utility for predicting poor prognosis in whiplash associated disorders [33] and differentiating pain mechanisms in musculoskeletal pain conditions [18,23,34,35]. These two clinically relevant nociceptive stimuli can form part of a shorter QST protocol by limiting participant burden and improving time efficiency [36].

The large birth cohort investigated here provided an opportunity to capture more precise sex specific pressure and cold pain threshold estimates for young, pain-free adults. The aims of this study were: (1) to provide sex-specific reference values of pressure and cold pain thresholds in young pain-free adults; (2) to examine the association of site, sex, ethnicity, height, weight, smoking, health related quality of life, psychological factors and physical activity levels with pain threshold values.

2. Methods

2.1. Study Population

Cross-sectional data for this study was obtained from the Western Australian Pregnancy Cohort (Raine) Study (http://www.rainestudy.org.au). This is an ongoing birth cohort study that commenced with 2900 women who enrolled in the study before the 18th gestation week and 2868 children born, entered the initial birth cohort. Data has been collected at 1, 2, 3, 5, 8, 10, 14, 17, 20 and 22 years. The characteristics of the active participants were compared with census data collected in 2011 on all similarly aged young adults in Western Australia. The comparison showed that the sample remains widely representative for a range of variables including education level, employment status, income, marital status, number of offspring, hours worked and occupation. The 22 year follow-up data collection ran between March 2012 and July 2014. Further detail on full measures collected can be found at http://www.rainestudy.org.au/for-researchers/cohort-follow-ups/ [37].

2.2. Recruitment, sampling and data collection

All data used in this study were obtained at the 22 year follow-up. Data were collected as part of 4 h of testing followed by an overnight sleep study. For this follow up, 1065 individuals participated in pressure pain and cold pain threshold testing. Of the 970 participants who had pressure and cold pain threshold data, and completed questionnaire and physical assessment data on nominated correlates, 617 (280 female and 337 male) were classified as pain free and were included for analysis. Participants were considered pain free if they answered "no" to the question "do you have any current body pain?" from the Orebrö Musculoskeletal Pain Questionnaire (OMPQ).

Questionnaires were filled in before physical assessments and were checked for completion. Anthropometry measures and pressure and cold pain threshold testing were part of the physical assessment protocol conducted by twelve Raine research staff, all of who were thoroughly trained in the data collection procedures and used standardised protocols.

2.3. Quantitative sensory testing

Due to time constraints allowed for collecting data and to minimise the already significant participant burden, the sensitivity measures considered most clinical relevant were collected. A standardised protocol for QST consistent with current best practice recommendations [12,17], was used to measure PPT and CPT. All QST measurements were taken from the right side of the body, as side to side consistency in pain threshold measurements have been shown in people with [38] and without pain [12]. All testing was done in the early evening minimising the influence of circadian rhythms on pain sensitivity [39] and the order of testing was PPT, followed by CPT, as applying cold first has been found to increase the risk of mechanical hyperalgesia [40]. This testing sequence has been used previously [23]. Both PPT and CPT have demonstrated inter-examiner and intra-subject reliability with reasonable levels of standard error of measurement [41–43]. Excellent inter-rater and intrarater reliability for PPT testing by the Raine research staff has been demonstrated, with the caveat that an absence of any confounding of study estimates by rater should be checked due to a systematic rater bias identified [44].