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Original

# Agreement between single and mean of three craniofacial pressure pain threshold measurements: feasibility in healthy adults

**Rosana Tieka Miyazaki Brancucci[1], Vanda de Lelis[1], Georgia Westenhofen[1], Ida Fortini[1], Gabriel Taricani Kubota[1], Gianluca Coppola[2], Mario Fernando Prieto Peres[1]**

[1]University of São Paulo, São Paulo, São Paulo, Brazil
[2]Sapienza University of Rome Polo Pontino, Latina, Italy

Mario Fernando Prieto Peres
mariop3r3s@gmail.com

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Marcelo Moraes Valença

**Abstract**

**Background**
Pressure pain threshold assessment is used to quantify pain sensitivity in headache disorders, reflecting peripheral and central sensitization of the nociceptive system. Traditional protocols involve multiple measurements to ensure reliability, but these protocols are time-consuming and may cause participant fatigue and discomfort.

**Objective**
To evaluate the agreement and reliability between a single Pressure Pain Threshold (PPT) measurement and the mean of three measurements in the craniofacial of individuals without a history of headache disorders, using a digital algometer.

**Methods**
Cross-sectional methodological study with ten volunteers (60% female, mean age 43±8 years) without headache history. Pressure pain threshold was assessed at eight craniofacial sites (bilateral: occipital, temporal, masseter; central: frontal, vertex) using a digital algometer. Three consecutive measurements were performed at each site with 10-minute intervals. Reliability between measurements was assessed using Intraclass Correlation Coefficient (ICC), while agreement and systematic bias were evaluated using Bland–Altman analysis

**Results**
Intra-rater reliability ranged from moderate to good (ICC=0.54–0.96) across individual sites, with good-to-excellent reliability in bilateral occipital, temporal, and masseter sites (ICC=0.62–0.96). Reliability between the single measurement and the mean of three trials was uniformly excellent (ICC=0.93–0.98) Bland-Altman analysis showed minimal bias (mean differences near zero) and relatively narrow limits of agreement in peripheral sites, with wider limits observed in central regions.

**Conclusion**
A single pressure pain threshold measurement demonstrated agreement comparable to the mean of three measurements, supporting the potential use of simplified assessment protocols.

**Keywords:**
Pressure pain threshold
Agreement
Intraclass correlation coefficient
Headache
Reproducibility

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## Introduction

Understanding the subjective experience of pain and its underlying neural mechanisms remains a constant challenge in both academic and clinical research. To investigate pain perception in humans, controlled external stimuli are frequently applied to replicate painful sensations (1,2). Among the various modalities of quantitative sensory testing (QST) (3), the Pressure Pain Threshold (PPT) is widely used to assess sensitivity to mechanical pain in deep somatic structures. The PPT is defined as the minimum amount of pressure required to elicit a painful sensation (3–6), which may be altered in different types of headache, including migraine and tension-type headache (7–11).

PPT assessment reflects peripheral and central sensitization of the nociceptive system. Peripheral sensitization refers to increased excitability of nociceptors at the site of injury, resulting in lowered thresholds and amplified local pain response. Central sensitization involves altered excitability of central nervous system neurons, leading to pain amplification and expansion of receptive fields, often manifested as secondary hyperalgesia and pain in areas distant from the original site (8–10).

By quantifying mechanical pain sensitivity, PPT has been applied in various pain conditions, including headache disorders, assisting in the quantification of pain sensitivity. Assessing pain sensitivity in cephalic regions is particularly relevant for understanding physiopathology and treatment response in patients with different headache types (9–15). However, PPT protocols commonly rely on repeated trials per site, typically averaging two or three measures to increase stability. Although widely used, this approach is time-consuming, increases participant burden, and may introduce re-exposure effects such as deficit habituation, anticipation, or discomfort, factors that are particularly relevant when multiple cephalic sites must be assessed (5,16).

Previous studies have demonstrated good intra- and inter-rater reliability of PPT in healthy volunteers (5,17–19) and across pain-related conditions (20). Reliability is typically quantified using the Intraclass Correlation Coefficient (ICC), with values commonly ranging from 0.80 to 0.95, indicating high reproducibility. Complementary indices such as the standard error of measurement (SEM) and absolute error also fall within acceptable ranges, often below 15% of the mean PPT value in healthy samples, supporting the methodological robustness of PPT for both clinical and research purposes (5,21–23). Despite these strengths, conventional protocols requiring multiple measurements per site increase assessment time and may contribute to participant fatigue or discomfort, particularly when several anatomical sites must be evaluated.

Given these considerations, the present study investigated whether a single PPT measurement in the craniofacial region of pain-free volunteers is in agreement with the mean of multiple consecutive trials obtained using a digital algometer (Neuro Cranio Cervical Device) (24). Establishing whether a simplified single-measure protocol can adequately represent repeated measurements has practical implications for studies of pain perception and headache research, as it may streamline data collection, reduce participant burden, and improve feasibility in protocols requiring multiple-site assessments.

## Methods

*Study design*

This cross-sectional methodological study evaluated the agreement between a single PPT measurement and the mean of repeated measurements obtained with a digital algometer in individuals without a history of headache disorders. In addition, intra-rater reliability across repeated trials was assessed to characterize measurement consistency. The primary outcome was the level of agreement between a single measurement and the reference standard defined as the mean of three repeated measurements at predefined craniofacial sites. The study adhered to established methodological standards for reliability research, including current recommendations for the design, statistical analysis, and interpretation of Intraclass Correlation Coefficients (ICC) (5,24,25) and Bland-Altman(26).

*Participants*

Adults aged ≥18 years were recruited from a convenience sample of medical students and healthcare professionals. Eligible participants had no history of migraine or other primary headache disorders, no acute or chronic pain conditions, and no major medical or psychiatric illnesses. All participants provided informed consent. The study protocol was approved by the Ethics Committee of the Hospital das Clínicas, Faculty of Medicine, University of São Paulo (CAAE: 4.293.550).

*Procedure*

The protocol consisted of PPT assessments to evaluate measurement reliability. All evaluations were conducted by a physiotherapist who completed standardized training to ensure consistent probe positioning and controlled pressure application at a fixed rate of 0.5 kPa/s.

*Pressure pain threshold assessment*

PPTs were measured using a digital algometer (NOD-Neuro Cranio Cervical Device; OT Bioelettronica, Turin, Italy) equipped with a 1 $cm^2$ hard-rubber circular probe. The device transmits data wirelessly via Bluetooth® to a tablet. Output values were expressed in kilopascals (kPa).

*Measurement sites and testing protocol*

Eight craniofacial sites were assessed using a standardized protocol: bilateral suboccipital muscle insertions, bilateral medial and ventral portions of the masseter and temporalis muscles, the central frontal region, and the cranial vertex. Each site was identified through anatomical palpation and marked with a dermographic pen to ensure precision and reproducibility.

PPTs were measured thrice in the following order: (1) 2/3 of the distance of a line drawn from the center of the mastoid to the external occipital protuberance occipital of the right occipitofrontal muscle (27), major occipital nerve; (2) right temporalis muscle, deep temporalis nerve; (3) right masseter muscle, masseteric nerve (4) frontal, between eyebrow, frontal muscle, medial branch of the supraorbital nerve; (5) vertex, central top of skull; (6) left occipital, major occipital nerve; (7) left temporalis muscle, deep temporalis nerve; (8) left masseter, masseteric nerve (28).

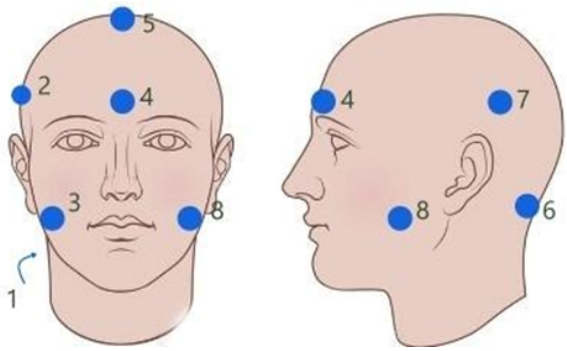


Figure 1. Eight craniolfacial sites measurement pressure pain threshold.

Participants received detailed instructions regarding the operation of the algometer and were seated comfortably with their forearms supported on the table. They underwent a preliminary trial for familiarization with the measurement of the PPT, applied to the ventral region of the finger extensor muscles of the dominant hand. Pressure was gradually increased until participants perceived the onset of pain and verbally indicated "stop," at which point the corresponding pressure value (kPa) was recorded. After a 10 minute interval, the experimental measurements commenced, consisting of three consecutive PPT assessments at each site, performed with 10 minute intervals between trials. In each assessment, the corresponding pressure value (kPa) was recorded (5).

*Reliability and agreement analysis*

Intra-rater reliability across repeated measurements was quantified using the Intraclass Correlation Coefficient (ICC) (5,25). A two-way mixed-effects model with single-measurement and absolute-agreement definition [ICC (1,3)] was applied, which is appropriate for repeated assessments performed by a single fixed examiner. ICC values were interpreted as <0.50 indicating poor reliability, 0.50–0.75 moderate, 0.75–0.90 good, and >0.90 excellent reliability.

Agreement between a single PPT measurement and the mean of three repeated measurements was also assessed using the ICC with absolute agreement. In addition, Bland–Altman analysis was performed to evaluate the level of agreement and to identify any systematic bias between the single-measure and the mean of repeated measurements.

*Statistical Analysis*

Statistical analyses were performed using IBM SPSS Statistics, version 28 (IBM Corp., Armonk, NY, USA). Intraclass correlation coefficients (ICCs) were computed to assess intra-rater reliability across the three repeated measurements (T1, T2, T3) at each craniofacial site. Agreement analyses compared a single PPT measurement (T1) with the mean of the three measurements (Tmean). Bland-Altman plots were generated using MedCalc, version 12.5.0.0, displaying 95% limits of agreement, the mean difference line, and the zero line to evaluate systematic and random bias between the single measurement and the mean (Tmean).

A significance level of $p < 0.05$ was adopted. The sample size was consistent with methodological studies indicating that intra-rater reliability of PPT can be estimated with acceptable precision in small samples (approximately 8–15 participants) when repeated trials are obtained under standardized conditions (5,25).

## Results

Fifteen individuals were screened, five of whom were excluded due to a history of pain, resulting in a final sample of ten participants. All participants provided written informed consent. Sociodemographic characteristics are summarized in Table 1 sociodemographic characteristics of the study participants.

Table 1. Sociodemographic characteristics of the study participants

| Variables | n | % |
|---|---|---|
| **Sex (n=10)** | | |
| Men | 4 | 40 |
| Women | 6 | 60 |
| **Age, mean ± SD** | 43.2 ± 8.0 | - |
| **BMI, mean ± SD** | 25.4 ± 3.2 | - |
| **Education (n=10)** | | |
| Undergraduate | 3 | 30 |
| Postgraduate | 7 | 70 |
| **Employment status (n=10)** | | |
| Part-time employment | 4 | 40 |
| Full-time employment | 6 | 60 |

Values are presented as absolute frequencies (n) and percentages (%). Age and BMI are expressed as mean ± standard deviation (SD)

Participants were predominantly female (60%), with a mean ± SD age of 43 ± 8 years and a mean body mass index (BMI) of 25.4 ± 3.2 kg/m$^2$. Most participants (70%) held a postgraduate degree.

Descriptive statistics for the three PPT measurements are presented in Table 2 Pressure pain threshold measurements across three trials at craniofacial sites. The distribution of PPT values across craniofacial sites is illustrated in Figure 2 relationship between sites and pressure pain threshold (kPa).

Table 2. Pressure pain threshold measurements across three trials at craniofacial sites

| Measure | Time 1 | | | Time 2 | | | Time 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| Pressure Pain Threshold (PPT) | Average | SD | Sum | Average | SD | Sum | Average | SD | Sum |
| Occipitalis right | 423.3 | 172.9 | 4233 | 347.5 | 162.4 | 3475 | 395.4 | 165.3 | 3954 |
| Occipitalis left | 387.4 | 235.1 | 3874 | 378.4 | 200.9 | 3784 | 426.8 | 200.8 | 4268 |
| Temporalis right | 223.0 | 79.9 | 2230 | 243.6 | 61.1 | 2436 | 254.2 | 97.1 | 2542 |
| Temporalis left | 209.7 | 72.1 | 2097 | 191.3 | 57.2 | 1913 | 195 | 80.9 | 1950 |
| Masseter right | 146.2 | 69.7 | 1462 | 149.3 | 51.3 | 1493 | 142.5 | 58.4 | 1425 |
| Masseter left | 159.1 | 74.6 | 1591 | 123.6 | 49.9 | 1236 | 135.1 | 50 | 1351 |
| Frontal | 282.1 | 81.1 | 2821 | 255.9 | 74.6 | 2559 | 278 | 66.7 | 2780 |
| Vertex | 351.2 | 127.8 | 3512 | 395.3 | 181.1 | 3953 | 358.7 | 127.5 | 3587 |
| Sum | 2182 | 913.2 | 21820 | 2084.9 | 838.7 | 20849 | 2185.7 | 846.6 | 21857 |

Values are presented as mean (Average), standard deviation (SD), and summed PPT values for each trial. The row labeled Sum represents the total PPT for all sites within each trial

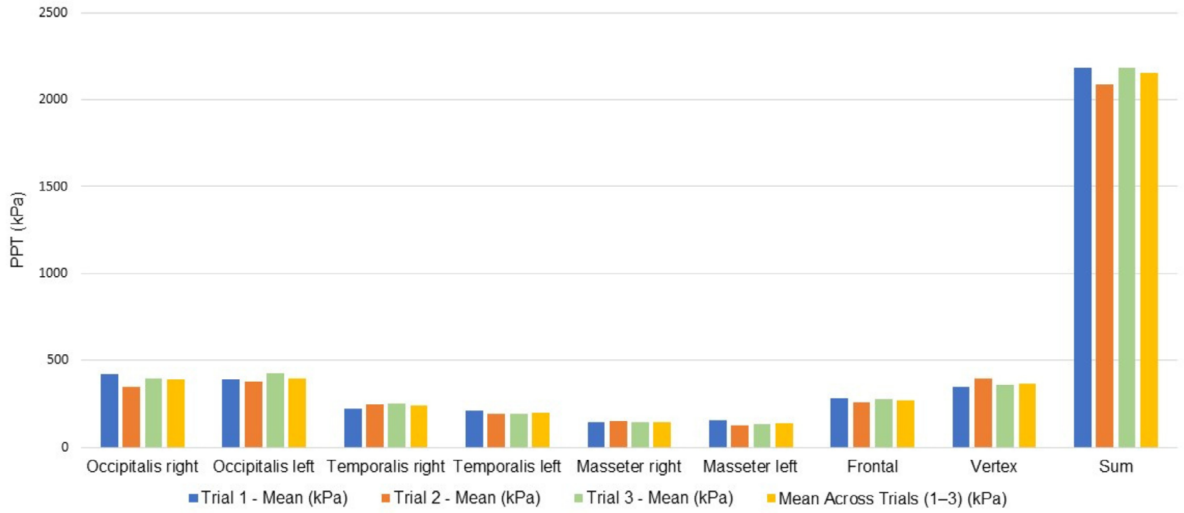


Figure 2. Relationship between sites and pressure pain threshold (kPa).

Comparison between the single PPT measurement and the mean of three trials demonstrated moderate-to-excellent consistency across anatomical sites. PPT measurements in kPa bilaterally at the occipital, temporal, and masseter sites demonstrated excellent reliability between the first measurement and the mean of three repetitions, with intraclass correlation coefficients (ICC > 0.85, up to 0.984 in left occipital). Bland-Altman analysis revealed minimal bias (means of differences near zero, including -17.3 kPa in right temporal, which remains clinically acceptable) and reasonably relatively narrow limits of agreement in peripheral regions, with wider limits observed in central cranial sites (e.g., -45.2 to 45.6 kPa in right masseter), indicating high reproducibility in PPT measurements. The frontal and vertex sites showed good reliability (ICC 0.74 to 0.92), with moderate bias (10.1 and 31.1 kPa) and wide limits of agreement (-92.0 to 112.2 kPa frontal; -113.9 to 79.5 kPa vertex); notably, frontal threshold measurements lay within the limits of agreement with a random data pattern, as did right and left masseter and right and left occipital measurements, indicating greater variability and reduced precision, particularly in central cranial regions. All data presented are shown in Table 3 Intraclass correlation coefficient and Bland-Altman analysis between the first measurement and the mean of the three measurements.

Bland-Altman plots for the eight anatomical sites (bilateral occipital, temporal, masseter, central frontal, and vertex) are shown in Figures 3-10, and the overall sum is shown in Figure 11.

Table 3. Intraclass correlation coefficient and Bland-Altman analysis between the first measurement and the mean of the three measurements

| Measurement PPT (kPa) | ICC (95% CI) | Bland-Altman | |
|---|---|---|---|
| | | Mean difference | 95% LoA of mean differences |
| Frontal | 0.7402 (0.2491 – 0.9285) | 10.10 | -92.0 – 112.2 |
| Right masseter | 0.9342 (0.7592 – 0.9833) | 0.20 | -45.2 – 45.6 |
| Left masseter | 0.8560 (0.5238 – 0.9622) | 19.80 | -47.5 – 87.1 |
| Right occipital | 0.9807 (0.9247 – 0.9952) | 34.60 | -29.9 – 99.0 |
| Left occipital | 0.9836 (0.9357 – 0.9959) | -10.10 | -89.0 – 68.7 |
| Right temporal | 0.8753 (0.5776 – 0.9675) | -17.30 | -91.4 – 56.9 |
| Left temporal | 0.8954 (0.6363 – 0.9729) | 11.00 | -48.8 – 70.9 |
| Vertex | 0.9237 (0.7245 – 0.9805) | 31.10 | -113.9 – 79.5 |
| Sum (overall) | 0.9959 (0.9836 – 0.9990) | -17.20 | -86.6 – 148.9 |

ICC: intraclass correlation; 95% CI (confidence interval): 95% LoA (limits of agreement); PPT: pressure pain threshold; kPa: kilopascal

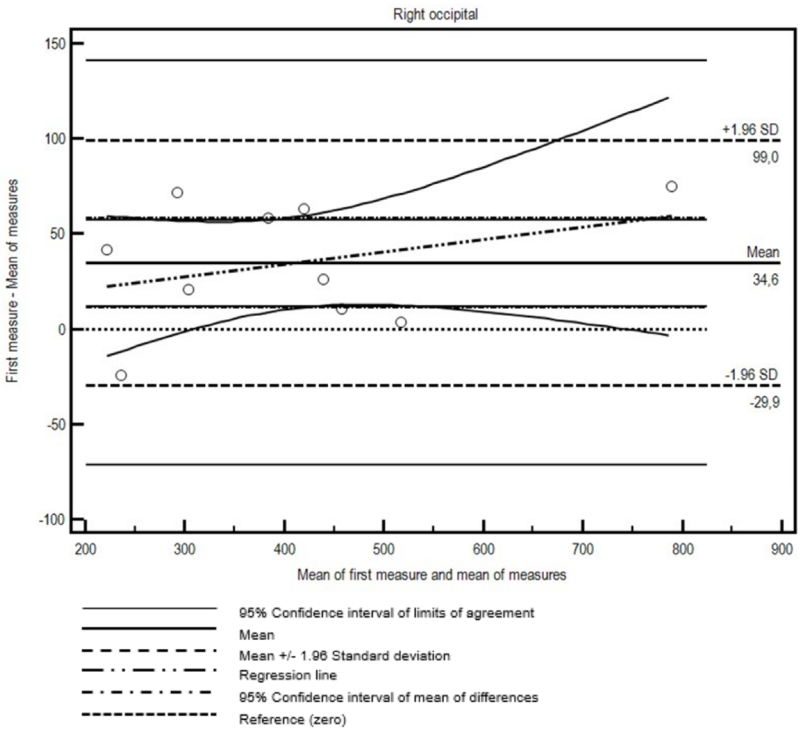


Figure 3. Bland-Altman analysis for right occipital measurement.

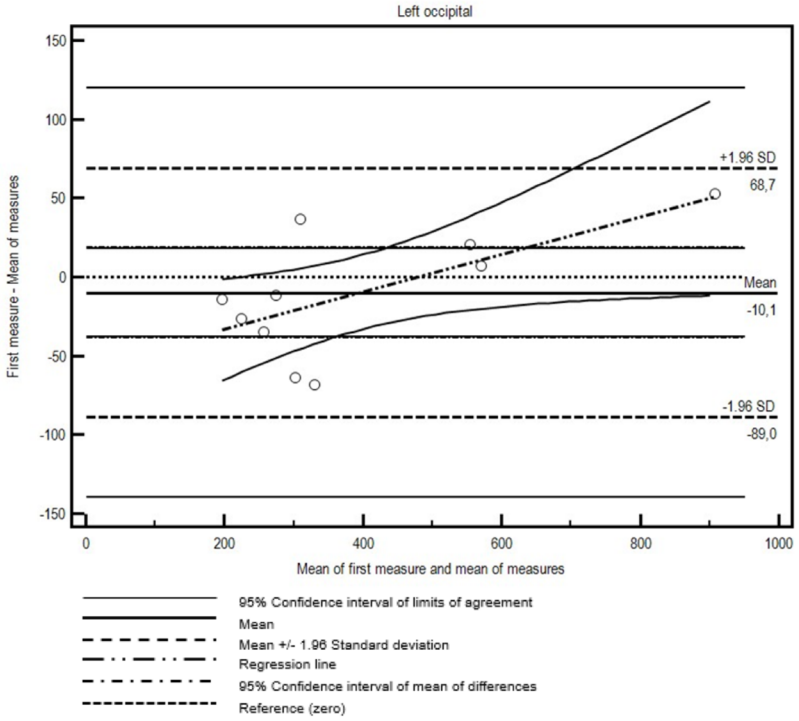


Figure 4. Bland-Altman analysis for left occipital measurement.

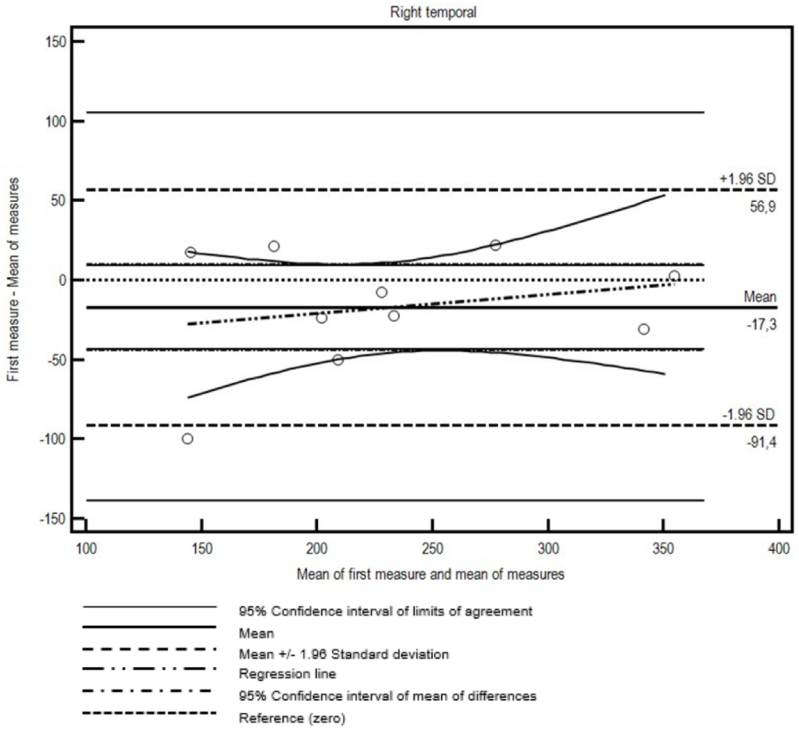


Figure 5. Bland-Altman analysis for right temporal measurement.

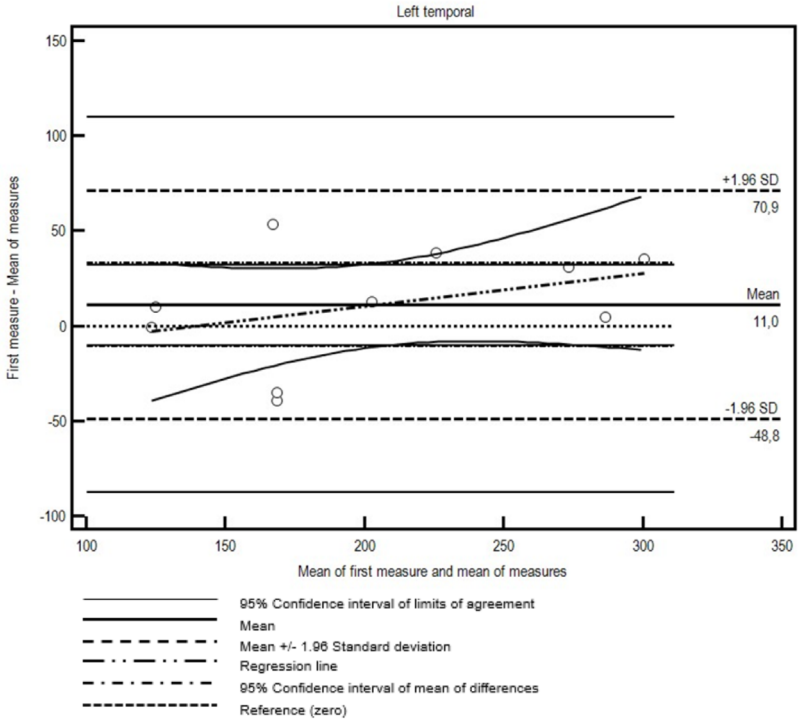


Figure 6. Bland-Altman analysis for left temporal measurement.

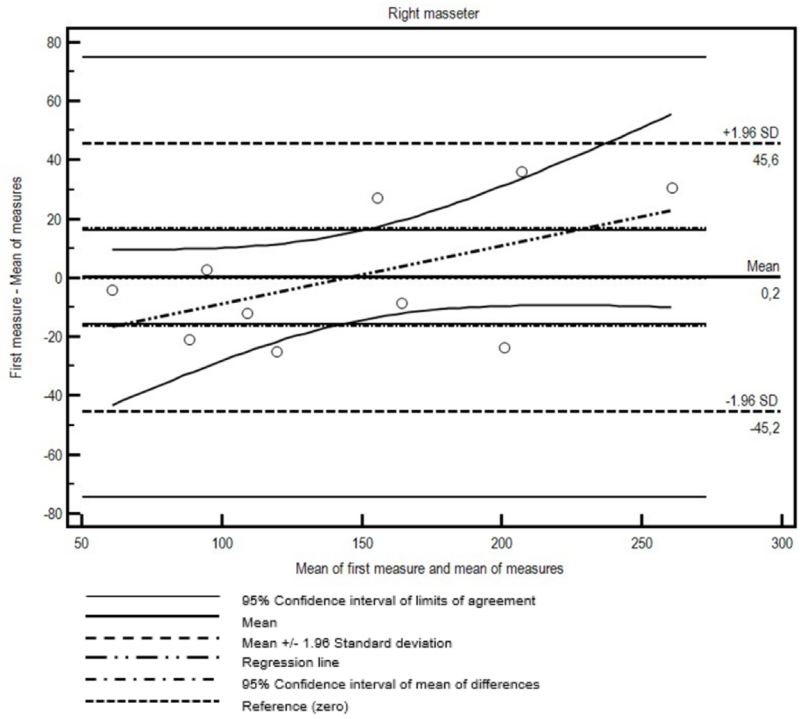


Figure 7. Bland-Altman analysis for right masseter measurement.

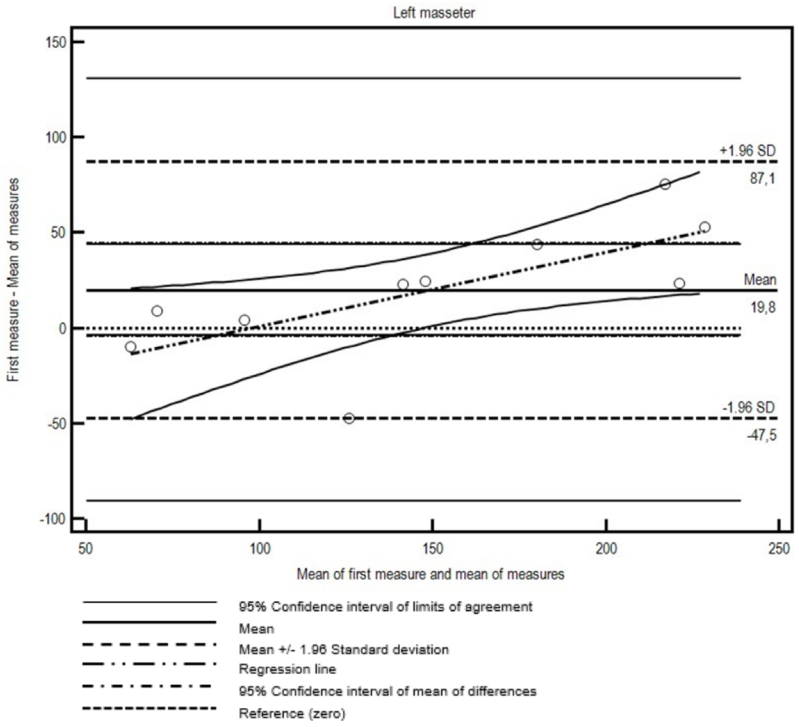


Figure 8. Bland-Altman analysis for left masseter measurement.

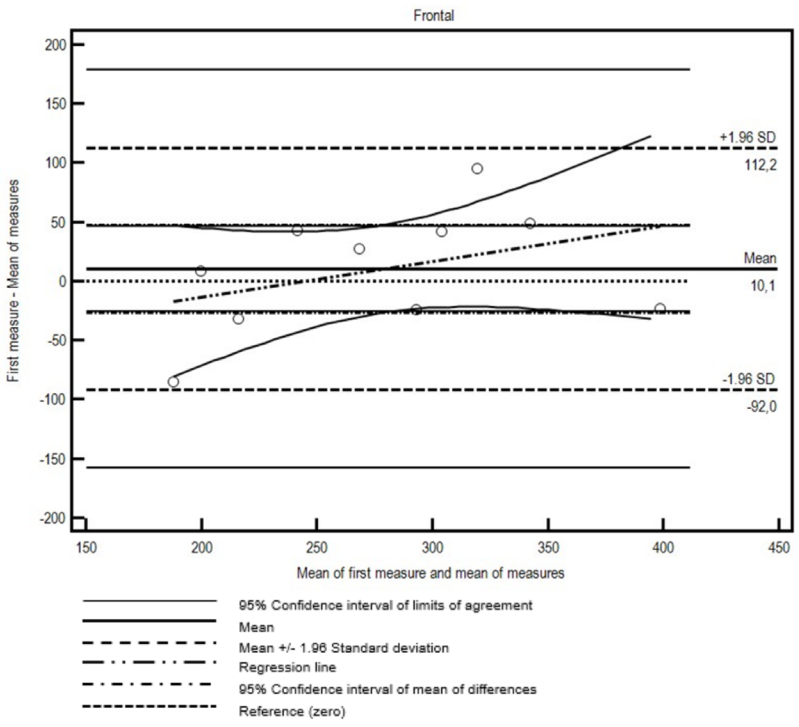


Figure 9. Bland-Altman analysis for frontal measurement.

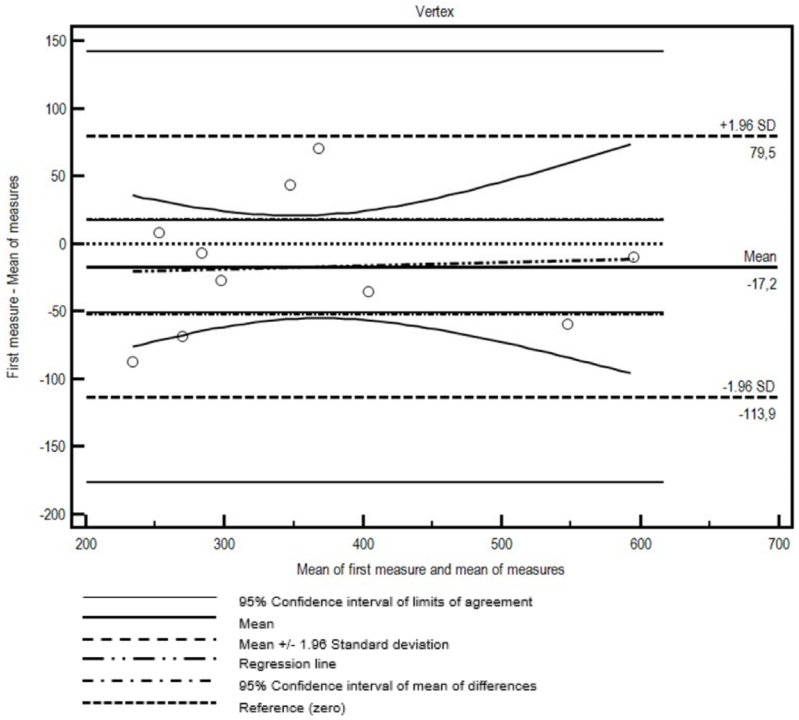


Figure 10. Bland-Altman analysis for vertex measurement.

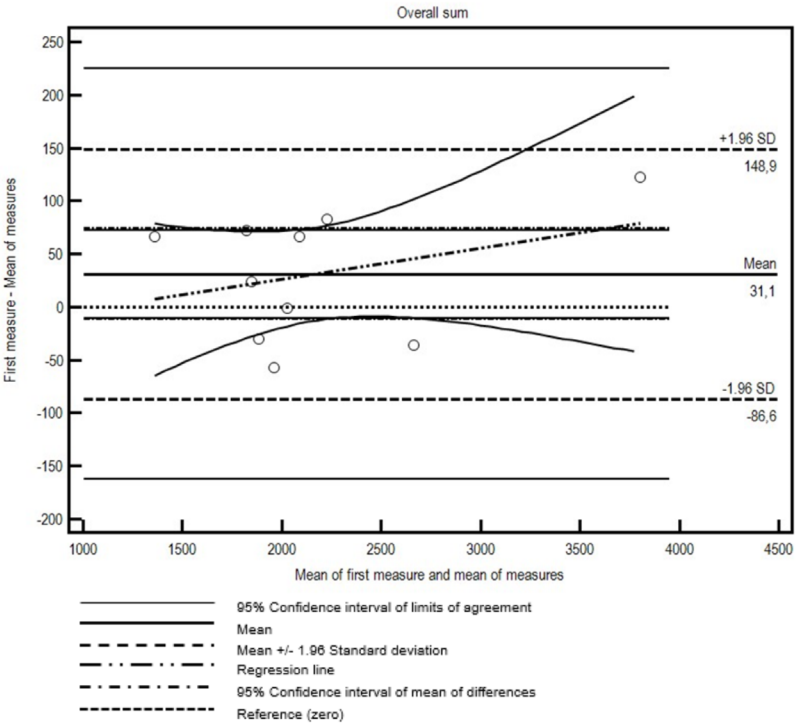


Figure 11. Bland-Altman analysis for overall sum.

Reliability of the mean PPT values across trials is presented in Table 4 Intraclass Correlation Coefficients (ICC) for sum scores of pressure pain threshold values across trials. ICCs for summed comparisons were uniformly excellent: Trial 1 versus Trial 2 (ICC = 0.96; 95% CI 0.86–0.99), Trial 1 versus Trial 3 (ICC = 0.98; 95% CI 0.93–0.99), and Trial 2 versus Trial 3 (ICC = 0.93; 95% CI 0.74–0.98), with excellent reliability across comparisons.

Table 4. Intraclass Correlation Coefficients (ICC) for sum scores of pressure pain threshold values across trials

| Trial comparison | ICC | Interpretation | 95% CI |
|---|---|---|---|
| 1 vs. 2 | 0.96 | Excellent | 0.86-0.99 |
| 1 vs. 3 | 0.98 | Excellent | 0.93-0.99 |
| 2 vs. 3 | 0.93 | Excellent | 0.74-0.98 |

ICC values represent intra-rater reliability for the total PPT score (sum of all craniofacial sites) calculated between pairs of trials. Reliability was classified according to established thresholds, where ICC ≥ 0.90 indicates excellent agreement

Although ICC values were high, the wide limits of agreement observed in central regions (frontal and vertex) suggest limited precision at the individual level, which should be considered in clinical interpretation.

## Discussion

This study demonstrated moderate-to-excellent agreement between a single PPT measurement and the mean of three consecutive trials in the cephalic region. In addition, repeated measurements showed moderate-to-excellent intra-rater reliability. These findings suggest that a single-trial protocol may adequately represent repeated measurements under standardized conditions, with potential implications for reducing participant burden in research and clinical settings.

Previous studies have reported high intra- and inter-rater reliability of PPT when calculated as the average of multiple trials, with ICC values often between 0.90 and 0.95 (21–23). The results extend this literature by showing that a single-trial approach can achieve reliability estimates within a similar range, particularly in the occipital region. Variability across anatomical sites, with lower reliability observed in the frontal and vertex regions, may reflect differences in tissue composition, participant perception, or probe stabilization.

Internal validity was strengthened by the use of standardized procedures, consistent probe application, and assessments performed by a single trained examiner, thereby eliminating inter-rater variability. The 10-minute interval between trials also (5) helped limit potential sensitization. Nevertheless, some sources of measurement variability cannot be fully excluded, including anticipatory responses, localized tissue differences, and subtle fluctuations in participant attention or posture.

Migraine is characterized by deficient habituation to repetitive sensory stimulation, a phenomenon consistently demonstrated across nociceptive, visual, and somatosensory modalities. Multiple studies have shown reduced or absent habituation to repeated painful stimuli in individuals with migraine, possibly reflecting altered thalamo-cortical regulation and enhanced cortical responsivity (16,29). Repeated nociceptive trials may therefore increase discomfort, anticipation, or sensitization in this population, potentially influencing PPT measurements and contributing to greater within-session variability.

Although the present study was conducted in individuals without headache disorders, the observation that a single PPT measurement yielded reliability comparable to the average of three trials has implications for research in migraine populations. A simplified, single-trial PPT protocol may help limit exposure to repeated painful stimuli, reduce participant burden, and minimize confounding effects related to atypical habituation patterns in migraine. Such an approach may be particularly advantageous in studies requiring the assessment of multiple cephalic sites within a single session.

Reliability varied across anatomical sites, ranging from excellent in the bilateral occipital region and good in the right masseter to moderate in the temporal, frontal, and vertex areas. The greater stability observed in the occipital region may relate to its robust innervation by the greater occipital nerve, which converges onto second-order neurons within the trigeminocervical complex and provides consistent sensory input. Variability among other cephalic regions may reflect differences in tissue compliance, probe stabilization, or participant perception, which can influence threshold detection across repeated trials (30).

Sensory variability may also be influenced by regional differences in cutaneous mechanoreceptor distribution. The density and functional properties of fast-adapting (FA I/II) and slow-adapting (SA I/II) mechanoreceptors vary across body regions (31), which may partially explain the lower PPT values and reduced reliability observed in areas with thinner soft tissue or greater receptor heterogeneity. Although mechanoreceptive factors were not directly assessed in this study, they provide a plausible physiological basis for the site-specific differences in reliability.

This study has limitations. Although previous methodological work suggests that small samples can provide acceptable estimates of intra-individual PPT variance (5), the limited sample size restricts generalizability and precludes stratified analyses. The absence

of psychometric screening measures prevented examination of psychological or affective factors that may influence pain perception or threshold detection. Future studies should replicate these findings in larger and more diverse samples, including individuals with primary headache disorders. Evaluating test–retest reliability across sessions and examining the responsiveness of PPT to interventions will also be important for defining the utility of a single-trial protocol in both research and clinical contexts.

From a clinical and research perspective, reducing the number of PPT measurements per site may significantly decrease assessment time, improve participant tolerability, and enhance feasibility in protocols involving multiple craniofacial regions. This may be particularly relevant in headache populations, in which repeated nociceptive stimulation can influence sensory processing and measurement stability.

The clinical acceptability of the observed limits of agreement remains uncertain, as no established minimal clinically important difference (MCID) for PPT in craniofacial regions is available.

## Conclusion

A single PPT measurement demonstrated agreement comparable to the mean of three consecutive trials, while repeated measurements showed moderate-to-excellent intra-rater reliability. These findings support the potential use of a simplified PPT assessment protocol, although further validation in larger and clinical populations is warranted.

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Rosana Tieka Miyazaki Brancucci
https://orcid.org/0000-0002-9941-2288
Vanda de Lelis
https://orcid.org/0000-0002-5437-0360
Georgia Westenhofen
https://orcid.org/0000-0001-8563-558X
Ida Fortini
https://orcid.org/0000-0003-1084-340X
Gabriel Taricani Kubota
https://orcid.org/0000-0001-7790-8111
Gianluca Coppola
https://orcid.org/0000-0002-8510-6925
Mario Fernando Prieto Peres
https://orcid.org/0000-0002-0068-1905



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