Journal of Pain Research

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Effect of the Location of Tetanic Stimulation on Autonomic Responses: A Randomized Cross-Over Pilot Study

Pekka Talke[1], Isabel Talke[2]

[1]Department of Anesthesia and Perioperative Medicine, University of California San Francisco, San Francisco, CA, USA; [2]California Polytechnic State University, San Luis Obispo, CA, USA

Correspondence: Pekka Talke, Email talkep@gmail.com

Background: Tetanic stimuli are used as standardized noxious inputs to investigate nociception. Previous studies have applied tetanic stimuli to various anatomical locations without validating that the resulting physiological responses were independent of the location where tetanic stimuli were applied. Our aim was to investigate the effects of three anatomical tetanic stimulus application sites on physiological variables reflecting autonomic nervous system responses as measured by photoplethysmography (PPG).

Methods: Under general anesthesia, a five second, 100 hertz, 70 milliamp tetanic stimulus was applied to the ulnar nerve, medial side of the tibia, and thorax (T5 dermatome) (N=12). The effect of tetanic stimuli on PPG-derived variables (AC, DC, and ACDC) and pulse rate at each stimulus location was determined using repeated-measures analysis of variance (ANOVA) followed by Dunnett's post hoc test. Maximum tetanic stimulus-induced changes in PPG-derived variables and pulse rates were compared among the three stimulus locations using ANOVA.

Results: AC and ACDC values of PPG decreased, and the DC values of PPG increased in response to tetanic stimuli-induced vasoconstriction at each location ($p<0.001$ for all). The maximum changes in the AC, ACDC, and DC values did not differ between locations (p=NS). There were no significant changes in pulse rate (p=NS).

Conclusion: The results showed that tetanic stimulation at either of these three locations provides the same autonomic nervous system responses, as measured by PPG.

Clinical Trial Registration: ClinicalTrials.gov; NCT03648853.

Plain Language Summary: We studied how pain medications and anesthetics reduce pain in humans. The amount of pain experienced by a person can be assessed by administering a slightly uncomfortable test, such as a small electric shock to the skin. These tests are often performed before and after administering a person's pain medication or anesthesia. It is not known if the test results change when an electric shock is applied to different areas of the body (eg, hand, leg, or chest). In this study, we applied small electric shocks to three areas of skin. We measured the participants' responses to this test using a special medical equipment (pulse oximeter), which tells us how the body reacts to an uncomfortable stimulus. We found that the test results were the same regardless of the area where the electric shock was applied. This information will be useful for investigators studying pain and pain management.

Keywords: tetanic stimulus, antinociception, pain, anatomical location, photoplethysmography

Introduction

Surgery and painful intensive care unit (ICU) procedures elicit noxious stimuli that can cause hormonal, metabolic, and autonomic changes.[1,2] To attenuate the resulting physiological stress responses, clinicians use various pharmacological and non-pharmacological interventions to optimize nociception-antinociception balance.[3–10]

Noxious input is needed to assess nociception-antinociception balance. Unfortunately, naturally evoked nociception, such as surgical stimulation and painful ICU care procedures, can be unpredictable in intensity, duration, and timing of

Received: 18 October 2023
Accepted: 28 December 2023
Published: 9 January 2024

occurrence, complicating its use to quantify nociception-antinociception balance. To overcome this limitation, a tetanic stimulus has been used as a "standardized" noxious stimulus to study autonomic nervous system activation, antinociceptive therapies, and to evaluate performance of nociception monitors.[3–13] Previous studies have applied the tetanic stimulus to various anatomical locations (ulnar-, median- and sural nerve, thoracic, lumbar and cervical dermatomes, finger and the forearm) with no prior validation that the resulting physiological responses are independent of the tetanic stimulus location.[3–11,13–17] Thus, the aim of this pilot study was to investigate the effects of three anatomical tetanic stimulus application sites on physiological variables that reflect the autonomic nervous system responses.

Materials and Methods

In a study, that confirmed to the Declaration of Helsinki, with approval of the University of California San Francisco Institutional Review Board (IRB# 18–25325, ClinicalTrials.gov NCT03648853) and written informed consent we studied 12 patients between October 3, 2018 and November 30, 2018, who were scheduled for elective neurological surgery under general anesthesia and were over 18 years of age. We excluded patients who were unable to provide informed consent, were taking opioids, or whose anticipated duration of general anesthesia was less than one hour. This study was conducted at the University of California, San Francisco Medical Center.

All the patients fasted overnight. Prior to the induction of anesthesia, a 20 g or 18 g intravenous catheter was inserted into the vein of the right hand to administer intravenous fluids and medications. Standard anesthesia monitors were used (5-lead electrocardiography, noninvasive blood pressure monitoring in the right upper arm, and a pulse oximeter probe on the finger of the right hand). A second pulse oximeter probe was applied to the distal phalanx of the left index finger to collect data. During the study, patients were placed in the operating room in a supine position covered with blankets and/or surgical drapes.

Patients received fentanyl (up to 100 µg) and midazolam (up to 2 mg) premedication. Baseline blood pressure and heart rate were recorded prior to anesthesia induction. After preoxygenation with 100% oxygen, anesthesia was induced with intravenous propofol as per the attending anesthesiologist. Rocuronium (minimum, 50 mg) was administered after loss of consciousness to facilitate endotracheal intubation and prevent movement during data collection. Anesthesia was maintained with inhaled oxygen (2 L/min) and sevoflurane, targeted at an ET of 2 vol%. An intravenous phenylephrine infusion was used if necessary to maintain the systolic blood pressure within 20% of the baseline values. Positive pressure ventilation was mechanically controlled using an 8 mL/kg tidal volume, and the respiratory rate was adjusted to maintain the end-tidal carbon dioxide between 30 and 35 mmHg.

In this single-blinded (patient) study, a five second, 100 hertz (Hz), 70 milliamp (mA) tetanic stimulus (Stimpod NMS450, Xavant Technologies, Pretoria, South Africa) was delivered sequentially to three anatomical locations. The stimuli were delivered using standard electrocardiogram electrodes applied to the area of the left ulnar nerve, tibia and thorax. Electrodes for the ulnar nerve site were placed so that the distal electrode was on the skin approximately one centimeter above the flexor crease of the wrist, and the other electrode was immediately proximal to the first electrode parallel to the flexor carpi ulnaris tendon. Electrodes for the tibial site were placed on the skin on the medial surface (bony area) of tibia. Electrodes were placed next to each other parallel to the axis of the tibia at the mid-tibia level. Electrodes for the thoracic site were placed next to each other parallel to the axis of the body at the T5 dermatome of midaxillary line. The positive electrodes were placed distally. Three sets of two electrodes and connecting wires were left in place throughout the study so that tetanic stimuli could be delivered using the same Stimpod device.

For randomization, two blocks of the six potential stimulus location sequences were placed in sealed envelopes according to a randomly generated sequence. One of the sequentially numbered envelopes was opened by the principal investigator at the beginning of each trial. Randomization of the stimulus location was designed to reduce potential biases due to the stimulus sequence or time effects. The stimulation sequence was repeated twice for each participant. Each participant received six tetanic stimuli. The tetanic stimuli were delivered at a minimum of 2 min apart.

To achieve quasi-steady-state anesthesia and to minimize nociceptive inputs other than the tetanic stimuli used for study purposes, the study data collection was started at a minimum of 15 min after the beginning of anesthesia and endotracheal intubation and was completed before surgical incision.

Tetanic stimuli-induced peripheral vasoconstriction and changes in the pulse rate (PR) were measured using photoplethysmography (PPG). Infrared light transmitted through the fingertip was measured using a Masimo Radical-7 pulse oximeter (Masimo Corp., Irvine, CA, USA; Masimo SET software version 7.0.3.3), for which an adhesive LNCS Adtx sensor (Masimo Corp., Irvine, CA, USA) was placed on the left index finger. The sensor was optically isolated from ambient light by covering a pulse oximeter probe with black 6 mil plastic. PPG data were recorded continuously throughout the study period using an automated data-acquisition system.

The pulse oximeter sensor contains a low-voltage, low-intensity light-emitting diode that emits infrared light (approximately 910 nm). A portion of the light is transmitted through the finger. The detector photodiode in the sensor generates an electrical current proportional to the amount of light received.[18] This electrical current is low-pass filtered (10 Hz) and then converted into analog-to-digital converter counts. The generated electrical current data were transmitted to a computer, sampled at 62.5 Hz, and saved with no further signal processing. These data were recorded using Pulse Ox Automated Data Collection software (Masimo Corp., Irvine, CA, USA; ADC v3.1.1.0).

Sample size calculations were not performed for this pilot study because preliminary data were not available, and this study was meant to provide preliminary data for potential future studies. From the 62.5 Hz PPG data, we identified the minimum and maximum light transmittances for each cardiac pulse using programs written in MATLAB (MathWorks, Inc., Natick, MA). These data were used to determine the AC and DC values for each pulse (Figure 1).[18] The AC values signify the pulsatile portion of the light transmittance, and the DC values signify the nonpulsatile portion of the light transmittance. The AC and DC values were used to calculate the derived variables: ACDC = AC/DC × 100. The pulse rate was calculated using the beat-to-beat time interval data from the PPG recordings.

The baseline values for AC, DC, ACDC, and PR were defined as the median values of 12 heartbeats immediately before the beginning of the tetanic stimulus. To analyze the stress response, we included data from 60 heartbeats following the beginning of the tetanic stimulus. We averaged the data from the two PPG recordings at each site. AC, DC,

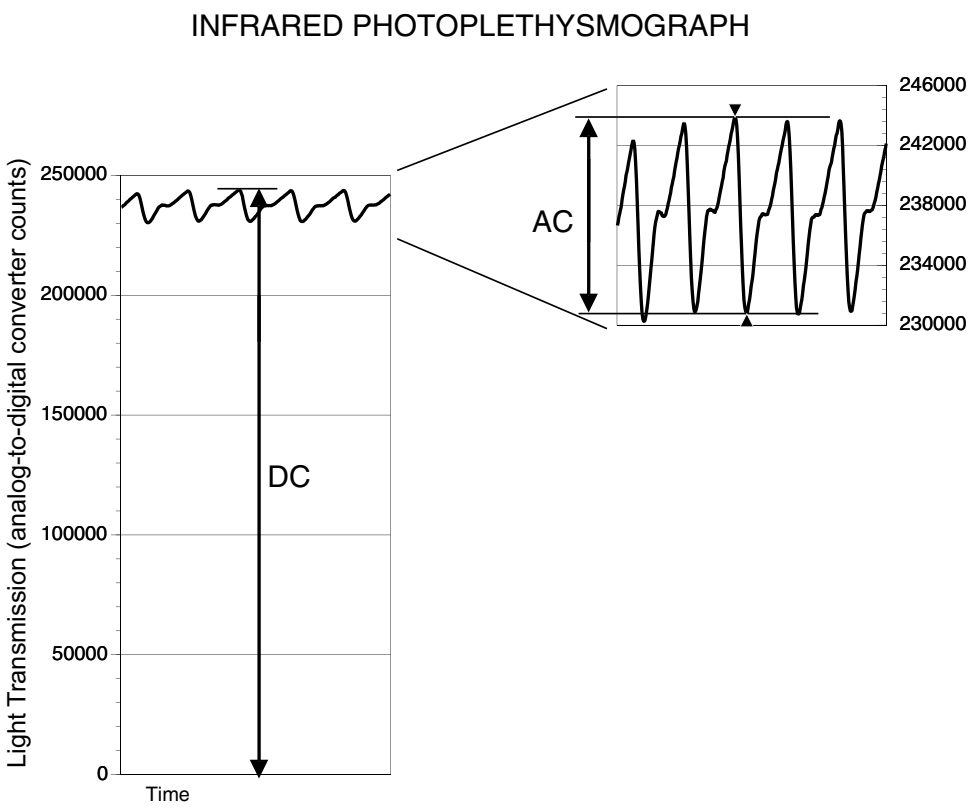

Figure 1 Illustration of photoplethysmogram DC and AC components. The DC value corresponds to the smallest blood volume in the finger (end diastole), which corresponds to the highest light transmission value of each pulse through the finger. The AC values correspond to the difference between the highest (end diastole) and lowest (end systole) light transmission values of each pulse representing the pulse added volume of blood in the finger.

and ACDC data are expressed as percent changes relative to the baseline values. The maximum DC and PR, and minimum AC and ACDC values were defined as the highest and lowest values during the 60-heartbeat recording period, respectively.

For the primary endpoint, the maximum percent changes in AC, DC, ACDC, and PR values from baseline were compared among the three stimulus locations using ANOVA. The effect of tetanic stimuli on PPG measurements at each stimulus location was determined using repeated-measures ANOVA followed by Dunnett's post hoc test. The AC, DC, ACDC, and PR baseline values and times to reach the post-stimulus maximum or minimum values were compared among the three stimulus locations using ANOVA. Data are reported as the mean ± standard deviation (SD), with $p < 0.05$ signifying statistical significance.

Results

Out of 12 subjects, data from 2 subjects were excluded from the analysis. One subject had no clearly defined responses and one study was aborted because the surgical procedure started before data collection was complete (protocol violation).

The patient characteristics and baseline hemodynamic and medication data of the remaining 10 subjects are shown in Table 1. A representative PPG recording of tetanic stimulus-induced vasoconstrictive response is shown in Figure 2.

The AC, DC, ACDC or PR baseline values did not differ significantly between the stimulus locations (p=0.99, 0.99, 0.99 and 0.98 for AC, DC, ACDC and PR respectively). The AC and ACDC values decreased, and the DC values increased in response to tetanic stimuli-induced peripheral vasoconstriction at each location (p<0.001 for all) (Figure 3). The maximum changes (primary outcome) in AC, DC, and ACDC values did not differ significantly between locations (p=0.36, 0.39 and 0.06 for AC, DC and ACDC respectively; Figure 4). The PR values did not change significantly in response to tetanic stimuli at any location (p=0.37).

Tetanic stimulus-induced AC, DC, and ACDC vasoconstrictive responses started during the 5 s tetanic stimulation. There were no significant differences in the times for AC, DC, or ACDC values to reach maximum changes between the stimulus locations (p=0.68, 0.07 and 0.07 for AC, DC and ACDC respectively; Figure 5).

Discussion

Our results show that the anatomical location at which a tetanic stimulus is applied does not affect autonomic nervous system-mediated physiological responses, as measured using PPG. Our results further show that under these experimental conditions, changes in heart rate are not reliable indicators of the stress response. These results should be extrapolated with caution to anatomical locations other than those tested in this study.

Table 1 Patient Characteristics, Baseline Hemodynamic and Medication Data

N	10
Age (years)	48 ± 17
Sex (M/F)	3 / 7
Weight (kg)	85 ± 19
Height (cm)	170 ± 8
Baseline hemodynamics	
SBP (mmHg)	138 ± 14
DBP (mmHg)	76 ± 7
PR (bpm)	80 ± 10
Medications	
Fentanyl (μg/kg)	1.2 ± 0.7
Midazolam (mg)	1.2 ± 0.9
Propofol (mg/kg)	2.4 ± 1.3

Note: Data reported as means ± SDs.
Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; PR, pulse rate.

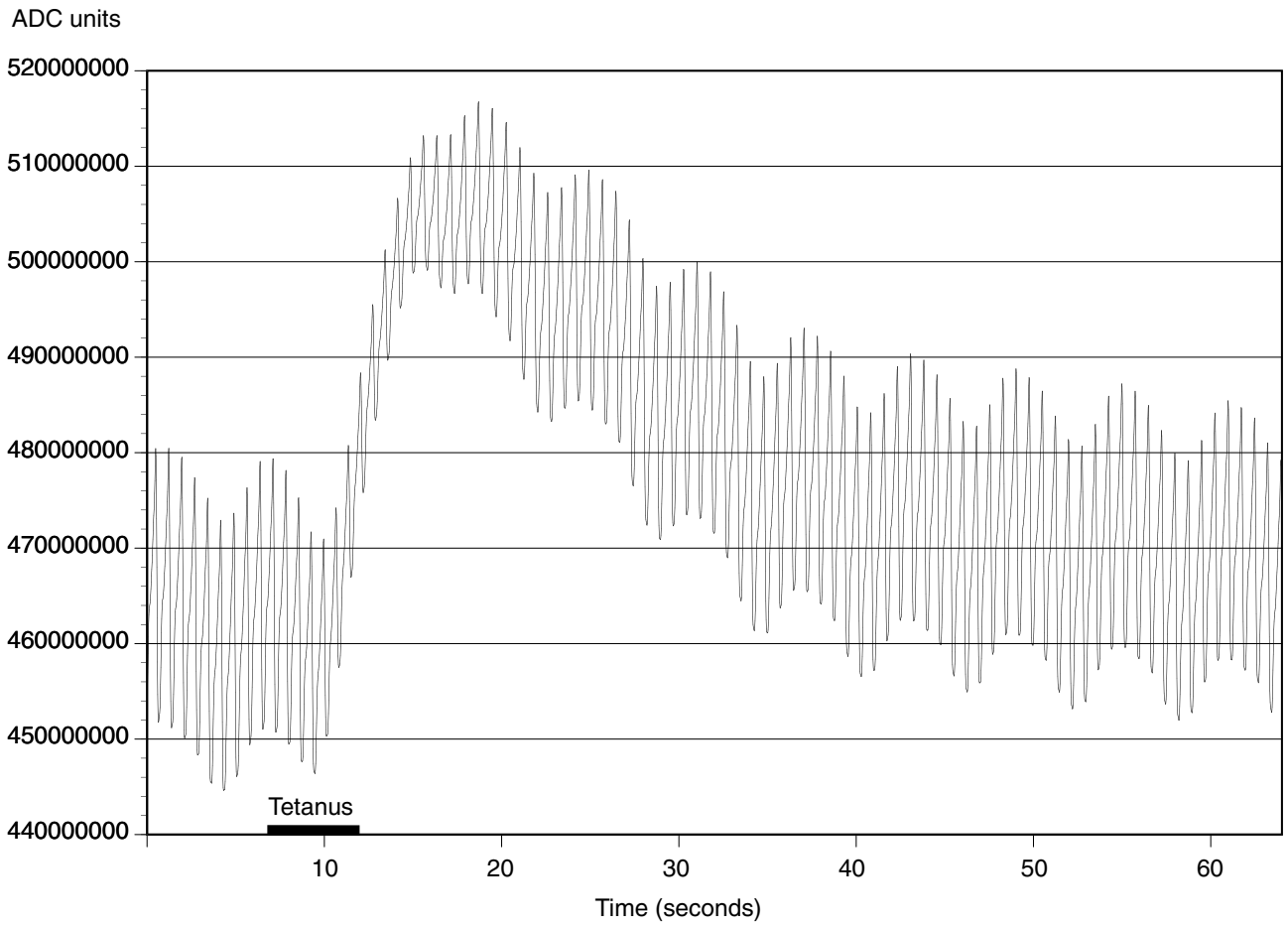

Figure 2 A representative PPG recording of one tetanic stimulus induced vasoconstrictive response. Tetanic stimulus induced vasoconstriction results in an increase in light transmittance through finger. The data are in analog-to-digital converter units (ADC units). The slower (7–8 heartbeats) PPG oscillations are due to mechanical ventilation.

There are several reasons for studying the effects of tetanic stimulation sites on autonomic response. First, the distribution and density of the peripheral endings of polymodal primary sensory neurons are inhomogeneous.[2] Thus, there are theoretical reasons why electrical stimuli may not induce similar levels of nociception when applied to different anatomical locations. Second, it is not feasible to place stimulating electrodes at a singular anatomical location in every subject for clinical or research purposes. Our results provide options for three sites at which the application of tetanic stimulus yields similar physiological responses. Third, tetanic stimulus-induced muscle contraction may be undesirable in certain situations and may cause additional sympathetic nervous system activation.[2] Therefore, we included stimulation sites that would elicit minimal muscular contraction (tibia, thorax). However, since our subjects underwent complete neuromuscular blockade to optimize PPG signal quality, future studies need to be conducted to determine whether our results apply when neuromuscular blockade is not used.

Nociception can cause hormonal, metabolic and autonomic changes. Autonomic nervous system activation induces physiological responses, such as increases in heart rate, blood pressure, peripheral vasoconstriction, changes in skin conductance, heart rate variability, and temperature.[1,2,19] These variables can be monitored continuously, in real time, and are being used in various devices. We chose to monitor changes in peripheral vasomotor tone and heart rate using PPG, which is currently used for surgical and postoperative pain assessments.[3–5,7,13,20] PPG allowed us a unique possibility to use high-frequency data recordings to analyze the peak stress responses and beat-by-beat time course of the stress response.

A PPG has two components, commonly referred to as AC and DC. The AC component is caused by pulsatile changes in the tissue volume (mainly arterial pulsation). The DC component is due to transmission of light by nonpulsatile

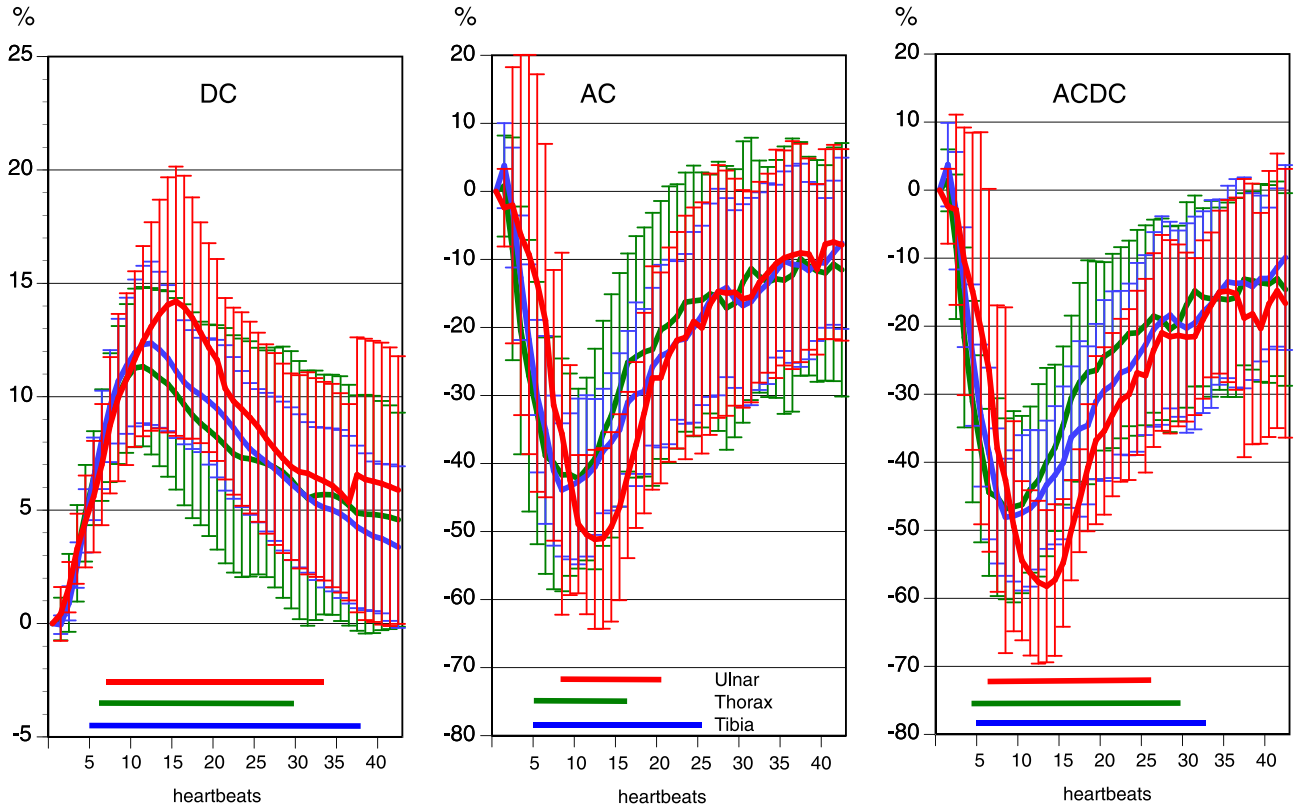

Figure 3 % change in PPG derived variable data (DC, AC, ACDC) from baseline values. Data are means (thick lines) ± SD over 45 heart beats. Time zero is the beginning of the vasoconstrictive response. The horizontal bars at the bottom of the figure illustrate values that are significantly (p <0.05) different from baseline values.

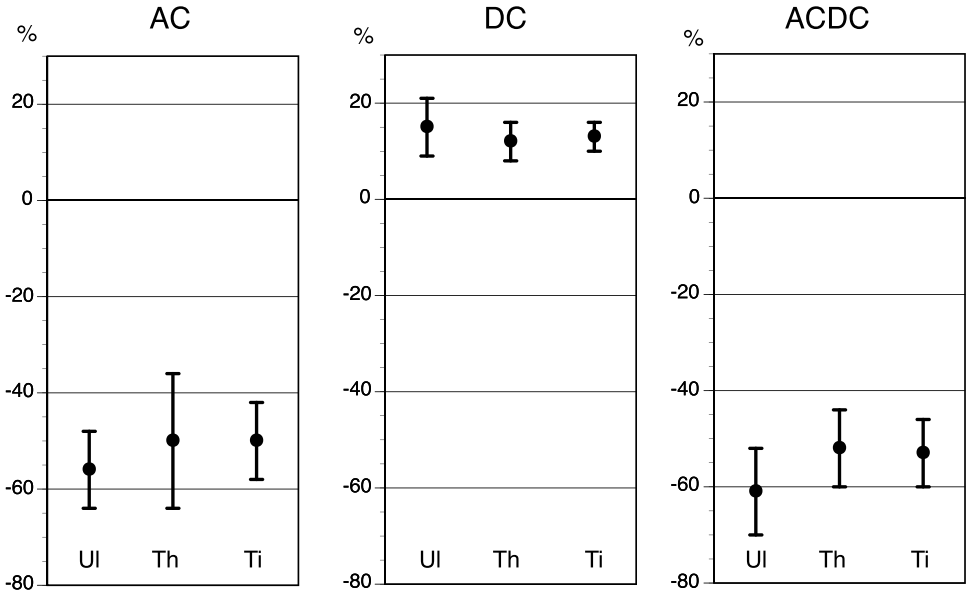

Figure 4 Maximum changes in AC, DC and ACDC values from baseline (in percent) after tetanic stimuli. Data reported as means ± SDs.
Abbreviations: Ul, ulnar; Th, thorax; Ti, tibia.

tissues, including venous blood and nonpulsatile portions of arterial blood.[18] Noxious stimuli-induced stress responses mediate peripheral vasoconstriction.[19,21–24] This in turn, should decrease the AC component (reduced arterial pulsation) and increase the DC component (reduced venous and arterial blood volume) of the PPG, as observed in this study.

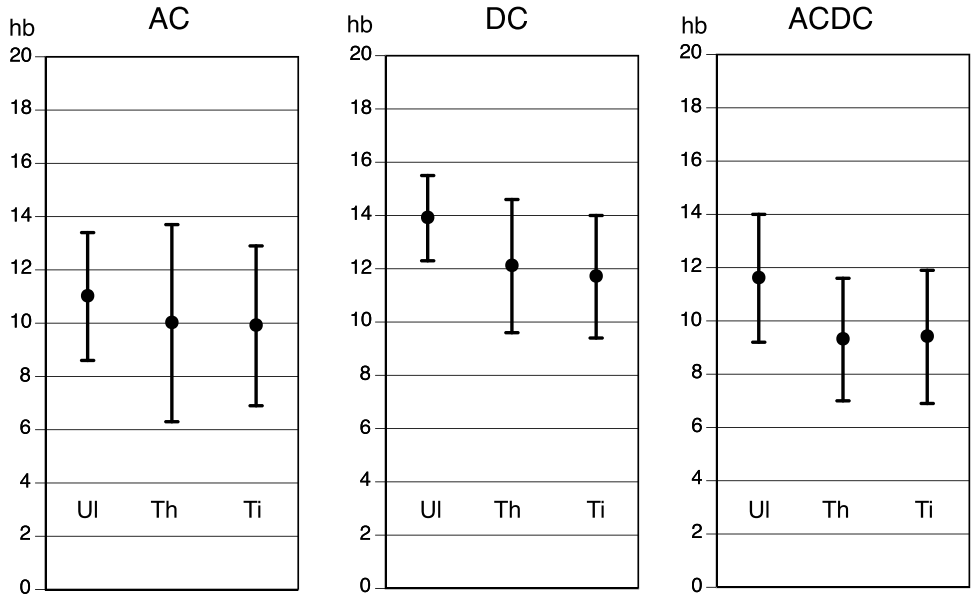

Figure 5 Number of heartbeats to reach maximum AC, DC and ACDC values after beginning of tetanic stimulus induced vasoconstriction. Data reported as means ± SDs.
Abbreviations: Ul, ulnar; Th, thorax; Ti, tibia; hb, heartbeat.

Peripheral vasoconstriction may have different effects on the AC and DC components of PPG, depending on the cause of vasoconstriction. For example, temperature-induced vasoconstriction has a larger effect on the DC than on the AC component of the PPG, whereas intubation-induced noxious stimuli have a larger effect on the AC than on the DC component.[20–24] Our study adds to the current literature by analyzing the effect of a tetanic stimulus on both the AC and DC components and a derived variable (ACDC) of the PPG. Our data demonstrated that tetanic stimulus-mediated peripheral vasoconstriction has a larger effect on the AC and ACDC components of the PPG than on the DC component.

In our study, peripheral vasoconstriction started within seconds after the beginning of the tetanic stimulus, peaked at an average of 10 heartbeats later, and lasted less than a minute. This fast time-course suggests a neural response mediated by norepinephrine release from presynaptic nerve terminals after the activation of the nociceptive medullary autonomic pathway. The time course of this vasoconstrictive response was identical to that observed intraoperatively after the surgical stimuli (personal observations). In addition to a relatively brief neural response, surgical noxious stimuli may activate catecholamine secretion from the adrenal medulla. The resulting hemodynamic changes can last several minutes beyond the end of the surgical stimulus that evokes the stress response, reflecting the pharmacokinetics of circulating catecholamines rather than the ongoing surgical stimuli.

Most available physiological measurements detect, but do not predict, inadequate nociception. This is a significant limitation of clinical anesthesia. This is partly due to the continuously changing surgical stimulation and variations in anesthetic concentrations. Instead of relying on unpredictable surgical noxious stimuli to assess the nociception-antinociception balance, we suggest that the use of periodic tetanic stimuli-evoked autonomic responses should be tested as a potential means to improve the predictability of antinociception monitoring.

Our study had several limitations. First, the sample size is small. No prior data were available for use in the sample size calculations. Power calculation using our ACDC data showed that this study had a 0.8 power (alpha=0.05) to detect a 30% difference between the measurement sites. The results of these pilot studies could be used to design future research. We measured peripheral vasomotor tone at the fingertip, the most commonly used site for pulse oximeter probes. As the magnitude of noxious stimulus-induced peripheral vasoconstriction is not the same in all vascular beds, our results are applicable only when PPG is measured from the fingertip.[19,22–30,] We applied tetanic stimuli to three anatomical locations. We cannot infer weather our results would be applicable to the other anatomical locations that have been used in previous studies.

Our study had two subjects that were obvious outliers. One subject (not analyzed) had no clearly defined responses to any of the six tetanic stimuli. The patient was taking an alpha-1 adrenoceptor blocker. The second outlier exhibited a typical initial peripheral vasoconstrictive stress response. However, this subject's recovery from vasoconstriction was significantly prolonged compared with that of the other subjects. This patient was taking a selective serotonin reuptake inhibitor (SSRI), suggesting the potential for reduced norepinephrine or neuropeptide Y reuptake from the synaptic cleft. These outliers contribute to concerns regarding concomitant medications that may affect nociceptive monitoring.

Conclusions

In Conclusion, this pilot study showed that the magnitude of peripheral vasoconstriction was independent of the location where tetanic stimulus was applied. These results should aid in the development and use of nociception-antinociception balance monitors and in conducting pain research using electrical noxious stimuli.

Data Sharing Statement

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

Funding

Funding was provided by departmental funding.

Disclosure

Neither author has any conflicts of interest in this research.

References

1. Cowen R, Stasiowska MK, Laycock H, et al. Assessing pain objectively: the use of physiological markers. *Anaesthesia*. 2015;70(7):828–847. doi:10.1111/anae.13018
2. Shoemaker JK, Badrov MB, Al-Khazraji BK, et al. Neural control of vascular function in skeletal muscle. *Compr Physiol*. 2015;6:303–329.
3. Coulombe M-A, Décary E, Maximos S, et al. Assessing the antinociceptive effect of nitrous oxide to tetanic stimulation in anaesthetised patients with new intra-operative nociception monitors: an observational study. *Eur J Anaesthesiol*. 2021;38(5):512–523. doi:10.1097/EJA.0000000000001431
4. Ellerkmann RK, Grass A, Hoeft A, et al. The response of the composite variability index to a standardized noxious stimulus during propofol-remifentanil anesthesia. *Anesth Analg*. 2013;116(3):580–588. doi:10.1213/ANE.0b013e31827ced18
5. Funcke S, Sauerlaender S, Pinnschmidt HO, et al. Validation of innovative techniques for monitoring nociception during general anesthesia: a clinical study using tetanic and intracutaneous electrical stimulation. *Anesthesiology*. 2017;127(2):272–283. doi:10.1097/ALN.0000000000001670
6. Guglielminotti J, Grillot N, Paule M, et al. Prediction of movement to surgical stimulation by the pupillary dilatation reflex amplitude evoked by a standardized noxious test. *Anesthesiology*. 2015;122(5):985–993. doi:10.1097/ALN.0000000000000624
7. Renaud-Roy E, Stöckle PA, Maximos S, et al. Correlation between incremental remifentanil doses and the Nociception Level (NOL) index response after intraoperative noxious stimuli. *Can J Anaesth*. 2019;66(9):1049–1061. doi:10.1007/s12630-019-01372-1
8. Sahinovic MM, Eleveld DJ, Kalmar AF, et al. Accuracy of the composite variability index as a measure of the balance between nociception and antinociception during anesthesia. *Anesth Analg*. 2014;119(2):288–301. doi:10.1213/ANE.0000000000000274
9. Struys MMRF, Vanpeteghem C, Huiku M, et al. Changes in a surgical stress index in response to standardized pain stimuli during propofol-remifentanil infusion. *Br J Anaesth*. 2007;99(3):359–367. doi:10.1093/bja/aem173
10. Wennervirta J, Hynynen M, Koivusalo AM, et al. Surgical stress index as a measure of nociception/antinociception balance during general anesthesia. *Acta Anaesthesiol Scand*. 2008;52(8):1038–1045. doi:10.1111/j.1399-6576.2008.01687.x
11. Jozefowicz E, Sabourdin N, Fontaine V, et al. Prediction of reactivity during tracheal intubation by pre-laryngoscopy tetanus-induced ANI variation. *J Clin Monit Comput*. 2022;36(1):93–101. doi:10.1007/s10877-020-00624-6
12. Jeanne M, Clément C, De Jonckheere J, et al. Variations of the analgesia nociception index during general anaesthesia for laparoscopic abdominal surgery. *J Clin Monit Comput*. 2012;26(4):289–294. doi:10.1007/s10877-012-9354-0
13. Gruenewald M, Ilies C, Herz J, et al. Influence of nociceptive stimulation on analgesia nociception index (ANI) during propofol-remifentanil anaesthesia. *Br J Anaesth*. 2013;110(6):1024–1030. doi:10.1093/bja/aet019
14. Yang LL, Niemann CU, Larson MD. Mechanism of pupillary reflex dilation in awake volunteers and in organ donors. *Anesthesiology*. 2003;99(6):1281–1286. doi:10.1097/00000542-200312000-00008
15. von Dincklage F, Correll C, Schneider MHN, et al. Utility of nociceptive flexion reflex threshold, bispectral index, composite variability index and noxious stimulation response index as measures for nociception during general anaesthesia. *Anaesthesia*. 2012;67(8):899–905. doi:10.1111/j.1365-2044.2012.07187.x
16. Larson MD, Berry PD, May J, et al. Autonomic effects of epidural and intravenous fentanyl. *Br J Anaesth*. 2007;98(2):263–269. doi:10.1093/bja/ael335
17. Larson MD, Sessler DI, Ozaki M, et al. Pupillary assessment of sensory block level during combined epidural/general anesthesia. *Anesthesiology*. 1993;79(1):42–48. doi:10.1097/00000542-199307000-00009
18. Mannheimer PD. The light-tissue interaction of pulse oximetry. *Anesth Analg*. 2007;105(6):S10–S17. doi:10.1213/01.ane.0000269522.84942.54

19. Allen J. Photoplethysmography and its application in clinical physiological measurement. *Physiol Meas*. 2007;28(3):R1–39. doi:10.1088/0967-3334/28/3/R01
20. Yang Y, Seok HS, Noh GJ, et al. postoperative pain assessment indices based on photoplethysmography waveform analysis. *Front Physiol*. 2018;9:1–11. doi:10.3389/fphys.2018.01199
21. Talke P. The effect of tracheal intubation-induced autonomic response on photoplethysmography. *Anesthesiol Res Pract*. 2017;2017:1–5. doi:10.1155/2017/7646541
22. Korhonen I, Yli-Hankala A. Photoplethysmography and nociception. *Acta Anaesthesiol Scand*. 2009;53(8):975–985. doi:10.1111/j.1399-6576.2009.02026.x
23. Awad AA, Ghobashy MA, Ouda W, et al. Different responses of ear and finger pulse oximeter wave form to cold pressor test. *Anesth Analg*. 2001;92(6):1483–1486. doi:10.1097/00000539-200106000-00026
24. Nijboer JA, Dorlas JC. Comparison of plethysmograms taken from finger and pinna during anaesthesia. *Br J Anaesth*. 1985;57(5):531–534. doi:10.1093/bja/57.5.531
25. Jablonka DH, Awad AA, Stout RG, et al. Comparing the effect of arginine vasopressin on ear and finger photoplethysmography. *J Clin Anesth*. 2008;20(2):90–93. doi:10.1016/j.jclinane.2007.09.008
26. Shelley KH, Jablonka DH, Awad AA, et al. What is the best site for measuring the effect of ventilation on the pulse oximeter waveform? *Anesth Analg*. 2006;103(2):372–377. doi:10.1213/01.ane.0000222477.67637.17
27. Babchenko A, Davidson E, Ginosar Y, et al. Photoplethysmographic measurement of changes in total and pulsatile tissue blood volume, following sympathetic blockade. *Physiol Meas*. 2001;22(2):389–396. doi:10.1088/0967-3334/22/2/310
28. Allen J, Murray A. Similarity in bilateral photoplethysmographic peripheral pulse wave characteristics at the ears, thumbs and toes. *Physiol Meas*. 2000;21(3):369–377. doi:10.1088/0967-3334/21/3/303
29. Larsen PD, Harty M, Thiruchelvam M, et al. Spectral analysis of AC and DC components of the pulse photoplethysmograph at rest and during induction of anaesthesia. *Int J Clin Monit Comput*. 1997;14(2):89–95. doi:10.1007/BF03356582
30. Talke P, Snapir A, Huiku M. The effects of sympathectomy on finger photoplethysmography and temperature measurements in healthy subjects. *Anesth Analg*. 2011;113(1):78–83. doi:10.1213/ANE.0b013e318217f6b1