ORIGINAL RESEARCH

A mechanistic study of the tremor associated with epidural anaesthesia for intrapartum caesarean delivery.*

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Abstract:

Background: It is not known if the tremor associated with an epidural top-up dose for intrapartum caesarean delivery is thermoregulatory shivering. A tremor is only shivering if it has the same frequency profile as cold stress-induced shivering. Thermoregulatory shivering is a response to a reduction in actual body temperature, whereas nonthermoregulatory shivering may be triggered by a reduction in sensed body temperature. This mechanistic study aimed to compare: (1) the frequency profiles of epidural top-up tremor and cold stress-induced shivering; and (2) body temperature (actual and sensed) before epidural top-up and at the onset of tremor.

Methods: Twenty obstetric patients received an epidural top-up for intrapartum caesarean delivery and 20 nonpregnant female volunteers underwent a cold stress. Tremor, surface electromyography, core temperature, skin temperature (7 sites) and temperature sensation votes (a bipolar visual analog score ranging from -50 to +50 mm) were recorded.

Results: The mean (SD) primary oscillation (9.9 (1.9) Hz) frequency of epidural top-up tremor did not differ from that of cold stress-induced shivering (9.0 (1.6) Hz; *P*=0.194), but the mean (SD) burst frequency was slower (6.1 (1.2) x 10^{-2} Hz and 6.9 (0.7) x 10^{-2} Hz, respectively; *P*=0.046). Before the epidural top-up dose, the mean (SD) core temperature was 37.6 (0.6)° C. Between the epidural top-up dose and the onset of tremor the mean (SD) core temperature did not change (-0.1 (0.1)° C; *P*=0.126), the mean (SD) skin temperature increased (+0.4 (0.4)° C; *P*=0.002) and the mean (SD) temperature sensation votes decreased (-12 (16) mm; *P*=0.012).

Conclusions: These results suggest that epidural top-up tremor is a form of nonthermoregulatory shivering triggered by a reduction in sensed body temperature.

Keywords: body temperature; caesarean delivery; epidural anaesthesia; temperature sensation; tremor; shivering

Introduction:

Tremor is a common side effect of epidural anaesthesia for intrapartum caesarean delivery which has a negative impact upon maternal satisfaction.[1,2] The term "shivering" is often used to describe epidural top-up tremor, but it is unclear if this form of tremor is the same as cold stress-induced shivering. Tremors are identified by their frequency profiles and their triggers.[3] For example, Parkinsonian tremor has a frequency of 4–6 Hz and is triggered by inactivity.[3] Consequently, in order for epidural top-up tremor to be considered a form of shivering, the frequency profile of its oscillation must match that of cold stress-induced shivering in the unanaesthetised state[4] and it must be triggered by the perception of hypothermia within the hypothalamus.[5] The tremor associated with neuraxial blockade in nonpregnant volunteers is shivering triggered by a reduction in tissue temperature.[4] However, epidural top-up tremor is morphologically different to other neuraxial blockade associated tremors[2] and, as labour is a heat stress, it is unlikely to be triggered by tissue hypothermia.[6] Consequently, it cannot be assumed that epidural top-up tremor is a form of shivering.

Cold stress-induced shivering is the "physiological" form of shivering and is therefore the control against which all potential forms of shivering must be compared.[4] It is a unique, amplitude modulated oscillation with a primary oscillation of 7.1–14 Hz and an amplitude modulation frequency (burst frequency) of 3.5–8.5 x 10^{-2} Hz (Figure 1).[7,8] It is generated by coordinated muscle activity and so the oscillation and burst frequencies of the surface electromyography (EMG) signal are also characteristic.[7,9] The tremor associated with neuraxial blockade in nonpregnant volunteers has the same oscillation and EMG characteristics as cold stress-induced shivering and is triggered by a reduction in mean body temperature,[4] and is therefore a form of shivering.

Shivering is categorised as thermoregulatory or nonthermoregulatory by the tissue temperature at its onset.[10] Thermoregulatory shivering occurs at reduced tissue temperatures and its trigger is increased cold thermoreceptor activity.[11] Nonthermoregulatory shivering occurs at normal or

increased tissue temperatures, it is nonphysiologic and it has a number of triggers. For example, rigors are a form of nonthermoregulatory shivering triggered by a prostaglandin E_2 mediated increase in the hypothalamic set-temperature.[11] Neural blockade in hyperthermic individuals is also a potential trigger; the hypothalamus may interpret the loss of warm thermoreceptor activity as a reduction in body temperature and therefore be tricked into activating the efferent arm of the shivering reflex.[12] Labour epidural analgesia is associated with hyper- rather than hypothermia[13] and so it is unlikely that epidural top-up tremor is triggered by a fall in tissue temperature. However, as labour is a heat stress,[6] it is possible that the epidural top-up dose blocks warm thermoreceptor activity and that epidural top-up tremor is triggered by the resulting reduction in sensed body temperature.

The aims of this mechanistic study were twofold. The first aim was to determine whether epidural top-up tremor is a form of shivering by comparing the frequency profiles of epidural top-up tremor and cold stress-induced shivering; epidural top-up tremor was recorded from obstetric patients and cold stress-induced shivering from nonpregnant female volunteers. The second aim was to investigate the trigger for epidural top-up tremor by comparing obstetric patients' actual and sensed body temperature before the epidural top-up dose and at the onset of tremor. It was hypothesised that epidural top-up tremor is nonthermoregulatory shivering triggered by a reduction in sensed body temperature. This study was a planned primary analysis, but data from obstetric patients were collected concurrently with an investigation of the effect of epidural top-up on cutaneous vasomotor tone.[14]

Methods:

Ethical approvals and recruitment procedures

Ethical approval was obtained from Imperial College Research Ethics Committee (nonpregnant female volunteers; ICREC_13_2_12) and from the London – Fulham NRES Committee (obstetric patients; 13/LO/0672). Approval from two ethical committees were required as data collection from the nonpregnant volunteers occurred on university property whereas data collection from obstetric patients occurred in an NHS hospital. All study subjects gave their written informed consent in accordance with the Declaration of Helsinki. Nonpregnant females volunteered to participate after viewing advertising posters in the study centre. Potential recruits were screened for eligibility at the time of volunteering on days when study personnel were available. Consent was obtained on the day of study participation. Obstetric patients were identified in the delivery suite following epidural catheter insertion. Consent was obtained after the duty obstetrician had obtained consent for delivery via intrapartum caesarean delivery. Thus, patients were pain free throughout the consent process and had a minimum of one hour to consider study participation.

Study population

Twenty nonpregnant female volunteers and 20 obstetric patients were recruited. The nonpregnant volunteers undertook a cold stress protocol and the obstetric patients received a standardised epidural surgical top-up dose. Nonpregnant female volunteers were chosen as the comparison group as exposing pregnant females to cold stress is not without risk. Inclusion criteria for the nonpregnant volunteers and obstetric patients were age ≥18 years and body mass index (BMI) >18 kg/m^2. Additional inclusion criteria for obstetric patients were established labour (regular contractions resulting in cervical dilation of at least 4 cm), effective epidural analgesia (0.1% levobupivacaine and 2 μg/mL^1 fentanyl; midwife delivered boluses) and a decision to deliver via intrapartum caesarean delivery (category 2 or 3[15]). Exclusion criteria for all participants were cardiovascular or neurological disease (including preeclampsia) and antibiotic administration for suspected infection. Obstetric

patients' data collection was terminated if the estimated blood loss exceeded 1500 mL. Data collected prior to the declaration of major haemorrhage were included in the final analysis.

Protocol – nonpregnant female volunteers

The measurement apparatus (accelerometer and EMG electrodes) was applied during a 30-min acclimatisation period in the laboratory. When acclimatisation was complete, 5 min of baseline data were recorded whilst the subject lay motionless on an examination couch. Cold exposure then commenced by encasing the study subject in a water-circulating mattress and blanket for 45 min (Meditherm iii, Stryker, Kalamazoo, MI) with the water temperature preset to 4° C. The mattress and blanket covered the entire body surface except the face. After 45 min, the water temperature was reset to 41° C and subjects were rewarmed for 75 min.

Protocol – obstetric patients

The measurement apparatus (accelerometer, EMG electrodes, core and skin thermocouples) was applied whilst the patient lay supine on the operating table tilted 15° to the left. The patient was then instructed to remain motionless whilst 5 min of baseline data were recorded. Upon completion, 15–20 mL of lignocaine-bicarbonate-adrenaline mixture (final concentrations 1.8%, 0.8% and 1:200,000 respectively)[16] were administered via the epidural catheter ("epidural top-up dose"). The dose was titrated to obtain a distribution of sensory blockade (light-touch sensation) up to and including the T5 dermatome bilaterally.[16] Surgery proceeded when this level of anaesthesia was attained. During the epidural top-up administration, patients received a 500 mL crystalloid (Plasmalyte™) coload, followed by a maintenance infusion at 125 mL/h. Phenylephrine boluses (50 μg) were administered if the systolic blood pressure fell by more than 10% of the baseline value or if the patient reported feeling lightheaded or nauseated. Following delivery, 5 IU of oxytocin were administered intravenously as a bolus and 40 IU (diluted in 500 mL 0.9% saline) were infused intravenously over 4 hr. All drugs and intravenous fluids were administered at room temperature.

Measurements

Oscillation, EMG and temperature data were sampled continuously (at 2 kHz) from the start of the baseline period until either the end of rewarming (nonpregnant female volunteers) or the end of caesarean delivery (obstetric patients) by a data acquisition interface (Power 1401+ and Spike2 software, Cambridge Electronic Design, Cambridge, UK). Oscillations were recorded with a unipolar accelerometer (EGCS-D1S, Entran Devices Inc., NJ, USA) positioned over the pectoralis major muscle in the midclavicular line, 3 cm inferior to the left clavicle. The accelerometer signal was filtered (1 Hz, high-pass). The accelerometer was aligned to record motion in an anterior-posterior direction. EMG activity was recorded with pairs of Ag/AgCl surface electrodes (ARBO blue, 2 cm diameter, Henleys Medical Supplies Ltd., Welwyn Garden City, UK) positioned over the mid-fibres of left trapezius and biceps brachii (biceps) muscles. Electrode pairs were placed parallel to the muscle fibres with a 3 cm separation. EMG signals were filtered (50 Hz to 1 kHz[17]) and amplified (x 1000, D-360 Isolated Patient Amplifier, Digitimer, Welwyn Garden City, UK). Accelerometer and EMG recording sites were chosen above the expected level of motor blockade (T4) in locations minimally contaminated by voluntary movement (in the upper limb, voluntary movement is most common in the forearm and hand). Core temperature was recorded (limits of error, +/- 0.01° C) with a tympanic T-type thermocouple (TTS-TC, Smiths Medical, Ashford, UK). Skin temperature was recorded (+/- 0.01°C) at seven sites on the patient's left side (head, chest, forearm, index finger, thigh, calf and great toe) with T-type thermocouples (Sable Systems, Las Vegas, NV, USA). All thermocouples were connected to a self-calibrating thermocouple meter (TC 2000, Sable Systems, Las Vegas, NV, USA). Mean skin temperature was calculated as the area weighted average of the seven skin temperature recording sites.[18] Mean body temperature was calculated as the volume weighted average of the core and the mean skin temperatures.[19] Obstetric patients' cutaneous heat flux and skin blood flow were recorded as described previously for a concurrent investigation of cutaneous vasomotor tone and were previously reported separately.[14]

Relevant clinical data were recorded including mass, height, BMI, American Society of Anesthesiologists physical status (ASA PS) classification and the indication for caesarean delivery.

Temperature sensation was assessed with temperature sensation votes, a bipolar visual analog scale (VAS) with the anchors “most cold imaginable” (-50 mm), “neutral” (0 mm) and “most hot imaginable” (+50 mm).[20] Thermal pleasantness was assessed with thermal pleasantness votes, a bipolar VAS with the anchors “very unpleasant” (-50 mm), “unpleasant” (-25 mm), “indifferent” (0 mm), “pleasant” (+25 mm) and “very pleasant” (+50 mm).[21] Temperature sensation votes and thermal pleasantness votes were recorded at 5 min intervals.

Signal processing

Accelerometer and EMG data were processed with bespoke scripts (MatLab software, MathWorks, Cambridge, UK). Periods of shivering and epidural top-up tremor were identified when three criteria were satisfied: the subject reported shivering, the investigator observed an oscillation and increased power was identified in the peak frequency-time plot (1 Hz bin width, 60 s segments, 0% overlap, Hann window).[22] Preliminary analysis demonstrated that both shivering and epidural top-up tremor exhibit local stationarity, thus the presented values represent averages of the entire shivering/tremor period. The primary oscillation was analysed with a frequency domain technique.[23] Prior to analysis, EMG data were full-wave rectified. Power spectra were constructed with Welch’s overlapped segment method (0.25 Hz bin width, 2 s segments, 50% overlap, Hann window).[24] The oscillation frequency and the frequencies of coordinated EMG activity were determined by examining the power spectra for the presence of significant peaks.[23] Coordinated EMG activity is not always present during tremor and so the proportion of cases in which it was present is reported (incidence of coordinated EMG activity). Oscillation amplitude was calculated as the sum of the power in the frequency bins between the upper and lower limits of the peak half width.[23] Amplitude modulation was examined with a time domain technique.[7] Before time domain analysis, accelerometer and EMG data were root-mean-square (RMS) transformed and the mean baseline RMS amplitude subtracted from the shivering/tremor recordings.[7] Burst frequency was determined by calculating the frequency at which the “burst threshold” was exceeded.[7] Oscillation burst intensity was calculated as the mean burst intensity normalised to the mean non-burst intensity.[7]

Sample size and statistical analysis

A sample size of 40 was a convenience sample chosen based on previous investigations of thermoregulation during neuraxial blockade, in which 8 to 20 subjects per group were studied.[25] The final analysis of the oscillation and EMG data only includes those nonpregnant volunteers who shivered and those obstetric patients who experienced tremor. The final analysis of body temperature, temperature sensation votes and thermal pleasantness votes only includes obstetric patients who experienced tremor. Demographic and clinical data of all participants were analysed. Normality of data was examined with Shapiro-Wilk tests. Normally distributed data are presented as mean (SD). Skewed data are presented as median (IQR [range]). Demographic, clinical, oscillation and EMG data of nonpregnant volunteers and obstetric patients were compared with 2-tailed unpaired t-tests, Mann-Whitney rank sum tests and Chi-square tests. Obstetric patients' body temperatures, temperature sensation votes and thermal pleasantness votes were compared at 2 time points (before the epidural top-up dose and at the onset of tremor) with paired t-tests. Data were analysed with SigmaStat (Systat, CA, USA) software. Comparisons are not multiplicity adjusted.

Results:

Twenty nonpregnant volunteers were recruited between September 2013 and September 2014 and 20 obstetric patients were recruited between January and June 2016 (Figure 2). The indication for caesarean delivery was 'failure to progress' in 17 cases and fetal tachycardia in 3 cases. One patient was excluded from the final analysis because an attempt at instrumental delivery was made prior to caesarean delivery following the epidural top-up dose. A second patient's recordings were terminated after 75 min when the estimated blood loss exceeded 1.5 L; data collected prior to this time point are included. Nonpregnant volunteers' and obstetric patients' demographic and clinical data are presented in Table 1.

Tremor

No obstetric patients or non-pregnant volunteers shivered or experienced tremor during baseline recordings. Sixteen nonpregnant volunteers shivered, and tremor occurred following the epidural top-up dose in 16 obstetric patients. In nonpregnant volunteers, the median (IQR [range]) onset of shivering was 4 (2–29 [1–37]) min after the application of cold stress and the median (IQR [range]) duration of shivering was 42 (19–45 [13–48]) min. In obstetric patients, the median (IQR [range]) onset of tremor was 15 (9–20 [5–44]) min after epidural top-up dose. Tremor was ongoing at the end of the caesarean delivery in 7 patients and in the remaining 9 patients the median (IQR [range]) tremor duration was 34 (29–40 [25–46]) min. The primary oscillation characteristics of epidural top-up tremor did not differ from those of cold stress-induced shivering (Table 2). Amplitude modulation was present in both epidural top-up tremor and cold stress-induced shivering, but the burst frequencies of epidural top-up tremor were slower than those of cold stress-induced shivering.

Actual and sensed body temperature

Before the epidural top-up dose, the mean (SD) core temperature was 37.6 (0.6)° C, mean (SD) skin temperature was 33.7 (0.9)° C and mean (SD) mean body temperature was 36.8 (0.5)° C. At the onset of tremor, skin temperature was greater (P = 0.002) than its value prior to epidural top-up

dose, but neither core temperature (*P* = 0.126) nor mean body temperature (*P* = 0.165) were different from the baseline values (Figure 3). Before the epidural top-up dose the mean (SD) temperature sensation votes was 0 (11) mm and mean (SD) thermal pleasantness votes was +7 (18) mm. At the onset of tremor both temperature sensation votes (*P* = 0.012) and thermal pleasantness votes (*P* = 0.048) were less than before epidural top-up dose (Figure 4).

Discussion:

To our knowledge, this is the first study to investigate the tremor associated with an epidural top-up dose for intrapartum caesarean delivery. The novel findings are (1) the primary oscillation frequencies of epidural top-up tremor and cold stress-induced shivering did not differ, but the burst frequencies of epidural top-up tremor were slower; (2) obstetric patients were either normothermic (core temperature 36.5 – 37.5° C) or hyperthermic (core temperature >37.5° C) before the epidural top-up dose; and (3) at the onset of tremor obstetric patients' sensed body temperature decreased but actual body temperature did not.

The recorded tremor frequencies are similar to previous reports, but, due to the potential confounders, between-study comparisons of tremor frequency should be interpreted with caution. The primary oscillation and the amplitude modulation frequencies of cold stress-induced shivering are similar to previous observations in the shoulder (8.5–8.7 Hz) and upper limb (6.7–7.0 x 10^{-2} Hz).[7,8] We did not find any previous reports of tremor recording during intrapartum caesarean delivery, but the primary oscillation frequency observed in the current study is similar to that reported for thermoregulatory shivering during epidural anaesthesia in healthy individuals (9–12 Hz).[4] Amplitude modulation has been observed previously during epidural anaesthesia,[4] but this is the first time its frequency and amplitude have been quantified. However, tremor recording methodology (apparatus, recording site, signal processing) has a significant impact on the frequencies reported[8] and so the aforementioned between-study comparisons may be invalidated by the methodological differences. The current within-study comparison of epidural top-up tremor and cold stress-induced shivering is not affected by such methodological differences and is therefore a reliable method of tremor diagnosis.

The increase in actual body temperature and the reduction in sensed body temperature was predicted, but this pattern of temperature change is not observed with other forms of neuraxial blockade. The tremor associated with neuraxial blockade in healthy individuals,[4,26,27] nonobstetric

patients[28] and obstetric patients during elective caesarean delivery[29,30] is preceded by a reduction in actual body temperature and an increase in sensed body temperature. The likely reason for this disparity is the difference in actual body temperature prior to neuraxial blockade. In the present study patients were in labour and thus heat stressed,[6] but in the other scenarios neuraxial blockade is initiated from a thermoneutral baseline.[4,26-30] Actual body temperature changes following all forms of neuraxial blockade are a consequence of sympatholysis. When conducted from a thermoneutral baseline, neuraxial blockade interrupts active cutaneous vasoconstriction and as a result actual body temperature falls.[2,7,26,29-31] However, during hyperthermia, skin blood flow is almost exclusively regulated by the cholinergic pathway of the sympathetic nervous system, causing active cutaneous vasodilation.[32] Consequently, in such conditions neuraxial blockade limits cutaneous heat loss and actual body temperature increases.[14]

Thermoreceptors are the primary afferent neurons of temperature sensation and are classified as either warm or cold sensitive.[33] In thermoneutral conditions, cold thermoreceptors are active and warm thermoreceptors are quiescent.[12] Consequently, neuraxial blockade from a thermoneutral baseline results in an increase in sensed body temperature (despite a reduction in actual body temperature).[26,27] However, during hyperthermia, warm thermoreceptors are active and cold thermoreceptors are quiescent.[12] It is likely therefore that the observed decrease in sensed body temperature following an epidural top-up dose is a consequence of warm thermoreceptor blockade.

Collectively the results of the current study suggest that the tremor associated with an epidural top-up dose for intrapartum caesarean delivery is nonthermoregulatory shivering triggered by a reduction in sensed body temperature. The most plausible explanation for the oscillation and EMG results is that epidural top-up tremor is a modified form of shivering. The alternative explanation is that epidural top-up tremor is a unique entity unrelated to any other form of tremor, but this is less credible. The lack of difference in the primary oscillation frequencies of epidural top-up tremor and cold stress-induced shivering and the presence of amplitude modulation in the epidural top-up tremor signal support the former explanation. However, the *a priori* defined standard of tremor

diagnosis is not completely satisfied, as the amplitude modulation frequency of epidural top-up tremor was less than that of cold stress-induced shivering. Spontaneous fluctuations in tremor amplitude are a unique characteristic of shivering[3] and so, despite this frequency difference, it is unlikely that epidural top-up tremor is a distinct form of tremor. A more likely explanation is that the epidural top-up dose modifies the shivering neural pathway. Amplitude modulation is generated within the spinal cord[34] and is subject to numerous sensory and central inputs.[35] It is possible, therefore, that an epidural top-up dose partially blocks the afferent signal to this spinal central pattern generator and, as a result, the frequency of its output is altered.

The absence of both hypothermia (core temperature <35.0°C) and a reduction in body temperature indicates that epidural top-up tremor is not a physiological thermoregulatory response. However, the autonomous (shivering) and behavioural (temperature sensation) thermoregulatory responses use the same populations of thermoreceptors and so temperature sensation can be considered an index of activity within the afferent limb of the shivering reflex.[11] It is possible, therefore, that topping-up an epidural catheter triggers shivering by blocking warm thermoreceptors and thus creating the illusion of hypothermia within the hypothalamus.

The main limitation of this study is that a crossover design was not used; for safety reasons it was not possible for obstetric patients to undertake a cold stress. Consequently, obstetric patients were older and had a higher BMI and ASA PS classification than the nonpregnant female volunteers. It is not known if pregnancy per se affects tremor frequencies, but it is unlikely that the other between-group differences significantly affected the results. The decrease in tremor frequency with age is limited to the elderly[36] and body mass does not affect the frequency of tremors generated by coordinated muscle activity, such as shivering.[36] The difference in ASA PS classification is an anomaly created by pregnancy being classified as ASA PS 2.

A direct clinical implication of the results is that active warming should not be used to prevent tremor during intrapartum caesarean delivery. Patients were either normothermic or hyperthermic

throughout and further warming could adversely affect the foetus.[13] However, further work should be conducted to investigate when active warming is appropriate during emergency caesarean delivery. Clinicians may also use the study conclusions to provide patients with an explanation should tremor occur. An indirect clinical implication is the identification of a target for future interventional studies: sensed body temperature. Portable thermoelectric devices that alter sensed body temperature are available[37,38] and this study suggests a novel application; tremor might be prevented by switching on the device following an epidural top-up dose, thus averting the decrease in sensed body temperature.

In summary, this is the first mechanistic study of the tremor associated with epidural top-up doses for intrapartum caesarean delivery. The results suggest that the epidural top-up tremor is non-thermoregulatory shivering triggered by a reduction in sensed body temperature. Active warming should not be used to prevent shivering in this scenario, but devices that increase sensed body temperature may prove effective.

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Tables:

Table 1 Demographic and clinical data of obstetric patients and nonpregnant female volunteers.

	Obstetric patients (n = 20)	**Nonpregnant female volunteers (n = 20)**	***P*-value**
Age (years)	33 (5)	24 (5)	<0.001
BMI (kg/m^2)	25.8 (22.8–28.9 [20.1–39.4])	20.7 (20.0–24.0 [17.9–25.6])	<0.001
ASA PS	2 (2–2 [2–2])	1 (1–1 [1–2])	<0.001
Epidural analgesia duration (min)	755 (307)	-	-
Indication for caesarean delivery:			
- Failure to progress	16 (80%)	-	-
- Fetal tachycardia	4 (20%)	-	-

BMI = Body mass index; ASA PS = American Society of Anesthesiologists physical status classification.

Values are mean (SD); median (IQR [range]) and n (%).

Table 2 Oscillation and surface electromyography characteristics of epidural top-up tremor (obstetric patients) and cold stress-induced shivering (nonpregnant female volunteers).

	Obstetric Patients (n=16)	**Nonpregnant female volunteers (n=16)**	***P*-value**
Primary oscillation characteristics			
Primary oscillation frequency (Hz)	9.9 (1.9)	9.0 (1.6)	0.194
Oscillation amplitude $((m/s^2)^2)$	0.10 (0.06–0.72 [0.04–1.96])	0.07 (0.04–0.11 [0.02–0.66])	0.130
Incidence of coordinated EMG activity			
- Trapezius	7 (44%)	7 (56%)	0.724
- Biceps	9 (56%)	5 (31%)	0.285
Frequency of coordinated EMG activity (Hz)			
- Trapezius	10.0 (1.3)	9.2 (1.1)	0.169
- Biceps	9.4 (2.1)	7.7 (1.6)	0.147
Amplitude modulation characteristics			
Oscillation burst frequency (x 10^{-2} Hz)	6.1 (1.2)	6.9 (0.7)	0.046
EMG burst frequency (x 10^{-2} Hz)			
- Trapezius	4.3 (1.5)	5.4 (1.0)	0.024
- Biceps	4.2 (1.0)	5.1 (1.3)	0.048
Oscillation burst intensity	4.8 (4.6–5.1 [3.5–6.0])	5.2 (5.0–5.5 [4.6–8.2])	0.027

EMG = electromyography. Values are mean (SD); median (IQR [range]) and n (%).

Illustrations:

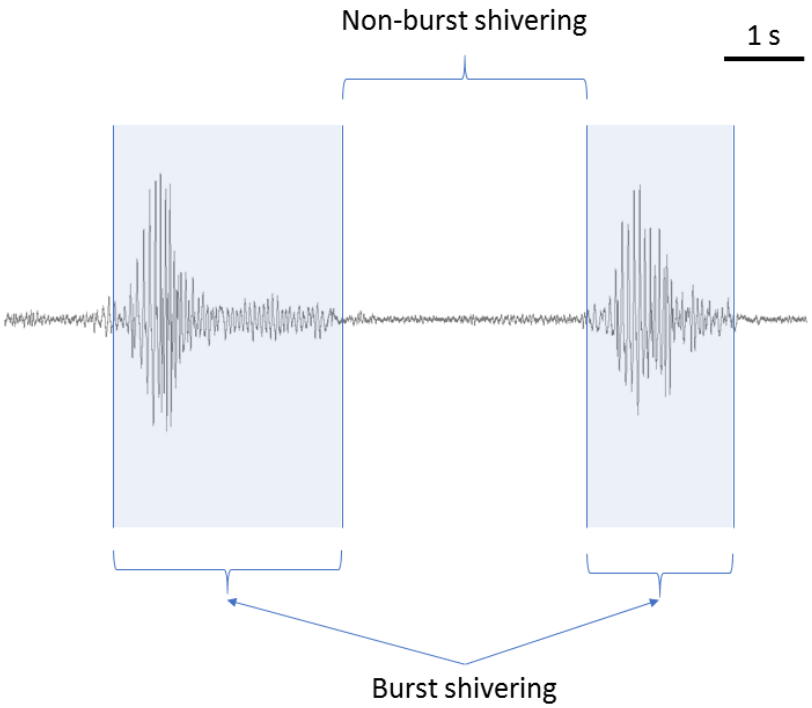

Figure 1 Schematic of 10 seconds (s) cold stress-induced shivering illustrating the high-frequency primary oscillation and the low-frequency amplitude modulation. Amplitude modulation frequency is the frequency at which at which burst shivering occurs.

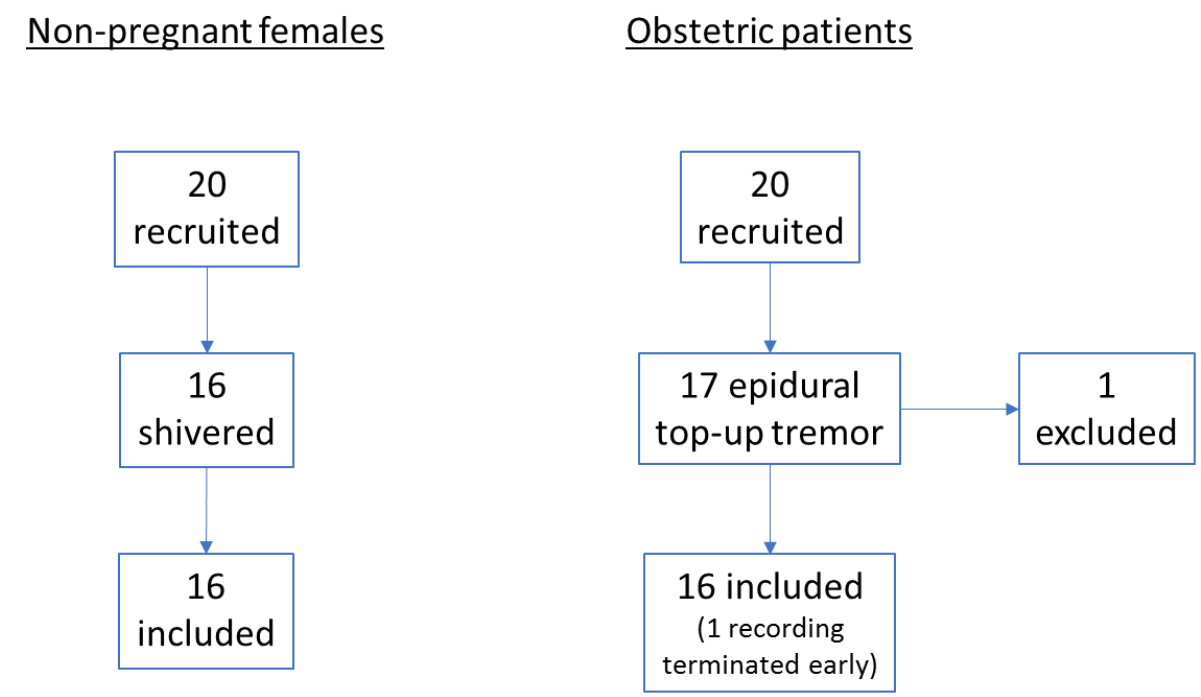

Figure 2 Flow chart of recruitment.

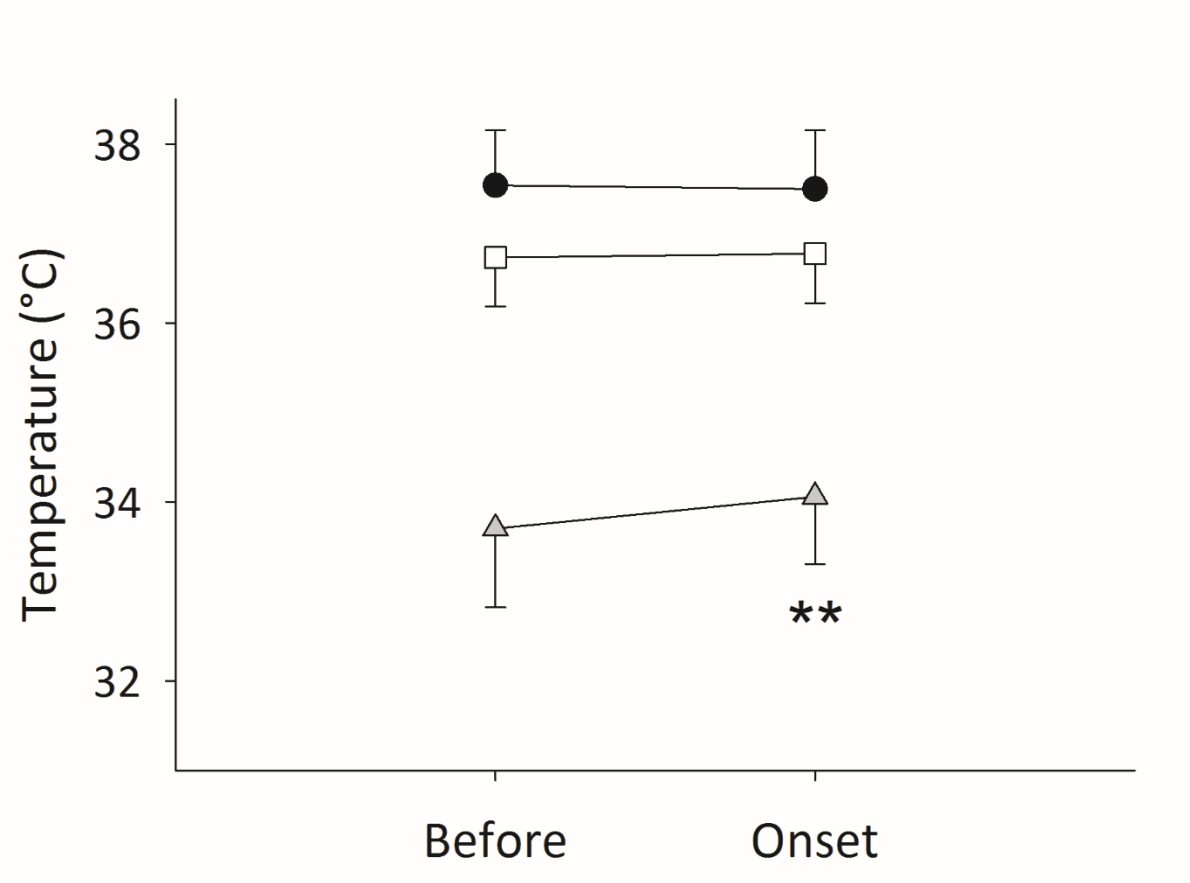

Figure 3 Obstetric patients' mean core (black circles), skin (grey triangles) and mean body (white squares) temperatures before the epidural top-up dose and at the onset of tremor (n = 16). Whiskers denotes standard deviations. ** indicates significant difference to the before epidural top-up value (*P* = 0.002).

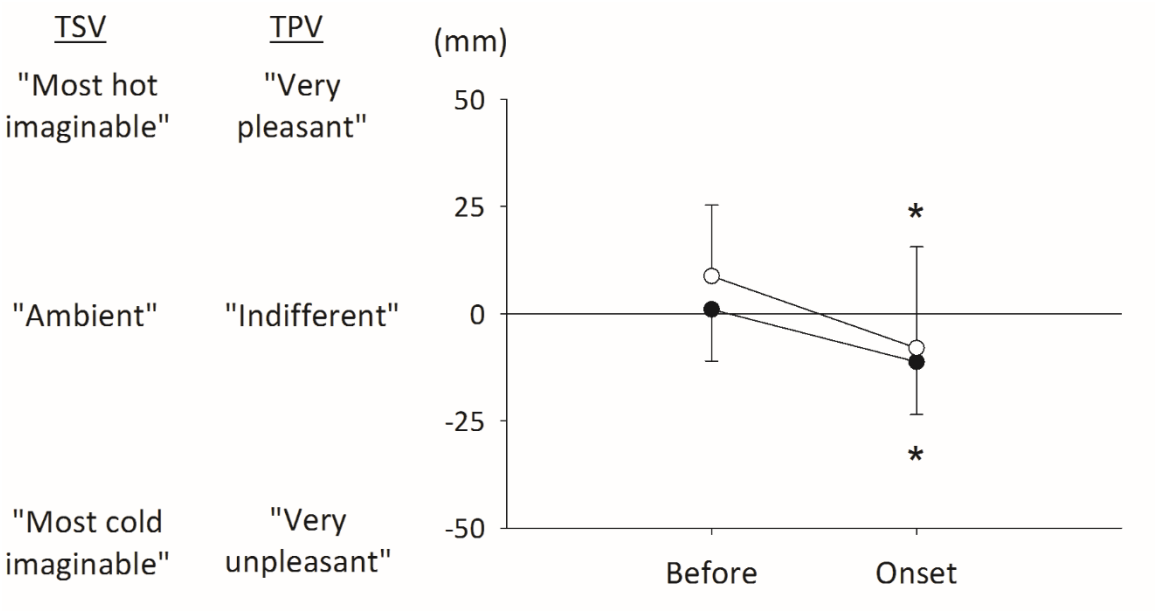

Figure 4 Obstetric patients' mean (SD) temperature sensation votes (TSV; black circles) and thermal pleasantness votes (TPV; white circles) before the epidural top-up dose and at the onset of tremor (n = 16). Whiskers denote standard deviations. * indicates significant difference to the before epidural top-up value ($P < 0.05$).