—Original—

The Current Perception Thresholds In Normal Pregnancy

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Abstract

The purpose of this study was to evaluate a quantitative analysis of the nociceptive threshold, using the current perception threshold (CPT), in women with normal pregnancies and to assess the relationship between nociceptive thresholds and ovarian sex steroids. The subjects consisted of 10 women with singleton pregnancies and 14 age-matched healthy female volunteers. The CPTs (5,250, and 2,000 Hz) of the dominant ankle section were determined with a Neurometer CPT/C (Neurotron, Baltimore, MD). Blood samples were collected after these examinations, and the total 17 β-estradiol (E_2) and progesterone concentrations in sera were measured. The present findings clearly indicated that the CPTs at 2,000 Hz in women at term in normal pregnancies were significantly higher than those in nonpregnant women ($p < 0.05$). At 5 and 250 Hz, there was no significant difference between pregnant and nonpregnant women. While there was also no significant correlation between CPT and E_2, and progesterone, there was significant correlation between CPT and the ratio of 17 β-estradiol/progesterone (E_2/P) at 2,000 Hz ($p < 0.05$, $r = 0.67$). We suggest from these data that changes in pressure sensitivity occur at term in pregnancy, and that other factors, possibly stimulated by both E_2 and progesterone, may play an important role in this change.
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Key words: pregnancy, current perception thresholds, 17 β-estradiol, progesterone

Introduction

The enhancement and mechanism of pain tolerance during pregnancy has not been clearly elucidated. In pregnant rats, a progressive increase in pain tolerance has been reported[1], and the administration of 17 α-estradiol (E_2) and progesterone has been observed to result in similar elevated nociceptive response thresholds in nonpregnant ovariectomized rats[2,3]. Additionally, it has been reported that E_2 and progesterone amplify the antinociceptive consequence of spinal κ/δ neurotransmission[4–6], and it has been suggested that the increase in pain thresholds was the result of a pregnancy-related increase in the endorphin system[1].

While several tactile threshold studies have been reported in pregnant women[7,8], no correlative studies on ovarian sex steroids and pain threshold have been reported. It is well known that E_2 and progesterone concentrations are higher in the third trimester and term of pregnancy than in the first and second trimesters, and that furthermore, progesterone concentration in cerebrospinal fluid is higher than in nonpregnant women[9]. Therefore, in clarifying the relationship between pain threshold and ovarian sex steroids, the enhancement and mechanism of pain tolerance during term in pregnancy should also be

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Table 1 Clinical characteristics of women with normal pregnancies and nonpregnant women

Characteristics	*nonpregnant women* (n = 14)	*women with normal pregnancies* (n = 10)
Age(y)	28.1 ± 5.2	29.4 ± 3.7
Body mass index (before conception)	20.8 ± 0.64	24.4 ± 0.54 (20.6 ± 0.50)
Parity	0.6	0.6
Weeks' gestation at study	—	38.3
Weeks' gestation at delivery	—	39.8

elucidated.

The aim of the present study was to determine whether current perception threshold (CPT) was increased at term in pregnancy, as well as to evaluate the relationship between the CPT and ovarian sex steroids.

Materials and Methods

The subjects in this study were 10 women with singleton pregnancies seen at our institution between July and August 2001 and fourteen agematched healthy female volunteers as control group (**Table 1**). All of the subjects were healthy nonsmokers with no history of drug use. The pregnant women underwent a nociceptive examination at 37～39 weeks' gestation (mean, 38.3 weeks); the interval between examination and delivery was 3～15 days (mean, 10.2 days). Subjects with neurologic, metabolic and endocrinological diseases such as diabetes mellitus, hyperthyroidism and gestational complications were excluded from this study. The study was approved by the ethics committee at our institution, and the subjects gave oral informed consent for the examinations.

Nociceptive threshold was measured with a Neurometer CPT/C (Neurotron, Baltimore, MD). The subjects and controls were examined following 15 min of resting time in a quiet environment, and were placed in a supine position. Nociceptive threshold was estimated from the dominant ankle section (lumbar/sacral sites). The device emits sinusoidal alternating currents at 2,000, 250 and 5 Hz at intensities from 0 to 10 mA. This constant current output automatically compensates for alterations in skin resistance and provides a standardized stimulus independent of different skin thickness, degree of skin dryness or perspiration, or drying of the electrode paste. Electrical stimulus was initially increased until any sensation at all was reported by the subject. Short stimuli were then applied at progressivery lower amplitudes until a minimal, but consistant threshold was detected. One CPT value corresponded to 10 μA[10]. To exclude inter-observer error, all examinations were performed by a single investigator. All examinations were carried out without maternal movements. After examination, 4 m*l* of blood was collected and centrifuged at 500 g for 10 min, and the supernatant was collected and stored at −20℃ until further analysis. Total E_2 and progesterone concentrations in sera were measured by radioimmunoassay using regents supplied by Diagnostic products corporation (Los Angeles, CA). The lower limits of sensitivity for E_2 and progesterone detection were 3.0 pg/m*l* and 0.2 ng/m*l* respectively. Concentrations lower than the limits of detection were taken as 0 pg/m*l* and 0 ng/m*l*.

Data are presented as mean±standard error. Statistical analyses were performed with the Welch's *t*-test and Peason's correlation coefficient test for the comparison of CPT values and E_2 and progesterone. Differences were considered significant at $p < 0.05$. Simple regression lines were performed to assess the correlation of the CPT values and the ratio of E_2/progesterone (E_2/P), with $p < 0.05$ and $r > 0.4$ considered significant.

Table 2 Ankle CPT values in nonpregnant women and women with normal pregnancies

	Nonpregnant women (n = 14)	Women with normal pregnancies (n = 10)
5 Hz		
Mean ± SE	42.7 ± 3.3	48.2 ± 7.1
Range	23—64	27—102
250 Hz		
Mean ± SE	53.0 ± 5.3	49.2 ± 7.7
Range	27—106	27—100
2,000 Hz		
Mean ± SE	174.5 ± 11.8	239.6 ± 30.2 *
Range	104—260	90—374

* Significant difference from values for nonpregnant women ($p = 0.01$; Welch's t-test).

Results

As shown in **Table 2**, the mean CPT values of lumbar/sacral sites at 5,250 and 2000 Hz were 42.7 ± 3.4, 53.0 ± 5.3 and 174.5 ± 11.8 in nonpregnant women and 48.2 ± 7.1, 49.2 ± 7.7 and 239.6 ± 30.2 in women with normal pregnancies respectively. Although there was no significant difference between nonpregnant women and women with normal pregnancies in CPT values at 5 and 250 Hz of stimuli, the approximately 1.4-fold increase at 2,000 Hz in pregnant women was markedly statistically significant ($p < 0.05$).

No significant correlation was found between CPT values at 2,000 Hz in women with normal pregnancies and E_2 ($p = 0.83$, $r = 0.4$), and progesterone ($p = 0.24$, $r = 0.08$) (**Fig. 1**). The correlation between CPT values of lumbar/sacral sites at 2,000 Hz in women with normal pregnancies and the ratio of E_2/P was found to be significant ($p < 0.05$, $r = 0.67$) (**Fig. 2**).

Discussion

Our findings showed that the CPT values at 2000 Hz in women at term in normal pregnancies were significantly higher than those in nonpregnant women. At 5 and 250 Hz, there was no significant difference between pregnant and nonpregnant women. CPTs 5 Hz stimulus selectively excites Type C unmyelinated fibers, the 250 Hz stimulus selectively excites Type Aδ small myelinated fibers, and the 2,000 Hz stimulus selectively excites Type Aβ large

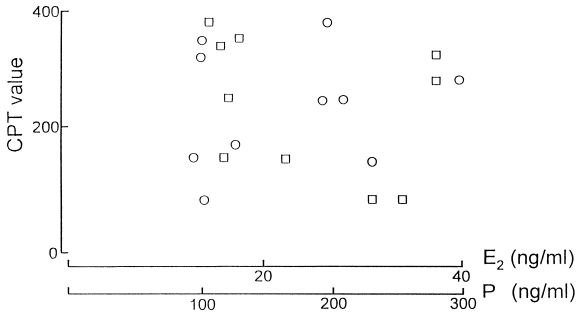

Fig. 1 Plot of current perception threshold (CPT) values of lumbar/sacral sites at 2,000 Hz in women with normal pregnancies on the basis of 17 β-estradiol (E_2), progesterone. Open circles, open squares indicate E_2, progesterone.

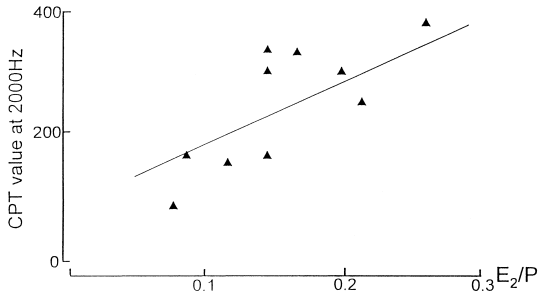

Fig. 2 Plot of current perception threshold (CPT) values of lumbar/sacral sites at 2,000 Hz in women with normal pregnancies on ratio of E_2/P. Closed triangles indicate the ratio of E 2/P. Correlation between CPT values and the ratio of E_2/P was significant ($p < 0.05$, $r = 0.67$) : $y = 1,088\ x + 75.5$.

myelinated fibers[11]. Stimulation in Type C unmyelinated fibers is sensed as temperature, slow pain and post ganglionic sympathetic nerves; in Type Aδ small myelinated fibers it is sensed as mechanorecepter pressure, temperature, and fast pain; in Type Aβ large myelinated fibers it is sensed as cutaneous touch and pressure. Our results showed that the approximately 1.4-fold increase at 2,000 Hz at term in pregnant women was markedly statistically significant. This finding suggests that changes in pressure tolerance may be abrupt in vaginal delivery in late stage pregnancies, and female specific physiological features have been reported to be associated with antinoception[7,8]. During the late stage of pregnancy, pain thresholds, or sensory thresholds have been reported to be increased in both rats[1,12-18] and humans[7,8,19,20], in response to noxious stimuli including electric[1], heat[21], and pressure stimuli[7,8]. This is the first report confirming these phenomena by quantitative analysis with CPT values obtained from term pregnant women. This pregnancy associated antinociception is considered to be the result of mediation, in part, by the spinal cord dynorphin/κ antinociceptive system[15,17].

In nonpregnant animals, simulating a blood concentration of E_2 and progesterone profiling pregnancy produces an opioid antinociception which closely approximates that of actual pregnancy[4].

The antinociception of both pregnancy and pseudopegnancy is multifactorial and requires spinal and peripheral components. Moreover, non-mechanical factors such as an increase in progesterone concentration may alter the susceptibility of the nerve to local anesthetics during pregnancy in humans[22]. There is a gradual increase in the levels of plasma progesterone as well as those of estradiol and estriol in normal human pregnancy[23]. An increase in progesterone during pregnancy is thought to be the probable reason for increased sensitivity to local anesthetics[24,25]. It is known that progesterone has the effect of decreasing electrical excitability in the central and peripheral nervous system in both animals and humans. Other investigators have reported that large doses of steroids, including progesterone and pregnanediol, had anaesthetic effects[26,27], and that progesterone raised the electroshock seizure threshold[28]. An increased threshold to painful stimulus was also observed in ovariectomized rats treated with progesterone[29]. Our data showed there were no corelationships between E_2 and progesterone, and CPT values in term pregnant women. Previous reports have shown that the pregnant blood concentration of both E_2 and progesterone produce an opioidmediated elevation in nociceptive thresholds in animals[2,3]. As there was a significant correlation between CPT values and the ratio of E_2/P, possible nociceptive agents may be stimulated when both E_2 and progesterone concentrations are above the levels of their executive threshold.

In summary, our data affirmed an approximate 1.4-fold increase in nociceptive sensitivity during the antepartum period in humans, similar to that described in animals. Moreover, as our findings showed a co-relationship between CPT values and the ratio of E_2/P, we suggest that an increase in E_2 and progesterone concentration and its balance is the probable reason for sensitivity to CPT values in term pregnant women.

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