ORIGINAL ARTICLE

Can second to fourth digit ratio (2D:4D) predict sensitivity to pain?

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Abstract

OBJECTIVES: Sexually dimorphic index 2D:4D (digit length ratio between the second and fourth finger) is believed to reflect prenatal effect of gonadal hormones. Higher index in women results from prenatal exposure to lower level of testosterone whereas lower index in men results from higher testosterone level We hypothesized that more masculine index will be associated with lower sensitivity and more feminine index with higher sensitivity to pain.

METHODS: Thirty four subjects (18 women and 16 men) underwent two thermal nociceptive tests: stimulation of fingers with the beam of radiant heat until appearance of withdrawal reaction and the cold pressor test (CPT - immersion of non-dominant hand into water 2°C for 2 min). Intensity of perceived cold pain was assessed in 15 s intervals on visual analogue scale.

RESULTS: In thermal pain, we found no significant gender differences and no correlation between digit ratio and withdrawal latency from heat stimulus. In CPT, pain intensity correlated positively with digit ratio and women experienced more intensive pain than men.

CONCLUSION: From these results it can be concluded that sexually dimorphic index 2D:4D is probably more associated with affective than with sensory component of pain.

Introduction

Men and women differ in their perception of pain. Females are more sensitive to experimentally induced pain relative to males and their responses to noxious stimuli vary across the menstrual cycle (Fillingim & Ness 2000). In adulthood, circulating sex hormones have an activational effect whereas during prenatal period they have an organizational effect and can also influence development of nociceptive system.

Experimental studies on animals bring a lot of facts about bidirectional effects of sex hormones on endogenous opioid system and vice versa. Prenatal or early postnatal manipulation with opioids changes sexual behavior and vice versa, manipulation with sex hormones changes responses to painful stimuli. In rodents, adult female rats neonatally treated with testosterone displayed enhanced morphine analgesia relative to controls (Cataldo *et al* 2005). On the other hand, prenatal exposure to morphine feminizes (Gagin *et al* 1997) whereas prenatal naltrexone (antagonist of opioid receptors) facilitates male sexual behavior in adulthood (Cohen *et al* 1996).

Sexually dimorphic index 2D:4D (digit length ratio between the second and fourth finger) is believed to reflect prenatal effect of testosterone and estrogens. Higher index in women (= or > 1) results from prenatal exposure to lower level of testosterone whereas lower index in men (< 1) results from higher testosterone level (McIntyre 2006).

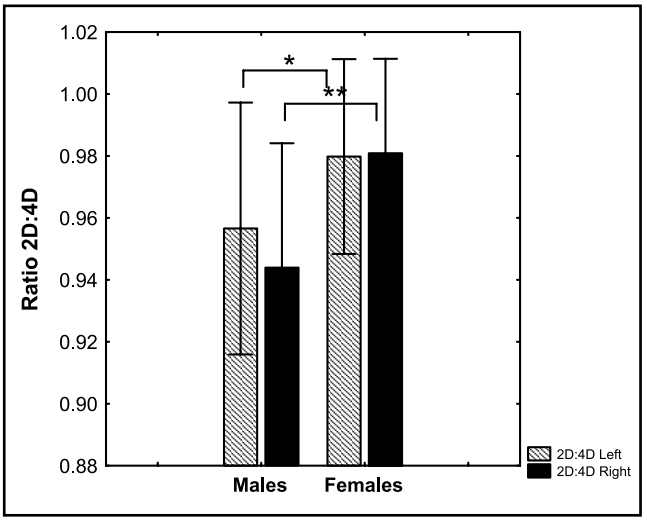

Fig. 1. Ratios of the length of the second and fourth digit in men and women. * $p < 0.05$, ** $p < 0.01$.

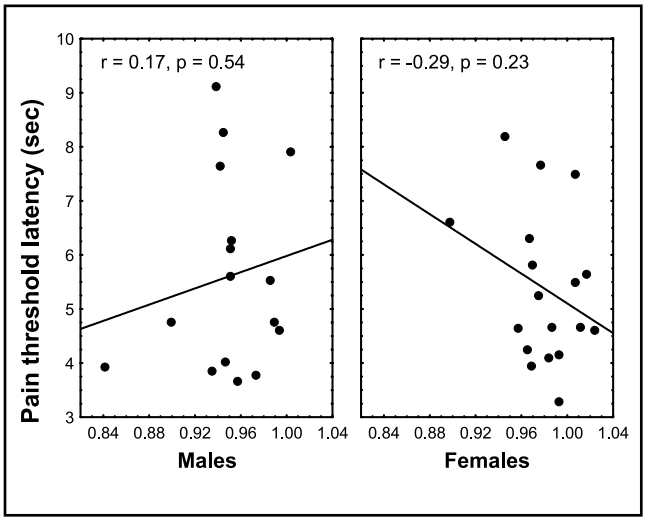

Fig. 2. Correlation between heat pain threshold and digit ratio for males and females.

The aim of present study was to compare nociceptive sensitivity in adult men and women in dependency on digit ratio. We hypothesized that more masculine index will be associated with lower sensitivity to pain and more feminine index with higher sensitivity to experimentally induced pain.

Methods

Eighteen women (mean age 23.1 years) and sixteen men (mean age 23.4 years), were recruited among students of the Faculty of Medicine. Twelve women were taking contraceptives; one woman and two men were left handed. Because of small sample size, we did not evaluate the effect of the menstrual cycle phase. Digit ratios were calculated from the photocopies of both hands.

The pain threshold was measured at rest condition using the Analgesia Meter (IITC Life Science USA Model 33), which applies radiant heat of constant intensity to an area of 1cm^2. The pain threshold was measured on all fingers (except of thumb) of both hands from the dorsal and ventral sides. Average of all measurements was used in the analysis. Participants were instructed to withdraw their finger when the heat becomes painful. The time from start of the radiant heat to the finger withdrawal was measured as thermal pain threshold latency. During the CPT, participants were asked to keep their non-dominant hand immersed in ice-water mixture maintained at 1–3° for 2 minutes. Intensity of cold pain was assessed in 15 s intervals by a 10 cm visual analogue scale (VAS) with the left extreme labeled as 'no pain' and the right extreme as 'maximum possible pain'.

Gender differences in thermal pain threshold and 2D:4D were analyzed using Student's t-test. ANOVA for repeated measures was used for the analysis of pain intensity assessed on visual analogue scale. Relationship between 2D:4D and thermal pain threshold and pain intensity in CPT was expressed using Pearson correlation. Data are presented as mean ± SD.

Results

Means and standard deviations for all measures are summarized in ***Table 1***. The digit ratio, as expected, was higher in women than in men (***Fig. 1***). We found no significant sex differences in the thermal pain and no significant correlation between withdrawal latency from the heat stimulus and finger ratio (women: $r = -0.30$, $p = 0.23$; men: $r = 0.17$, $p = 0.54$) (***Fig 2***).

During CPT women experienced more intensive pain than men (main effect of gender: $F_{(1,29)} = 4.72$; $p = 0.038$). Three women who withdraw their hand before 2 min limit were not included into analysis. Changes in pain intensity during 2 min of cold exposure were in both genders similar (ANOVA: $F_{(11,319)} = 0.73$, $p = 0.7$) (***Fig. 3***). Overall pain intensity during CPT, computed from the area under the curve, correlated positively with the finger ratio ($r = 0.38$, $p < 0.05$) when the data obtained from men and women were analyzed together (***Fig. 4***). When the data were analyzed for each gender separately, a weak correlation was still present in men ($r = 0.44$, $p = 0.08$), but disappeared in women ($r = 0.08$, $p = 0.79$) (***Fig. 5***).

Discussion

Results obtained from the thermal pain did not support our hypothesis that more masculine index will be associated with higher pain threshold. We did not find any significant correlation between pain threshold and 2D:4D neither in men nor in women, moreover in men, the more feminine index was associated with the higher pain threshold. Thus, we can suppose that perception of short phasic pain is probably more dependent on actual hormonal levels than on hormones which were

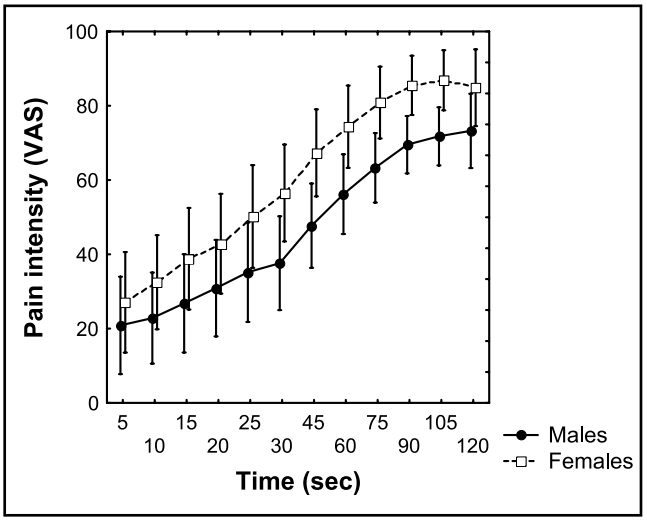

Fig. 3. Females (dashed line) showed significantly higher pain rating than males (solid line) during the cold pressor test.

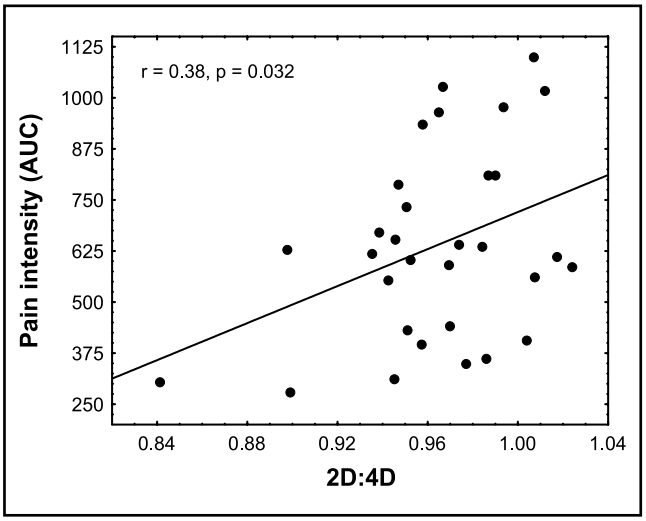

Fig. 4. Correlation between pain intensity in the cold pressor test and digit ratio for all subjects.

important during the development. Although several studies showed significant negative correlation between 2D:4D and adult testosterone in men (Roney *et al* 2004) or positive correlation with estradiol levels in women (McIntyre *et al* 2007), recently published meta-analysis of 2D:4D and adult hormone levels did not find any association between these two variables (Hönekopp *et al* 2007).

The development of nociceptive system including antinociceptive one are controlled by gonadal steroids. Manipulation with hormonal levels at critical period can change sensitivity to opioid and/or non opioid analgesics in adulthood and affect intensity of stress-induced analgesia (e.g. cold pressor test). The individual strength of antinociceptive system can roughly be estimated from the pain intensity during CPT. As we expected, the pain intensity of the whole sample correlated with 2D:4D positively, although separate analyses in men and women showed that this correlation was close to significant in men only. According to our knowledge, there is only one study which analyzed a relationship between CPT and 2D:4D ratio (Keogh *et al* 2007). Contrary to our results, they found a positive correlation between the sexual dimorphic index 2D:4D and the pain threshold in women but not in men.

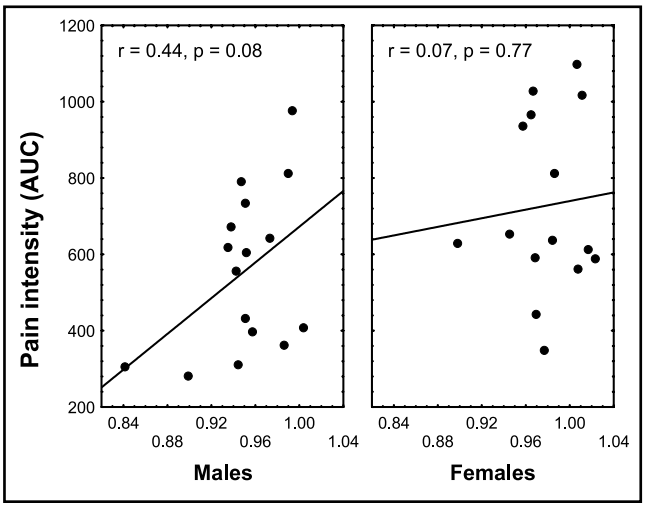

Fig. 5. Correlation between pain intensity in the cold pressor test and digit ratio for males and females

Recently, Schwerdtfeger and Heer (2008) described that association between digit ratio and pain perception seemed to depend on stimulus intensity. They observed a significant association for the higher-intense electrical stimuli but not for the lower-intense stimuli.

Table 1: Means and standard deviations for digit ratio and pain measures for men and women

	Male	Female	t-value	p
Left hand 2D:4D	0.97 ± 0.04	0.98 ± 0.03	-1.87	0.07
Right hand 2D:4D	0.94 ± 0.04	0.98 ± 0.03	-3.04	0.01
Average 2D:4D	0.95 ± 0.04	0.98 ± 0.03	-2.53	0.02
Skin temperature (°C)	32.1 ± 4.0	31.2 ± 4.0	0.65	0.52
Pain threshold latency (sec)	5.61 ± 1.78	5.37 ± 1.4	0.43	0.67
Pain intensity in CPT (AUC)	556 ± 209	728 ± 231	-2.17	0.04

In present study we did not analyze hormonal levels. In women, right hand 2D:4D was positively correlated with average estradiol level measured serially over the course of menstrual cycle (McIntyre *et al* 2007). Although progesterone level was not predicted with 2D:4D ratio, it plays important role in pain modulation in healthy women. In CPT, progesterone level positively correlated with pain intensity, which, on the other hand, was significantly reduced with increasing levels of estradiol (Stening *et al* 2007). From the point of view of continual hormonal changes over the menstrual cycle and consequently parallel changes in nociception, it is almost impossible to explain perceived pain with single hormone. Therefore the 2D:4D ratio cannot be considered a trait marker of stoicism or increased sensitivity to pain.

From our results we can conclude that sexually dimorphic index 2D:4D might be more associated with the perception of long lasting tonic pain which is more dependent on structural and functional background of whole nociceptive system (sensory and affective) than with the short lasting phasic pain.

Acknowledgements

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