学　位　論　文　要　旨

論文題名

Comparison of fetal gross movements between male and female fetuses with the use of a fetal movement acceleration measurement recorder
- An exploratory study-

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はじめに

男女の神経学的発達の違いについては、よく知られているが、胎児期の神経学的発達の性差に関しては、あまり知られていない。神経系の発達を評価するうえで、胎動は重要であると考えられている。これまでに、女児の方が男児よりも多く胎動を有するという報告や、女児よりも男児の方がより活動的であるとする報告があるが、見解は一致していない。その原因は、長時間の胎動の測定が困難であったためであると考えられている。そこで今回、これまでの研究により長時間の胎動の測定を可能にしたFMAM recorderを用いて、胎動に男女差があるかどうかを研究した。

方　法

2008年から2015年の間に帝京大学病院産婦人科を受診した、妊娠28から分娩に至までの妊婦を対象とした。胎動計の記録方法は、センサーの使用方法の説明を受けた妊婦が自宅にFMAMrecorderを持ち帰り、夜間就寝前に２個あるセンサーのうちの１個を腹壁上に（胎動センサー）、残りの１個は母体の動きをモニターすることを目的に大腿部に（母体動センサー）装着、記録開始のスイッチを入れ、就寝してデータを記録した。データの解析は、一晩あたり4時間以上胎動記録が可能であったものを検討し、記録をFMAM recorder用に開発された胎動解析プログラム（NoruPro Light Systems, Inc.）で解析し、胎動センサーのみ信号がある場合を胎動と判定した。一晩の記録を10秒ごとの区画にわけ,全区画の中で胎動がある区画の出現頻度を一晩当たりの割合として胎動占有割合として算出した。これを男児・女児ともに前半・後半（妊娠28-33週・34-39週）に分けて、胎動占有割合に関して、Wilcoxon法とtwo-way ANOVA法を用いて解析を行った。

結　果

男児・女児ともに15症例ずつの記録を得た。記録回数は合計205回であった。99例が男児（前半群が42例、後半群が57例）、女児が106例（前半群が54例、後半群が52例）であった。それぞれ男児の胎動占有割合の中央値が13.75%（min 2.54, max 33.11）、女児が12.72%（3.38, 35.96）であり、両者には有意差を認めなかった(p = 0.6879)。また、男児前半群、女児前半群の胎動占有割合の中央値(min, max)はそれぞれ17.99%(6.96, 33.11）、16.76%（4.16, 35.96)、男児後半群、女児後半群は8.44%（2.54, 22.7）、9.25%（3.38, 27.32)であり、これら

についても、それぞれ有意差を認めなかった（$p < 0.0001$）。さらに two-way ANOVA 法を用いて解析を行ったところ、妊娠期間に関しては、前半よりも後半の方が有意差を持って胎動占有割合が減少しており、性差に関しては有意差を認めなかった。

考　察

FMAM recorder は長時間の胎動の測定が可能であった。そのため、胎児の睡眠・覚醒のサイクルによる胎動占有割合の補正は、必要なかった。Ten Hof らは、60 分間の超音波検査を行い、胎動の評価している。この研究結果でも妊娠週数の経過とともに胎動が減少することが報告されている。これは今回の研究結果と非常に近いものであった。胎動は、胎児の well-being を評価するのに重要であることが知られており、現在広く用いられている Biophysical profiling score（BPS）の項目にも胎動と関連するものが含まれている。さらに近年、Kurjak らや、Morokuma らの報告によって、胎児の運動が神経学的発達と関連していることが認識されている。これらの報告から、今回の結果は、胎児の well-being を評価する際には男女について同様の評価を行うべきであることを示唆している。さらに、妊娠週数の経過とともに胎動が減少することは、胎児の神経学的な発達を示している可能性があると考えられた。しかし、これらは正常例に関する報告である。Paolozza らは胎児のアルコールスペクトル障害について、男児と女児で眼球運動が異なるパターンを示すことを報告している。他にも、男児の方が脳性麻痺の発症頻度が高いことは一般的にも知られている。このことからわかるように男児と女児の神経学的発達については複数の側面があり、今後のさらなる研究が必要であると考えられた。

結　論

FMAM recorder を用いて、長時間の胎動の測定が可能であった。胎動は、胎児の well-being のみならず、胎児の神経系の発達とも関連していることが知られている。今回の研究によって、正常例においては胎動に性差がなく、妊娠週数の経過とともに胎動が減少することが示された。今後、異常例を含めた胎動の性差についても更なる研究が必要であると考えられた。

Comparison of fetal gross movements between male and female fetuses with the use of a fetal movement acceleration measurement recorder

- An exploratory study-

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Abstract

Background: To investigate whether fetal gross movement counting differs between male and female fetuses by using a fetal movement acceleration measurement recorder. Methods: Fetal movements of thirty pregnant women were recorded after 28 weeks gestation. All data were divided into 10-s epochs. An epoch was judged positive for movements (a positive epoch) when maternal abdominal wall oscillations were detected within the epoch. The proportion of positive epochs to all epochs each night was calculated and compared between boys and girls. Moreover, gestational age was divided into earlier (28–33 weeks) and later periods (34–39 weeks), and comparisons were made for both periods. Results: A total of 205 recordings was obtained. The median proportion of positive epochs (minimum, maximum) was 13.75% (2.54, 33.11) in boys and 12.72% (3.38, 35.96) in girls, with no difference ($p = 0.6879$). The proportion in the earlier period for boys and girls was 17.99% (6.96, 33.11) and 16.76% (4.16, 35.96) respectively, and 8.44% (2.54, 22.7) and 9.25% (3.38, 27.32) for the later period with no difference in either period ($p = 0.4123$ and $p = 0.5421$, respectively). Conclusions: There were no differences in gross fetal movements after 28 gestational weeks between boys and girls.

Key words: fetal gross movements, FMAM recorder, fetal movement acceleration measurement recorder, neurological development, sex difference.

Introduction

It is well known that there are neurological differences during development between males and females. As for fetuses, however, little is known about developmental differences between the sexes. There have been few studies reporting differences of fetal gross movements between male and female fetuses, and results have been conflicting. Ten Hof et al. [1)] showed that with advancing gestation, female fetuses moved more than male fetuses. On the contrary, Di Pietro et al. [2)]found male fetuses to be more active than female fetuses at 38-39 weeks. However, they failed to replicate these results in a subsequent study.

Medina PGR et al. [3)] observed fetal gross movements in 123 normal fetuses, over 60 min, at 15-17 and 27–28 weeks of gestation, and over 2 h at 37–39 weeks by ultrasonography. The preliminary results showed that male fetuses had a higher movement incidence than female fetuses at 37–38 weeks. However, the difference tended to disappear with adjustment for the effect of the fetal wakefulness cycle, and the conclusion was that there was no evidence of any sex-related difference in fetal gross movements. They emphasized the importance of this adjustment in the discussion.

Fetuses do not move constantly. It is well known that the fetal wakefulness cycle develops as pregnancy progresses. Fetuses move depending on this cycle, especially at later gestational stages. Therefore, observing fetal movements for short periods is insufficient for precise assessment if the observing period is less than the cycle. Ultrasonography is not suitable to assess fetal movements over many hours in many cases not only from practical viewpoint but from safety concerns of bioeffects. There is no report of fetal movement differences between boys and girls by observing for many hours.

There were no practical and objective methods to allow for long-duration fetal movement counting; however, we have been developing a fetal movement acceleration measurement recorder (FMAM recorder) to count gross fetal movements [4-7]. The recorder is non-invasive. Today, FMAM recorder has made it possible to count gross fetal movements for hours at home.

The purpose of the study was to compare exploratorily whether fetal gross movement counting with the use of the FMAM recorder differs between male and female fetuses.

Methods

Subjects

A total of thirty singleton pregnant women who undertook prenatal care at Teikyo University Hospital from June 2008 to July 2015 were recruited for this study. There were 15 male fetuses and 15 female fetuses. Table I shows the characteristics of the pregnant women. Twenty-two women were nulliparous, and 8 women were multiparous. There were no maternal complications in any of the pregnancies or the deliveries. Twenty-three women underwent vaginal delivery, and seven women underwent cesarean delivery. All the newborns were delivered at full-term without anomalies or neurological problems, and their weights were appropriate for full-term births. There were no differences in the maternal or fetal characteristics in relation to fetal sex.

FMAM recorder

Figure 1 shows the FMAM recorder. The recorder has been described in detail elsewhere [4, 5]. The FMAM recorder has two acceleration sensors. In principle, the sensor detects acceleration caused by body movements. One sensor is a fetal movement sensor (FM sensor) that is attached to the mother's abdomen, while the other is a maternal movement sensor (MM sensor) attached to the mother's thigh (Figure 1). Both the sensors are similar in structure, and the sensitivity of the FM and MM sensors was set at 700 mV/0.1 G and 120 mV/0.1 G, respectively. When the FM sensor detects abdominal wall oscillations but the MM sensor does not detect any maternal movement, fetal movements are judged to have occurred. The recorder weighs 290 g, and is a handy, non-invasive device.

Fetal movement counting

Fetal movements were recorded by the mothers themselves at home. Each mother was asked to record fetal movements weekly from 28 weeks to term, as a previous study [4] has shown the recorder to be accurate after 28 weeks. Just before sleeping, the FM sensor was attached to the abdomen and the MM sensor to the thigh, and gross fetal movements were recorded overnight. All data were recorded in a secure digital card. The mothers brought the card to their hospital check-ups, and the data was transferred to a computer.

Data Analysis

We used data from recordings that lasted at least 4 h per night. All the data were analyzed mainly by using our computer analysis program, which has been described in detail elsewhere [4]. However, the program has not yet been completed, and minor errors in the computer analysis were revised by manual procedures. The recordings were divided into 10-second epochs (360 epochs per hour). All epochs were reviewed for gross movements. An epoch was judged to be positive for fetal gross movements (positive epoch) when the FM sensor detected abdominal wall oscillations and the MM sensor did not detect any maternal movements. The proportion of positive epochs to all epochs during one night was calculated. We divided the calculated data into boys and girls groups and examined correlation coefficients of the data to gestational age. Furthermore, gestational age was divided into early (28–33 weeks) and late periods (34–39 weeks), and the proportions were compared for both periods. Comparisons were made using the Wilcoxon method, and significant difference was set at $p < 0.05$. On top of that, we compared the proportions of positive epochs among the four groups divided by sex and gestational age differences using by the two-way ANOVA. All the mothers gave written informed consent, and this study was approved by the ethics committee at Teikyo University.

Results

We obtained a total of 205 recordings that lasted more than 4 h. There were 99 recordings for male fetuses (42 early, 57 late), and 106 recordings for females (54 and 52). Figure 2, 3 show scatter plots of the proportions of positive epochs respectively in boys and girls depending on gestational age. There were negative correlations both in boys and girls groups (-0.545 for male, and -0.456 for female). Figure 4-A shows the box plots of positive epoch proportions from 28 weeks to term. The medians (minimum, maximum) of the proportions were 13.75% (2.54, 33.11) in male fetuses and 12.72% (3.38, 35.96) in females, with no significant difference found ($p = 0.6879$). Figure 4-B compares medians at 28-33 weeks and 34-39 weeks. The proportions of positive epochs in the earlier period were 17.99% (6.96, 33.11) in males, and 16.76% (4.16, 35.96) in females, and 8.44% (2.54, 22.7) and 9.25% (3.38, 27.32), respectively, in the later period. The proportions in the early period were higher than those in the later period both in males ($p < 0.0001$) and females ($p < 0.0001$); however, there were no significant differences between boys and girls within each period ($p = 0.4123$, $p = 0.5421$). The comparison among the four groups by two-way ANOVA also showed statistical difference in gestational week between early group and late group (d. f. = 64.320, F = 1, $p < 0.0001$), but not between sexes (d. f. = 0.0832, F = 1, $p = 0.773$), and no interaction was detected between feeding sex and gestational age differences (d. f. = 0.9174, F= 1, p = 0.3393), similarly.

Discussion

The FMAM recorder made it easy to count fetal gross movement over many hours, which were sufficiently long when compared with the fetal wakefulness cycle; therefore, we did not need the cycle adjustment. We could count gross fetal movements directly for hours, and showed the proportions of epochs with fetal movements in the early gestational period were higher than those in the later period both in male and female fetuses, however; there were no differences between the sexes at earlier or later gestational ages.

Regarding the fetal gross movement changes during pregnancy, Ten Hof J et al. [8)] observed fetal movements with ultrasonography during 60 min biweekly from 24 to 36 weeks and during 120 min weekly after 36 weeks of gestation in 29 normal fetuses. They indicated that the median percentage incidence of fetal gross movements decreased from 17% at 24 weeks to about 7% near term. The pattern of these changes in their study was similar to that of this study. The incidence decline in fetal movements was thought to be caused by fetal neurological developments such as establishment of behavior state.

As for sexual difference, there were no differences in gross fetal movements after 28 weeks of gestation between male and female. Fetal movements have been recognized as important to estimate fetal well-being. It has been accepted worldwide that fetal heart rate accelerations combined with fetal movements are important signs for well-being in non stress test, and that fetal gross movements are one of the ultrasonographic indices in the biophysical profiling score to assess fetal well-being. Furthermore, fetal movements are counted by the mother themselves to reduce fetal death in some medical situations, though there has been no agreement as to whether this improves perinatal outcomes. Our results suggest that the above-mentioned methods for assessing fetal well-being do not need to consider gender differences.

On the other hand, it is well known that there are neurological differences during development between males and females. Voigt J et al. [11)] examined the weight of the brain in 0-18 year-old boys and girls, and showed that brains of girls were a little lighter than those of boys, even after adjusting for their physical differences. Allen LS et al. [12)] examined the human corpus callosum using MRI (magnetic resonance imaging), and showed that there were differences in its shape between adult men and women. The posterior region of the corpus callosum was more bulbous shaped in females and more tubular-shaped in males. Benbow CP et al. [13)] studied the mathematical reasoning ability of boys and girls for over twenty years. They showed that the standard deviation of ability was about 1.5-times larger in boys than in girls, and the ability of females was more balanced and narrowly focused.

As for fetuses, however, little is known about neurological differences between the sexes. There are differences in the hormonal environments between male and female fetuses, and this may affect neurological development. JM Reinisch et al. [14)] examined the effect of synthetic progestins with androgenic action - fetuses exposed to the drug showed a significantly higher potential for physical aggression than unexposed fetuses.

Recently, it has been recognized that fetal movements indicate neurological development. Kurjak et al. [9)] suggested a new scoring system for fetal movements by 3D/4D ultrasonography that may help in detecting fetal brain and neurodevelopmental alterations due to in-utero brain impairment. Morokuma et al. [10)] devised a brief ultrasound examination as an antenatal behavior-screening test that may make it possible to assess fetal brain function.

Consequently, we thought comparing movements between male and female fetuses might be useful to understand neurological differences during development between the two.

We compared fetal gross movements between boys and girls in the absence of complications; however, little is known about other behavior-related movements.

Hepper PG et al. [15] observed mouth movements in 39 normal fetuses, over 60 min, at 16, 18, and 20 weeks by ultrasonography, and showed that these increased with advancing gestational age, and females were found to move their mouths more than males.

On another angle, there may be complication-related behavioral differences between male and female fetuses from a pathological perspective. Paolozza A et al. [16] examined the accuracy and characteristics of saccadic eye movements in children with fetal alcohol spectrum disorder, and concluded that prenatal alcohol exposure had a sexually dimorphic impact on eye movement control, with males and females exhibiting different patterns of deficit. On top of that, it is known that male gender is a risk factor for cerebral palsy [17]. The developmental differences between male and female fetuses must have multiple aspects and further study is needed to understand these differences.

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Disclosure

The authors declare no conflict of interest.

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Figure legends

Figure 1

The FMAM recorder with two acceleration sensors. One sensor is a fetal movement sensor that is attached to the mother’s abdomen, while the other is a maternal movement sensor attached to the mother’s thigh.

Figure 2

A scatter plot showing individual proportions of positive epochs depending on gestational age for female.

Figure 3

A scatter plot showing individual proportions of positive epochs depending on gestational age for female for male.

Figure 4

A box plot showing the proportion of positive epochs for male and female fetuses.

A: Total period (28–39 weeks)

B: Earlier (28-33 weeks) and later period (34–39 weeks)

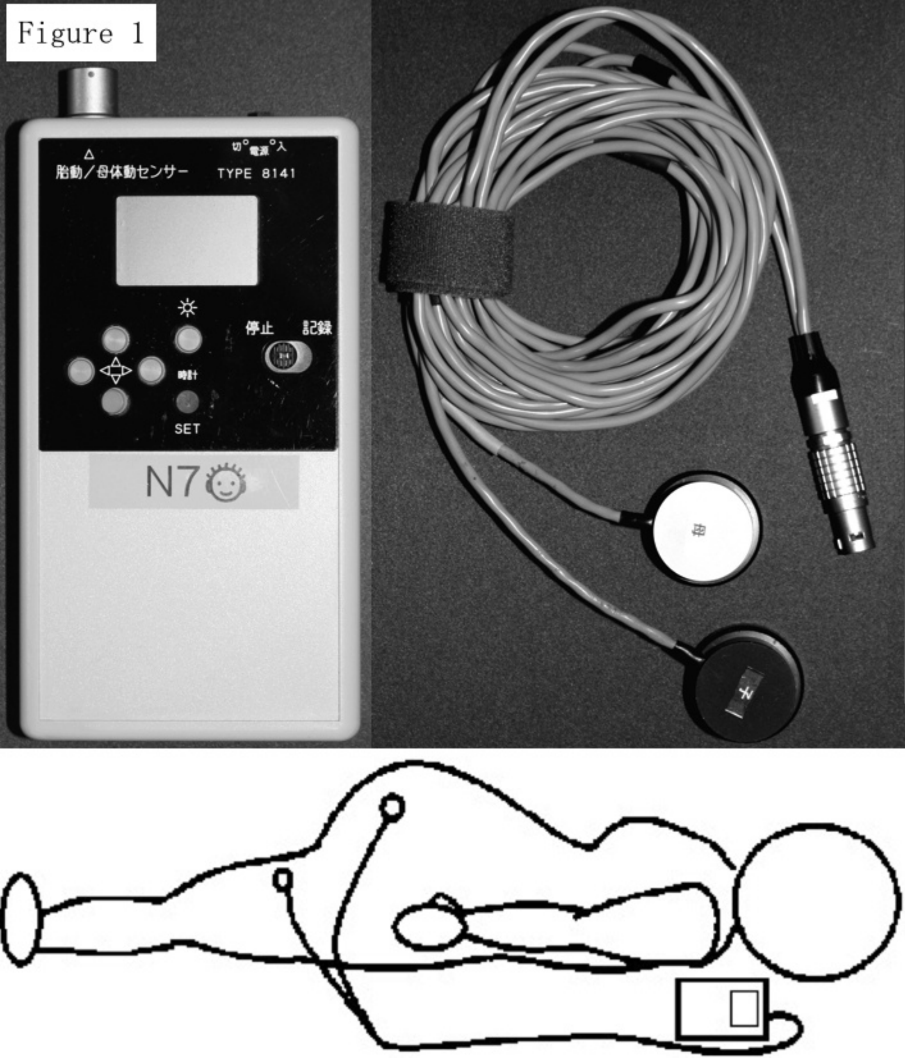
Table 1. Characteristics of the pregnant women and the newborns.

		Male (n = 15)	female (n = 15)	p-value
Characteristics of the mothers	Age	33.3（5.3）	33.4（4.9）	0.9716
	Nulliparaous	12	10	
	Multiparous	3	5	
	Height(cm)	158.6（3.2）	158（6.0）	0.7351
	Body weight (kg)	51.173（5.4）	52.7（8.9）	0.5818
	BMI	20.3（2.2）	21.0（2.8）	0.4675
Characteristics of the newborns	Gestational age at delivery (weeks and days)	39w1d（8d）	39w1d（8d）	0.9997
	Vaginal delivery	12	11	
	Cesarean delivery	3	4	
	Body weight (g)	3021.3（316.5）	3087.7（344.0）	0.5903
	UApH	7.285（0.056）	7.284（0.061）	0.9639
	Umbilical length(cm)	54.8（6.0）	56.8（15.1）	0.6439

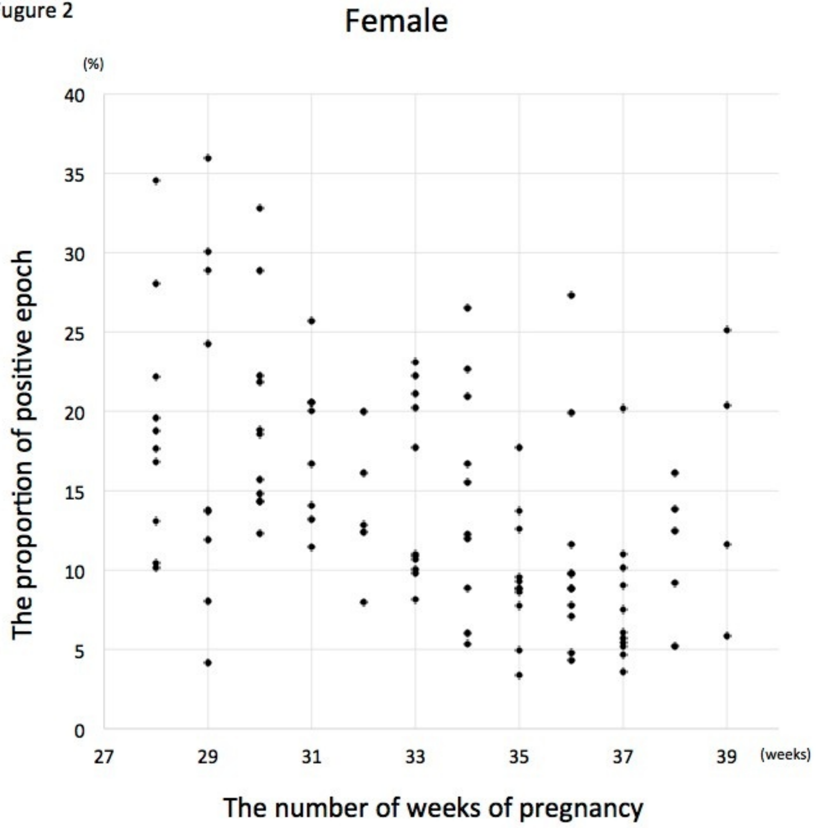
Data are presented as mean (S.D.)

*The comparisons between the two groups were done by student-*t* test and chi-square test.

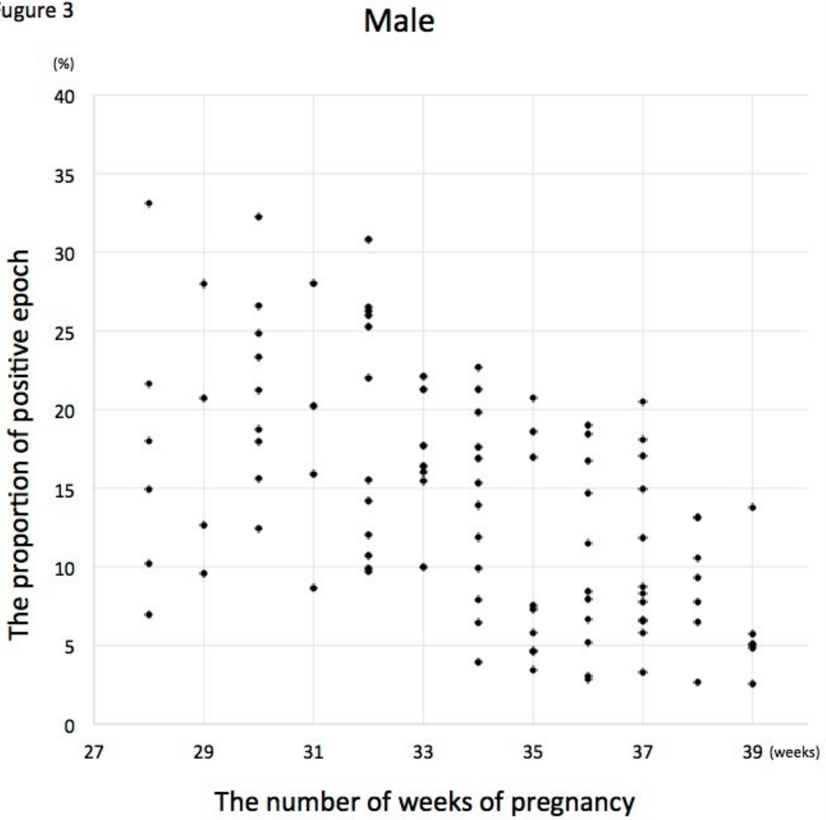
Figure 1



Fugure 2

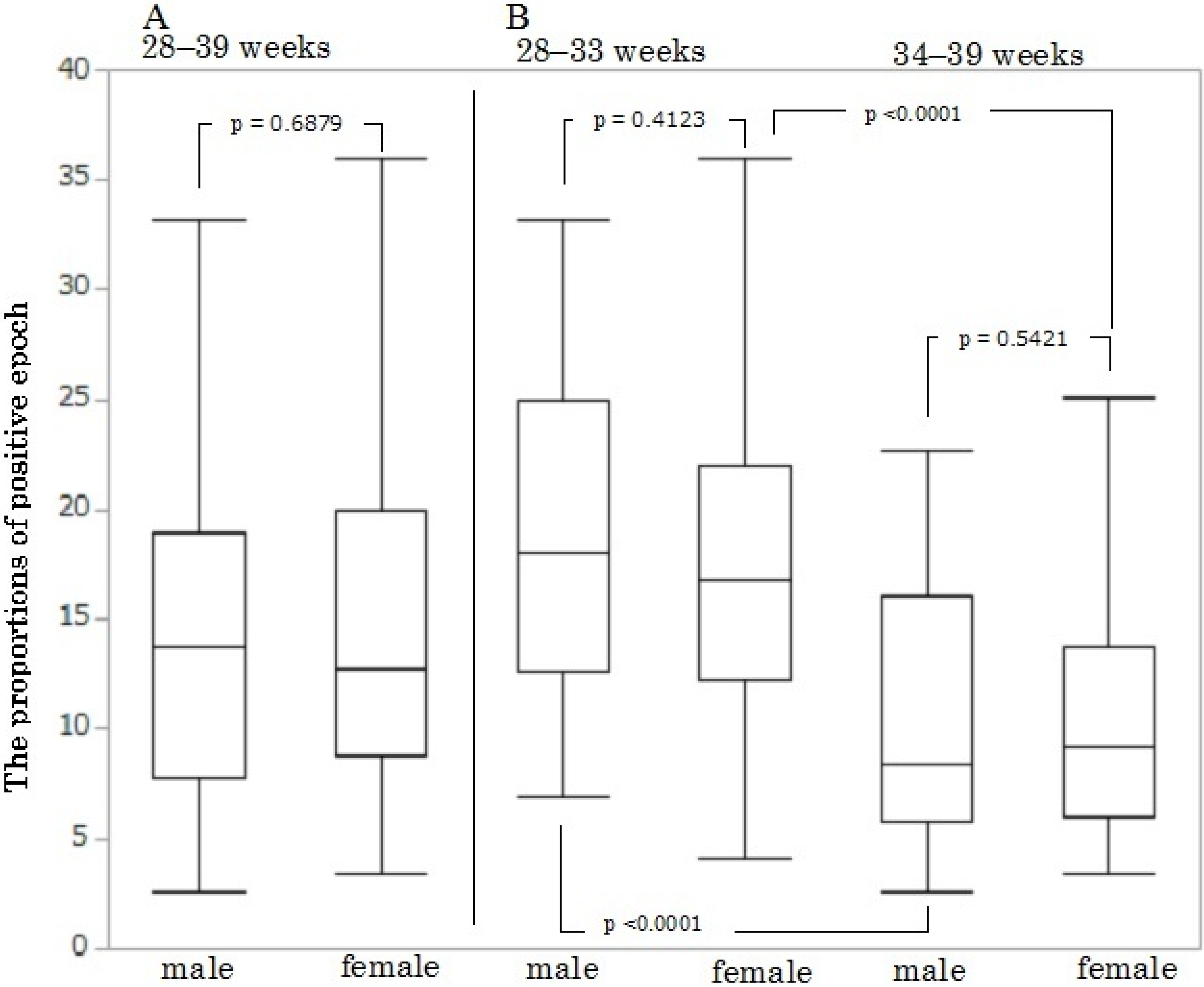

Female
(%)
40
35
30
25
20
15
10
5
0
The proportion of positive epoch
27
29
31
33
35
37
39
(weeks)
The number of weeks of pregnancy

Fugure 3



Male
(%)
40
35
30
25
20
15
10
5
0
The proportion of positive epoch
27
29
31
33
35
37
39 (weeks)
The number of weeks of pregnancy

Figure 4



A
28–39 weeks
B
28–33 weeks
34–39 weeks
p = 0.6879
p = 0.4123
p <0.0001
p = 0.5421
p <0.0001
The proportions of positive epoch
40
35
30
25
20
15
10
5
0
male
female
male
female
male
female