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学位論文

Fetal facial expressions in small-for-gestational-age and growth-restricted fetuses

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ORIGINAL ARTICLE

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Fetal facial expressions in small-for-gestational-age and growth-restricted fetuses

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ABSTRACT

Objective: To evaluate the frequencies of fetal facial expressions among appropriate-for-gestational-age (AGA), small-for-gestational-age (SGA), and growth-restricted (FGR) fetuses.

Methods: Four-dimensional (4D) ultrasound was used to examine the facial expressions of 50 AGA, 25 SGA, and six FGR fetuses between 28 and 35 weeks of gestation. The frequencies of seven facial expressions during 15-minute recordings were assessed. Comparison of facial expressions among the three groups was performed.

Results: Mouthing was the commonest facial expression at 28–35 weeks, and the frequency of mouthing was significantly higher than those of the other six facial expressions in AGA fetuses. Mouthing was the most frequent facial expression, but there was no significant difference in the frequency among mouthing, smiling and blinking in SGA fetuses. Moreover, mouthing displayed a significantly higher frequency than the other facial expressions, except for yawning, smiling, and blinking in FGR fetuses. However, there was no significant difference in the frequency of each facial expression among the three groups.

Conclusions: Our results suggest that the frequencies of fetal facial expressions are not decreased in either SGA or FGR pregnancies. The absence of a decrease in the frequency of each fetal expression in FGR fetuses may be due to increased brain blood flow because of the brain-sparing effect. Moreover, accelerated maturation and development of the brain function, especially the central dopamine system, might be suspected in SGA and FGR fetuses.

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4D ultrasound; fetal facial expression; AGA fetus; SGA fetus; FGR

Introduction

Fetuses with birth weights below the 10th percentile are usually defined as small-for-gestational age (SGA) infants [1]. However, SGA infants grow appropriately due to the intrinsic growth potential of each fetus [2,3], and usually show good perinatal outcomes [4]. Fetal growth restriction (FGR) is usually caused by the insufficient maternal–fetal exchange of respiratory gases, nutrients, and waste via the placenta, with limitation of fetal nutrition, oxygenation, or both [5]. FGR is clinically defined by the estimated fetal weight (EFW) below the 10th percentile for the standard growth curve, with a decreased middle cerebral artery pulsatility index (MCAPI), increased umbilical artery pulsatility index (UAPI), and/or decreased amniotic fluid index (AFI) [6]. Therefore, these differences in fetal nutrition and/or oxygenation between SGA and FGR may affect the fetal behavior, especially fetal facial expressions, because fetal behavior and facial expressions are thought to be indicators of the fetal brain function and development [7,8].

There have been several studies on conventional two-dimensional (2D) sonographic assessment of fetal behavior in FGR pregnancies [5,9–11]. However, these results are inconsistent. In uncomplicated FGR, the quantity and quality of general movements were the same as those in normal fetuses [10,11]. No difference in the quantity of general movements was noted between complicated FGR and normal fetuses [11]. Meanwhile, Bekedam et al. [9] reported that reductions in fetal movements were marked in FGR fetuses.

There is one major limitation of 2D sonographic assessment of fetal movements: fetal behavior outside the scanning plane cannot be displayed on the monitor because of the 2D character of conventional real-time ultrasound [12]. With the recent advent of four-dimensional (4D) ultrasound, fetal movements, behaviors, and facial expressions can be easily and readily

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assessed [7,8]. To the best of our knowledge, there has been only one report on 4D ultrasound assessment of fetal behavior in FGR fetuses [13]. In that study, a tendency for FGR fetuses to show lower-level behavioral activity than normal fetuses in all observed movement patterns was noted. However, the definition of FGR (abnormal 2D sonographic fetal biometry or abnormal 2D Doppler ultrasound measurements) is unclear. The aim of the present study was to evaluate the frequencies of fetal facial expressions among appropriate-for-gestational-age (AGA), SGA, and FGR fetuses using 4D ultrasound, and to assess whether the frequencies of facial expressions are decreased in SGA and FGR fetuses.

Materials and methods

Eighty-one pregnant Japanese women at 28–35 weeks' gestation who were scheduled to undergo routine ultrasound examinations between December 2013 and December 2016 were asked to take part in a 15-minute 4D ultrasound examinations of fetal facial expression cross-sectionally. The subjects were randomly recruited from the outpatient department and obstetric ward of Kagawa University Hospital. This study was approved by the ethics committee of Kagawa University Graduate School of Medicine, and all women gave standardized informed consent.

Four-dimensional ultrasound was used to examine the facial expressions of 50 AGA, 25 SGA, and 6 FGR fetuses between 28 and 35 weeks of gestation. AGA was defined based on EFW and the actual birth weights between the 10th and 90th percentiles, and SGA based on EFW and actual birth weights being under the 10th percentile of the standard Japanese growth curve [14,15]. FGR was defined as SGA with decreased MCAPI, increased UAPI, and/or decreased AFI [6]. All pregnancies were only examined once. None of the women were smokers or had any complicating diseases. Only singleton-pregnancy women were included in the study. Based on the first day of the last menstrual period, gestational ages were estimated. First-trimester or early second-trimester ultrasound examinations were performed to confirm these estimates. No neonate was found to have congenital anomalies, genetic disorders, or neurological disorders.

A Voluson E8 (GE Healthcare Japan, Tokyo, Japan) with 1–4-MHz transabdominal transducer was used for all 4D ultrasound examinations. Two experienced examiners (N.M. and M.A.M.A.) conducted all 4D ultrasound examinations. The device was switched to its 4D setting following a 2D examination. The transducer was set so that sagittal sections of the fetal face involving the forehead, nose, and mouth could be obtained. Images were obtained in the region of interest (ROI): a volume box, with parameters determined by the examiner, was superimposed over the 2D image, and a three-dimensional (3D) image corresponding to it was subsequently reconstructed. At a rate of 40 times per second (maximum), the crystal array of the transducer was automatically passed over the ROI with the generated 4D images shown on a monitor. All examinations were conducted over a total period of 15 minutes, and recorded on a USB. When inactive, we waited until the fetus became active. However, we did not apply any mechanical or acoustic stimulation during image acquisition. When the fetal face could not be visualized due to fetal movements, we did not include this time for analysis. A quiet temperature-controlled room was used for all examinations, performed in the morning.

As previously reported [16–18], on observing the USB recordings, seven types of facial expression (blinking, mouthing, yawning, smiling, tongue expulsion, scowling, and sucking) were examined. Good intra- and interclass correlation coefficients and intra- and interobserver agreements were confirmed in the previous investigation [19]. In the prior studies, each facial expression was described in detail [16–18]. The category of "mouthing movement" did not include other mouth movements such as yawning, smiling, tongue expulsion, scowling, or sucking. N.M., who has considerable experience in this area, assessed the frequency of each fetal facial expression, with the results presented as the median and ranges. Differences in the maternal age, gestational age at examination, EFW at examination, MCAPI value, UAPI value, AFI value, gestational age at birth, birth weight, umbilical artery pH (UApH), and placental weight were assessed by analysis of variance. The incidence of mechanical delivery, sex ratio, incidence of neonatal intensive care unit (NICU) admission, and incidence of pregnancy-induced hypertension (PIH) among the three gestational age groups was compared using the chi-square test. Differences in Apgar scores were investigated with the Kruskal–Wallis one-way analysis of variance. The frequencies of the facial expressions at 28–35 weeks of gestation were compared using the Kruskal–Wallis one-way analysis of variance by ranks and multiple comparisons in AGA, SGA, and FGR fetuses, respectively. Each facial expression frequency was compared using the Kruskal–Wallis one-way analysis of variance by ranks among AGA, SGA, and FGR fetuses, respectively. The statistical software SPSS, version 21, for Windows (SPSS Inc, Chicago, IL) was used for all calculations, with p-values of $< .05$ being significant.

Results

The clinical characteristics of the subjects are shown in Table 1. EFW at examination in FGR fetuses was significantly lower than those in AGA and SGA fetuses. MCAPI in FGR fetuses was significantly lower than that in AGA fetuses. UAPI in FGR fetuses was significantly higher than those in AGA and SGA fetuses. The gestational age at birth in FGR fetuses was significantly earlier than those in AGA and SGA fetuses. The time-interval until delivery in FGR fetuses was significantly shorter than those in AGA and SGA fetuses. The incidence of mechanical delivery in FGR fetuses was significantly higher than that in AGA fetuses. The birth weight in FGR fetuses was significantly lower than those in AGA and SGA fetuses, and that in SGA fetuses was lower than that in AGA fetuses. The Apgar score at 1 min in FGR fetuses was significantly lower than that in AGA fetuses. The placental weight in FGR fetuses was significantly lower than those in AGA and SGA fetuses, and that in SGA fetuses was lower than that in AGA fetuses. The incidence of NICU admission in FGR fetuses was significantly higher than those in AGA and SGA fetuses, and that in SGA fetuses was higher than that in AGA fetuses. The incidence of PIH in FGR fetuses was significantly higher than those in AGA and SGA fetuses, and that in SGA fetuses was higher than that in AGA fetuses. However, there were no significant differences in the maternal age, gestational age at examination, AFI, sex difference, Apgar score at 5 min, or UApH among the three groups.

The frequencies of the facial expressions in AGA, SGA, and FGR fetuses at 28–35 weeks of gestation are shown in Table 2. Mouthing was the commonest facial expression at 28–35 weeks, and the frequency of mouthing was significantly higher than those of the other six facial expressions in AGA fetuses (Figure 1). In AGA fetuses, the frequency of smiling was significantly higher than that of tongue expulsion (Figure 1). Mouthing was the most frequent facial expression, but there was no significant difference in the frequencies of mouthing, smiling, and blinking in SGA fetuses (Figure 2). Moreover, mouthing displayed a significantly higher frequency than the other facial expressions, except for yawning, smiling, and blinking, in

Table 1. Clinical characteristics of subjects.

Subject	*n*	Maternal age (y.o.) Mean (SD)	Gestational age at examination (weeks) Mean (SD)	EFW at examination (g) Mean (SD)	MCAPI Mean (SD)	UAPI Mean (SD)	AFI (cm) Mean (SD)	Gestational age at birth (weeks) Mean (SD)	Time-interval until delivery (weeks) Median (range)
AGA	50	30.8 (5.26)	32.5 (2.2)	1954 (420)^{a,b}	1.79 (0.36)^{c}	0.95 (0.16)^{d}	13.6 (4.8)	39.6 (1.4)^{f,g}	6.64 (1.1–12.3)^{i}
SGA	25	30.6 (5.88)	32.6 (2.44)	1585.9 (438.05)^{a}	1.70 (0.42)	1.00 (0.19)^{e}	11.35 (3.6)	38.47 (1.9)^{f,h}	5.57 (0.7–11)^{j}
FGR	6	31.5 (8.19)	31.9 (3.02)	1262.8 (444.2)^{b}	1.31 (0.2)^{c}	1.32 (0.4)^{d,e}	9.48 (4.0)	34.6 (3.4)^{g,h}	1.22 (0.1–11.4)^{i,j}
Significance		NS	NS	a–a, $p < .005$ b–b, $p < .005$	c–c, $p < .05$	d–d, $p < .001$ e–e, $p < .005$	NS	f–f, $p < .05$ g–g, $p < .001$ h–h, $p < .001$	i–i, $p < .005$ j–j, $p < .05$

Subject	Mechanical delivery (%)	Birth weight (g) Mean (SD)	Sex (male/female)	Apgar score 1 min Median (range)	Apgar score 5 min Median (range)	UApH Mean (SD)	Placental weight (g) Mean (SD)	NICU admission (%)	PIH (%)
AGA	22^{k}	3063.9 (406)^{l,m}	24/26	8 (5–9)^{o}	9 (8–10)	7.29 (0.07)	597.7 (131.6)^{p,q}	2^{s,t}	2^{v,w}
SGA	40	2192.5 (384.8)^{l,n}	9/16	8 (4–9)	9 (8–10)	7.28 (0.08)	453.9 (87.5)^{p,r}	40^{s,u}	28^{v}
FGR	66^{k}	1464.5 (485.4)^{m,n}	2/4	7.5 (5–8)^{o}	9 (7–9)	7.27 (0.08)	328 (85.3)^{q,r}	100^{t,u}	50^{w}
Significance	k–k, $p < .05$	l–l, $p < .001$ m–m, $p < .001$ n–n, $p < .001$	NS	o–o, $p < .05$	NS	NS	p–p, $p < .001$ q–q, $p < .001$ r–r, $p < .001$	s–s, $p < .001$ t–t, $p < .001$ u–u, $p < .01$	v–v, $p < .001$ w–w, $p < .001$

y.o: years old; SD: standard deviation; EFW: estimated fetal weight; MCAPI: middle cerebral artery pulsatility index; UAPI: umbilical artery pulsatility index; UApH: umbilical artery blood pH; AFI: amniotic fluid index; NICU: neonatal intensive care unit; PIH: pregnancy-induced hypertension; AGA: appropriate-for-gestational-age-fetus; SGA: small-for-gestational-age fetus; FGR: fetal growth restriction; NS: not significant.

Table 2. Frequency of fetal facial expressions among appropriate-for-gestational age, small-for-gestational age, and growth-restricted fetuses.

		Median (range)						
Subjects	*n*	Mouthing	Yawning	Smiling	Tongue expulsion	Scowling	Sucking	Blinking
AGA	50	3 (0–14)	0 (0–7)	1 (0–5)	0 (0–3)	0 (0–7)	0 (0–3)	0.5 (0–7)
SGA	25	2 (0–9)	0 (0–6)	1 (0–5)	0 (0–2)	0 (0–5)	0 (0–2)	0 (0–11)
FGR	6	3 (0–6)	1.5 (0–2)	0 (0–2)	0 (0–1)	0 (0–0)	0 (0–2)	0.5 (0–3)
Significance		NS	NS	NS	NS	NS	NS	NS

AGA: appropriate-for-gestational-age fetus; SGA: small-for-gestational-age fetus; FGR: fetal growth restriction; NS: not significant.

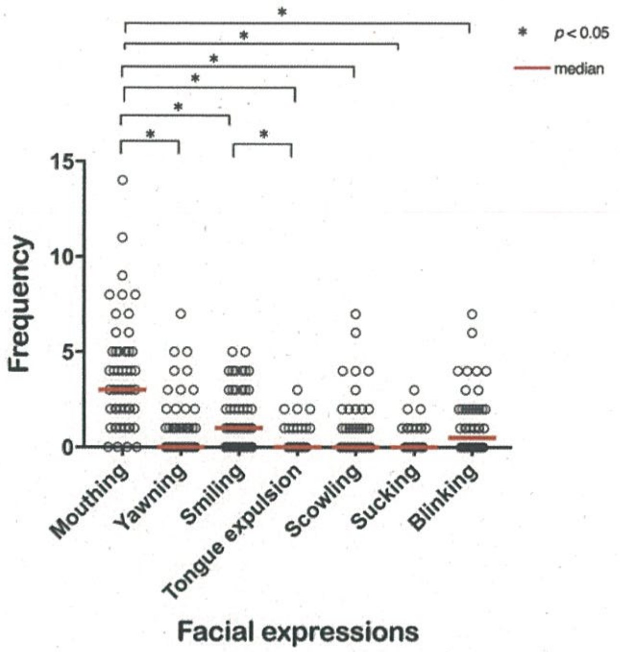

Figure 1. Comparison of the frequencies of fetal facial expressions in appropriate-for-gestational age fetuses at 28–35 weeks of gestation.

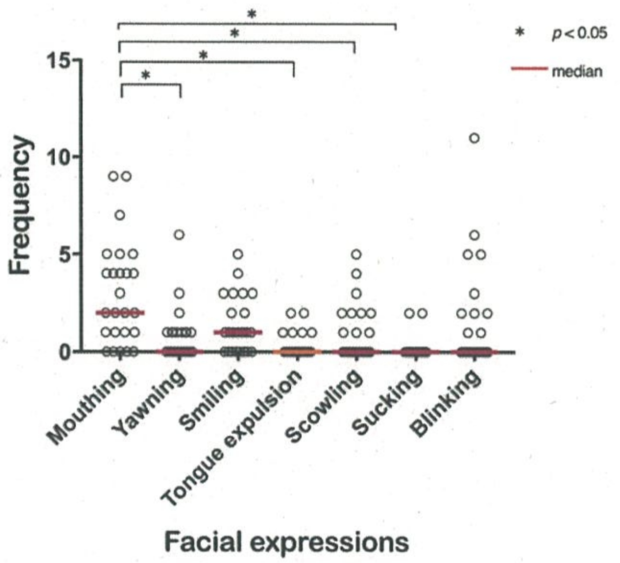

Figure 2. Comparison of the frequencies of fetal facial expressions in small-for-gestational age fetuses at 28–35 weeks of gestation.

FGR fetuses (Figure 3). However, there was no significant difference in the frequency of each facial expression among the three groups (Figure 4).

Discussion

In our previous investigation involving the 4D ultrasound assessment of seven fetal facial expressions in normal fetuses at 28–34 weeks of gestation, mouthing was significantly more frequent than any other facial expressions, but there were no significant differences in the other six facial expressions [16]. In the present study, the frequency of mouthing was also significantly higher than those of the other six facial expressions in AGA fetuses. Moreover, the frequency of smiling was significantly higher than that of tongue expulsion. The reason for the difference of fetal facial expressions between our previous report [16] and the present study is currently unknown. One possible explanation may be the difference in number of subjects studied (previous study: 10, and present study: 50 fetuses). Another possible explanation is the different devices used in the previous and present studies. The device used in the previous study is capable of capturing up to 25 frames per second depending on the defined angle range [16], whereas that used in the present study captures up to 40 frames per second (maximum). One further possible explanation may be the difference of observers between these two investigations. With respect to intra- and interobserver reproducibility for 4D ultrasound assessments of fetal facial expressions, good intra- and interobserver agreements were noted [19]. However, low-level interobserver variability may still remain because of the subjective judgment methods used by the examiners to assess the fetal expressions observed using 4D ultrasound.

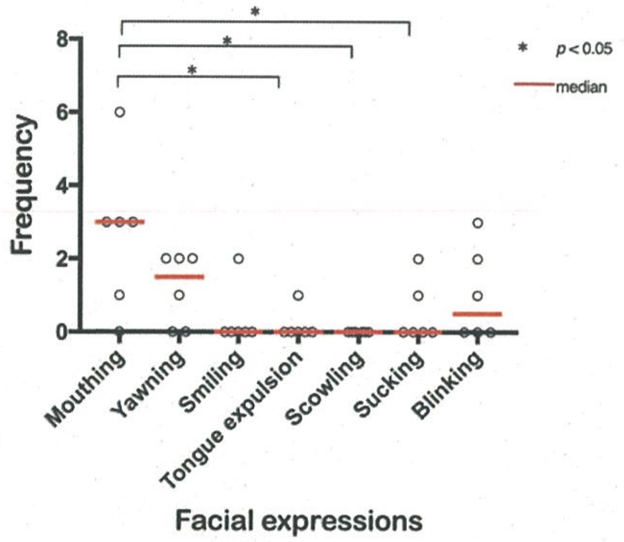

Figure 3. Comparison of the frequencies of fetal facial expressions in growth-restricted fetuses at 28–35 weeks of gestation.

With respect to the frequency pattern of fetal facial expression in SGA and FGR fetuses, mouthing was the most frequent facial expression, the same as in AGA fetuses. However, there was no significant difference in the frequency between mouthing and blinking in SGA or FGR fetuses, although the frequency of mouthing

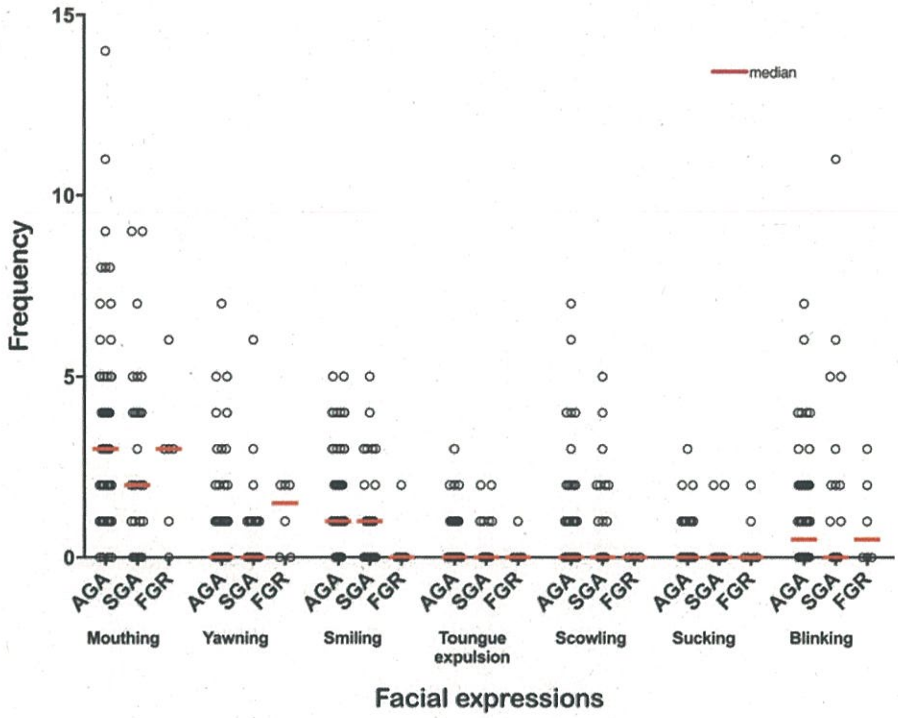

Figure 4. Comparison of the frequencies of each fetal facial expression among appropriate-for-gestational age, small-for-gestational age, and growth-restricted fetuses at 28–35 weeks of gestation.

was significantly higher than that of blinking in AGA fetuses. The increased frequency of fetal mouthing in the third trimester might indicate fetal neurological maturation [20], and fetal mouthing movements were absent in cases with fetal compromise [21]. Fetal blinking is also thought to be an important parameter of fetal brain functional development [8]. The brain function regulates the spontaneous blinking rate [22,23], and an increased spontaneous blinking rate is likely to be related to central dopamine system maturation [24,25]. Blinking occurs regularly during neonatal adaptation, and frequent blinking suggests neurological well-being [26]. It has been suggested that chronically stressed human fetuses with PIH and FGR show accelerated neurological development [27–29]. Therefore, the lack of a significant difference in the frequency between mouthing and blinking in SGA and FGR fetuses suggests the accelerated maturation and development of the brain function, especially the central dopamine system. However, the data and interpretation should be considered with some degree of caution because of the small number of subjects studied. Further studies involving a larger sample size are needed to confirm the neurodevelopmental maturation and brain function in SGA and FGR fetuses.

There has been one report on the conventional 2D sonographic evaluation of fetal yawning in SGA fetuses [30]. In this study, there was no significant difference in yawning patterns between normal and SGA fetuses. There were also no significant differences in the frequency of yawning among AGA, SGA, and FGR fetuses. Coordination between the brain stem and peripheral neuromuscular function regulates yawning [31]. "The frequency change of fetal yawning with advancing gestation suggests developmental stages of brain maturation and function with the rhythmic control of sleep and wake times" [8]. Therefore, these results may indicate that there is no difference in the rate of development of the brain stem and peripheral neuromuscular function among AGA, SGA, and FGR fetuses, maintaining their coordination.

There has been only one study on 4D ultrasound evaluation of fetal facial expressions such as mouthing, yawning, tongue expulsion, grimacing, and blinking in FGR fetuses [13]. According to that investigation, the frequencies of these facial expressions in FGR fetuses were significantly lower than those in AGA fetuses. In the present study, there were no significant differences in the frequencies of any of the facial expressions among AGA, SGA, and FGR fetuses. Qualitative and quantitative results of general movements in normal and FGR fetuses assessed by conventional 2D sonography were also inconsistent [5,9–11]. The reason for this discrepancy in the frequencies of fetal facial expressions in AGA and FGR fetuses between Andonotopo's and our studies is currently unclear. One possible explanation is the different 4D ultrasound machines used. The volume was obtained every 2 seconds in Andonotopo's investigation [13], whereas the mean frame rate was 2.2 per second (range, 1.4–5 per second) in our study. The relatively slow frame rates in his study may not be satisfactory for the observation of short-duration fetal movements, such as fetal facial expressions. Another possible explanation is the difference in sample size, especially the number of FGR cases, between the studies (Andonotopo's study: 50, and our study: 6 FGR cases). Certainly, the number of cases of FGR in our study was small. However, FGR cases (SGA with decreased MCAPI and increased UAPI and/or decreased AFI) are rare in our hospital. Moreover, the definition of FGR in Andonotopo's study is unclear. Further studies involving a larger sample size, especially a large number of FGR cases, are needed to ascertain the difference in the frequency of fetal facial expressions between AGA and FGR fetuses.

With respect to the difference in examination times, the time for examination in Andonotopo's investigation was 30 min [13], and it was 15 min in the present study. Thirty minutes for the examination time may be better than 15 min [18]. Fifteen minutes may be too short to detect differences in the frequency of fetal facial expressions among the study groups. However, the time for examination in recent 4D ultrasound studies on fetal facial expressions varied from 10 to 20 min [17,18,32–34] because of ethical issues regarding ultrasound exposure of the fetus (ALARA principle [35]) *in utero*. Further studies involving an extended examination period are required to assess the precise frequencies of fetal facial expressions among AGA, SGA, and FGR fetuses.

In conclusion, the present study suggests that the frequencies of fetal facial expressions are not decreased in SGA and FGR pregnancies early in the third trimester of pregnancy. The lack of a decrease in the frequency of each fetal expression in FGR fetuses may be due to increased brain blood flow because of the brain-sparing effect. Moreover, accelerated maturation and development of the brain function, especially the central dopamine system, may occur in SGA and FGR fetuses. However, the clinical importance and relevance of the described fetal facial expressions evaluated by 4D ultrasound remain unclear. Further, larger studies are mandatory to fully understand the neurodevelopmental maturation and brain function in SGA and FGR fetuses.

Disclosure statement

No conflicts of interest related to this study exist.

References

[1] Battaglia FC, Lubchenco LO. A practical classification of newborn infants by weight and gestational age. J Pediatr. 1967;71:159–163.

[2] Ott WJ. The diagnosis of altered fetal growth. Obstet Gynecol Clin North Am. 1988;15:237–263.

[3] Jones OW. Genetic factors in the determination of fetal size. J Reprod Med. 1978;21:305–313.

[4] Hata T, Kuno A, Akiyama M, et al. Detection of small-for-gestational-age infants with poor perinatal outcomes using individualized growth assessment. Gynecol Obstet Invest. 1999;47:162–165.

[5] van Vliet MAT, Martin CB Jr., Nijhuis JG, et al. Behavioural states in growth-retarded human fetuses. Early Hum Dev. 1985;12:183–197.

[6] Hata T, Aoki S, Manabe A, et al. Subclassification of small-for-gestational-age fetus using fetal Doppler velocimetry. Gynecol Obstet Invest. 2000;49:236–239.

[7] Hata T. Current status of fetal neurodevelopmental assessment: four-dimensional ultrasound study. J Obstet Gynaecol Res. 2016;42:1211–1221.

[8] AboEllail MAM, Hata T. Fetal face as important indicator of fetal brain function. J Perinat Med. 2017;45:729–736.

[9] Bekedam DJ, Visser GHA, de Vries JJ, et al. Motor behaviour in the growth retarded fetus. Early Hum Dev. 1985;12:155–165.

[10] Sival DA, Visser GHA, Prechtl HFR. The effect of intra-uterine growth retardation on the quality of general movements in the human fetus. Early Hum Dev. 1992;28:119–132.

[11] Sival DA, Visser GHA, Prechtl HFR. The relationship between the quantity and quality of prenatal movements in pregnancies complicated by intra-uterine growth retardation and premature rupture of the membranes. Early Hum Dev. 1992;30:193–209.

[12] Hata T, Dai S, Marumo G. Ultrasound for evaluation of fetal neurobehavioural development: from 2-D to 4-D ultrasound. Inf Child Develop. 2010;19:99–118.

[13] Andonotopo W, Kurjak A. The assessment of fetal behavior of growth restricted fetuses by 4D sonography. J Perinat Med. 2006;34:471–478.

[14] Japan Society of Ultrasonics in Medicine. Standardization of ultrasonic fetal biometry and Japanese reference values. J Med Ultrason. 2003;30:J415–J440.

[15] Ogawa Y, Iwamura T, Kuriya N, et al. Birth size standards by gestational age for Japanese neonates. Acta Neonat Jpn. 1998;34:624–632.

[16] Yan F, Dai SY, Akther N, et al. Four-dimensional sonographic assessment of fetal facial expression early in the third trimester. Int J Gynecol Obstet. 2006;94:108–113.

[17] Kanenishi K, Hanaoka U, Noguchi J, et al. 4D ultrasound evaluation of fetal facial expressions during the latter stages of the second trimester. Int J Gynecol Obstet. 2013;121:257–260.

[18] Sato M, Kanenishi K, Hanaoka U, et al. 4D ultrasound study of fetal facial expressions at 20–24 weeks of gestation. Int J Gynecol Obstet. 2014;126:275–279.

[19] AboEllail MAM, Tenkumo C, Mori N, et al. OP04.09: 4D ultrasound assessment of facial expressions and their reproducibility in the third trimester. Ultrasound Obstet Gynecol. 2017;50(Suppl 1):59.
[20] D'Elia A, Pighetti M, Moccia G, et al. Spontaneous motor activity in normal fetuses. Early Hum Dev. 2001;65:139–147.
[21] Pillai M, James D. Human fetal mouthing movements: a potential biophysical variable for distinguishing state 1F from abnormal fetal behavior: report of 4 cases. Eur J Obstet Gynecol Reprod Biol. 1991;38: 151–156.
[22] Fukuda K, Stern JA, Brown TB, et al. Cognition, blinks, eye-movements, and pupillary movements during performance of a running memory task. Aviat Space Environ Med. 2005;76(7 Suppl):C75–CC85.
[23] Siegle GJ, Ichikawa N, Steinhauer S. Blink before and after you think: blinks occur prior to and following cognitive load indexed by pupillary responses. Psychophysiology. 2008;45:679–687.
[24] Dreisbach G, Müller J, Goschke T, et al. Dopamine and cognitive control: the influence of spontaneous eyeblink rate and dopamine gene polymorphisms on perseveration and distractibility. Behav Neurosci. 2005;119:483–490.
[25] Colzato LS, van den Wildenberg WPM, van Wouwe NC, et al. Dopamine and inhibitory action control: evidence from spontaneous eye blink rates. Exp Brain Res. 2009;196:467–474.
[26] Hentschel J, Ruff R, Juette F, et al. Neonatal facial movements in the first minutes of life – eye opening and tongue thrust: an observational study. Am J Perinatol. 2007;24:611–618.
[27] Gould JB, Gluck L, Kulovich MV. The relationship between accelerated pulmonary maturity and accelerated neurological maturity in certain chronically stressed pregnancies. Am J Obstet Gynecol. 1977;127: 181–186.
[28] Amiel-Tison C. Possible acceleration of neurological maturation following high-risk pregnancy. Am J Obstet Gynecol. 1980;138:303–306.
[29] Hadi HA. Fetal cerebral maturation in hypertensive disorders of pregnancy. Obstet Gynecol. 1984;63: 214–219.
[30] Petrikovsky B, Kaplan G, Holsten N. Fetal yawning activity in normal and high-risk fetuses: a preliminary observation. Ultrasound Obstet Gynecol. 1999;13: 127–130.
[31] Walusinski O, Kurjak A, Andonotopo W, et al. Fetal yawning assessed by 3D and 4D sonography. Ultrasound Rev Obstet Gynecol. 2005;5:210–217.
[32] Reissland N, Francis B, Mason J, et al. Do facial expressions develop before birth? PLoS One. 2011;6:e24081.
[33] Reissland N, Mason C, Schaal B, et al. Prenatal mouth movements: can we identify co-ordinated fetal mouth and lip actions necessary for feeding? Int J Pediatr. 2012;2012:848596.
[34] Reissland N, Aydin E, Francis B, et al. Laterality of foetal selftouch in relation to maternal stress. Laterality. 2015;20:82–94.
[35] Kremkau FW. Contemporary ultrasound technology. Ultrasound Obstet Gynecol. 1995;6:233–236.