

Objective

The objective of the present study was to characterize the placental expression and DNA methylation of serotonin transporter gene (SLC6A) and serotonin receptor gene (HTR2A) in women with gestational diabetes mellitus (GDM).

Method

DNA and RNA were isolated from samples of tissue taken samples from the fetal side of the placenta immediately after delivery of 90 women. Thirty mothers were diagnosed with GDM and sixty mothers had normal glucose test (NGT). We analyzed DNA methylation patterns of 10 CpG sites within the SLC6A4 distal promoter region and 10 CpG sites within HTR2A region. DNA methylation was analyzed by bisulfite restriction analysis and pyrosequencing in placenta samples. SLC6A4 and HTR2A mRNA levels were measured by reverse transcription-quantitative PCR (RT-qPCR).

Result

Mean level of DNA methylation of placental SLC6A4 was higher in women with GDM than women with NGT (2.39 vs 1.76, $p < 0.001$). However, placental HTR2A was not significantly different between two groups. Placental SLC6A4 and HTR2A mRNA levels were positively associated with mean level of DNA methylation ($p = 0.017$ and 0.045 respectively). The association with glucose was significantly observed with SLC6A DNA methylation ($p = 0.05$).

Table 1. baseline characteristics of the study population

	GDM(n=30)	NGT(n=60)	p-value
Maternal age, years	35.77±2.89	33.68±4.06	0.014
Nulliparous	15(50)	40(66)	0.262
BMI, kg/m ²	26.84±4.52	22.07±4.04	<0.001
Gestation at birth, weeks	36.91±2.46	37.13±2.31	0.683
Weight gain	10.97±7.58	13.75±5.65	0.054
Birth weight, kg	3.03±0.76	2.86±0.72	0.300
Placenta weight, kg	0.70±0.21	0.64±0.20	0.192

Table 2. Methylation status of the study population

	GDM(n=30)	NGT(n=60)	p-value
SLC6A4 methylation	2.29±0.33	1.76±0.50	<0.001
HTR2A methylation	23.07±3.52	21.76±3.67	0.111

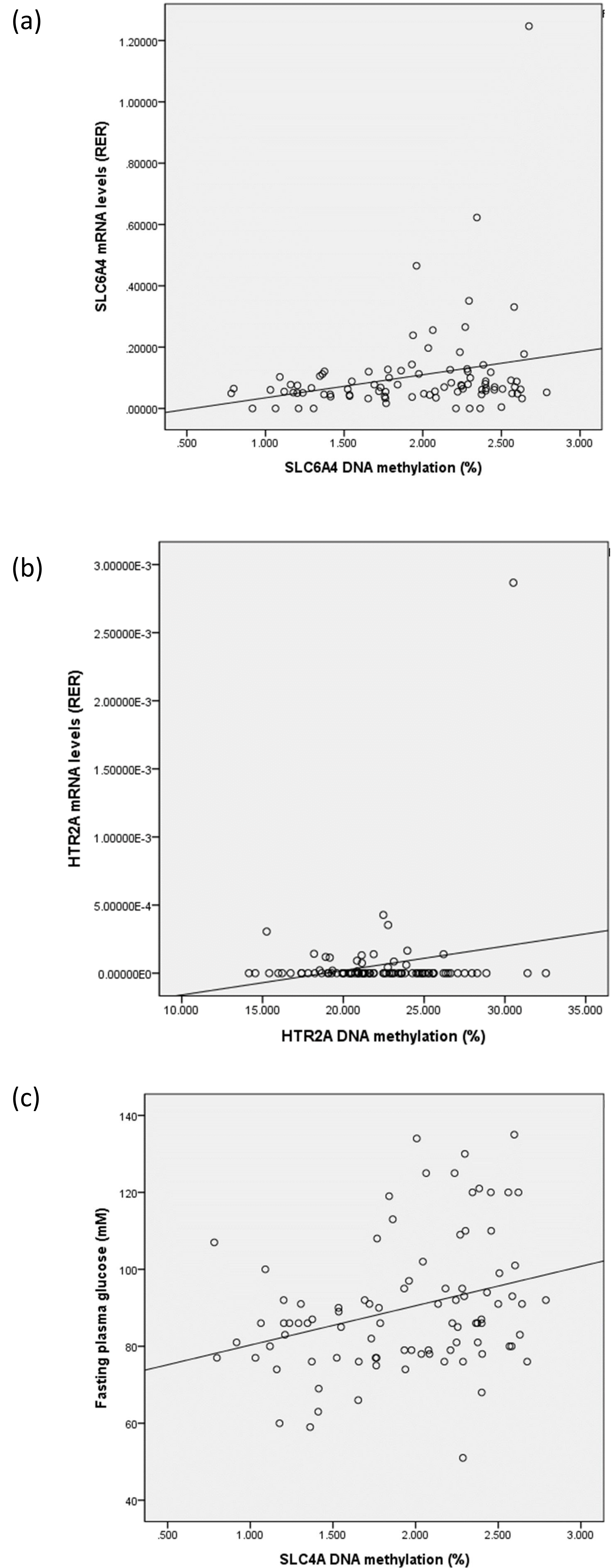


Figure 1. placental DNA methylation levels correlate with mRNA levels and fasting glucose concentration

(a) Placenta SLC6A4 DNA methylation correlated with SLC6A4 mRNA levels, (b) Placental HTR2A DNA methylation correlated with HTR2A mRNA levels, (c) Placenta SLC6A4 DNA methylation correlated with fasting glucose level

Conclusion

Our study's results suggest that the maternal diabetes in pregnancy is correlated to the DNA methylation of the placental SLC6A4 gene. Larger studies are needed to verify the association and determine to which degree of placental SLC6A4 changes may contribute to long-term outcomes of infants exposed to GDM.