The effect of neural immaturity after gestational diabetes on rapid auditory processing abilities in newborns

De Groot, E.R.[1], Ganga, R.[1*], Tataranno, M.L.[2], Wijnen, F.[1], Chen, A.[1]*
[1] Institute for Language Sciences, Utrecht University, The Netherlands,
[2] Department of Neonatology, UMC Utrecht, The Netherlands.
[*]These authors have contributed equally to this work.

Gestational diabetes mellitus (GDM) affects 5-13% of pregnancies worldwide (Zhu & Zhang, 2016). GDM leads to poorer fetal neural maturation and connectivity, which are associated with poorer cognitive development (Rodolaki et al., 2023) and recognition memory (deRegnier et al., 2000). Moreover, GDM impacts language development (Dionne et al., 2008; Sells et al., 1994). However, why GDM leads to language-related deficits is yet unknown.

As GDM only impacts children prenatally and the fetal neural language network is shaped by prenatal experiences, GDM-exposed children's postnatal language delays may be related to GDM's negative impact on fetal neural maturation. Neural immaturity affects the extent to and speed of sound processing. The ability to distinguish auditory stimuli presented in rapid succession, or rapid auditory processing (RAP) is impacted in infants with a family history of language impairments, explaining much variance in later language outcome (Benasich et al., 2006). We thus hypothesize that GDM affects newborns' RAP.

To test this hypothesis, adopting Benasich et al.'s (2006) EEG oddball paradigm and pure tone stimuli, we assessed RAP in 30 full-term newborns (10 GDM and 20 control; see table 1 for demographics) within 120 hours postnatally. The amplitude of the Mismatch Response (MMR) and the latency and peak amplitude of the Auditory-Evoked Potentials (AEP; N250), were assessed (Benasich et al., 2006).

There were no significant differences between the GDM-group and control group in N250 latency, peak amplitude and MMR amplitude. A clear positive MMR was seen in the right anterior region (see figure 1), similar to Benasich et al. (2006).

Blood glucose levels were well-regulated in the GDM group, which might serve as a protective factor against neural immaturity due to GDM. A larger GDM sample with more variation in blood glucose regulation is needed to validate these findings.

References

Benasich, A. A., Choudhury, N., Friedman, J. T., Realpe-Bonilla, T., Chojnowska, C., & Gou, Z. (2006). The infant as a prelinguistic model for language learning impairments: predicting from event-related potentials to behavior. *Neuropsychologia, 44*(3), 396-411. https://doi.org/10.1016/j.neuropsychologia.2005.06.004

deRegnier, R. A., Nelson, C. A., Thomas, K. M., Wewerka, S., & Georgieff, M. K. (2000). Neurophysiologic evaluation of auditory recognition memory in healthy newborn infants and infants of diabetic mothers. *The Journal of pediatrics, 137*(6), 777-784. https://doi.org/10.1067/mpd.2000.109149

Dionne, G., Boivin, M., Séguin, J. R., Pérusse, D., & Tremblay, R. E. (2008). Gestational diabetes hinders language development in offspring. *Pediatrics, 122*(5), e1073-e1079. https://doi.org/10.1542/peds.2007 -3028

Rodolaki, K., Pergialiotis, V., Iakovidou, N., Boutsikou, T., Iliodromiti, Z., & Kanaka-Gantenbein, C. (2023). The impact of maternal diabetes on the future health and neurodevelopment of the offspring: a review of the evidence. *Frontiers in Endocrinology, 14,* 1125628. https://doi.org/10.3389/fendo.2023.1125628

Sells, C. J., Robinson, N. M., Brown, Z., & Knopp, R. H. (1994). Long-term developmental follow-up of infants of diabetic mothers. *The Journal of pediatrics, 125*(1), S9-S17. https://doi.org/10.1016/S0022-3476(94)70 170-9

Zhu, Y., & Zhang, C. (2016). Prevalence of gestational diabetes and risk of progression to type 2 diabetes: a global perspective. *Current diabetes reports, 16,* 1-11. https://doi.org/10.1007/s11892-015-0699-x

Table 1. Demographics.

	GDM (n=10)	**Control (n=20)**	**P-value**
Gestational age at birth (weeks)	39.00 ± 1.02	39.94 ± 1.20	.044*
Postnatal age at EEG (days)	1.50 ± 1.43	1.05 ± 0.89	.506
Birthweight (grams)	3366.50 ± 380.49	3703.10 ± 424.89	.067
Head circumference (cm)	33.67 ± 1.52	34.57 ± 1.21	.114

Sex (%male)	20%	60%	.044*
Delivery mode *Emergency cesarean section* *Planned cesarean section* *Spontaneous vaginal birth* *Instrumental vaginal birth*	 10% 90%	 15% 30% 50% 5%	
Maternal age (years)	34.50 ± 4.72	32.85 ± 4.40	.366
Maternal pregnancy BMI	32.03 ± 5.07	25.86 ± 4.57	0.004**

The GDM and control group differed with regard to gestational age at birth, which is expected due to the relatively high birthweight of GDM infants, resulting in labor being frequently induced at a slightly lower gestational age. P-values are calculated using a Mann Whitney U test and Chi square test (latter only for sex at birth).

Figure 1. Topography of mismatch response in control (top) and GDM (bottom) groups. The mismatch response is calculated as the difference between the pre-deviant standard and the deviant stimulus.