Adverse neonatal outcomes predispose to exacerbated metabolic disturbances in childhood obesity

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The occurrence of **adverse neonatal outcomes** (i.e., prematurity, small for gestational age) is a significant contributing factor to the development of metabolic perturbations, which can persist throughout the lifespan and potentially lead to the onset of **childhood obesity**. Metabolomics has been employed in the past to investigate the pathophysiological mechanisms underlying those neonatal conditions. However, longitudinal studies elucidating the impact of neonatal determinants (i.e., gestational age, birth weight, birth length) on **later metabolic health** in general populations are scarce, and the **molecular mechanisms** underpinning their influence in the predisposition to obesity in children remain to be elucidated.

METHODS

Study design

- Gestational age at birth (GA)
- Birth weight (BW) and Z-scores (zBW)
- Birth length (BL) and Z-scores (zBL)

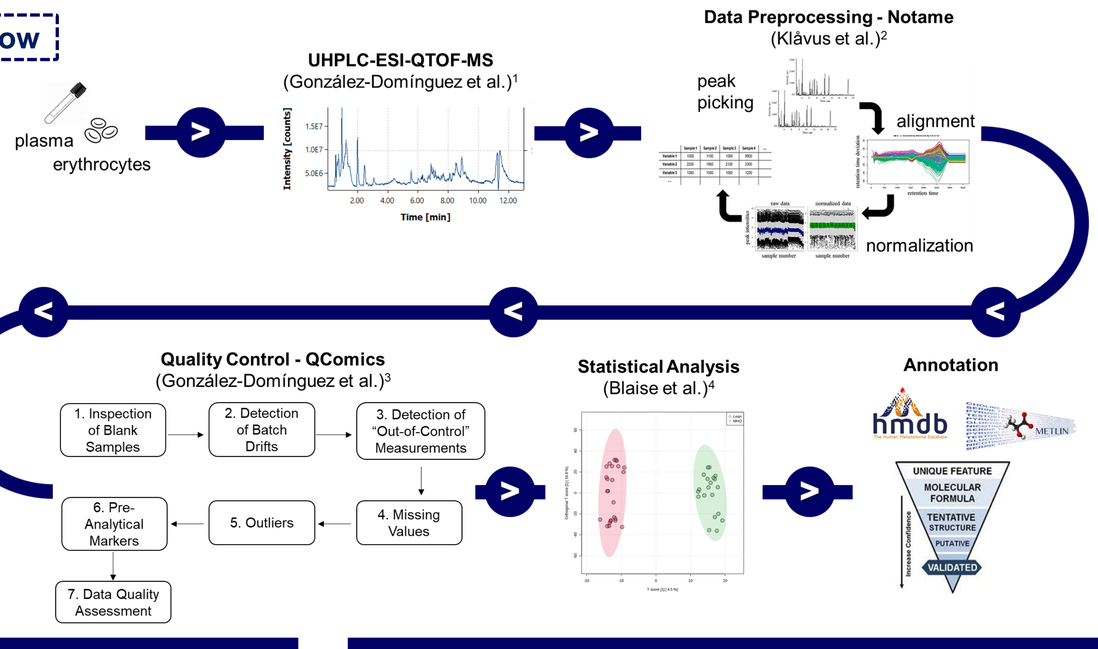
Inclusion criteria

- BMI > 2 SD
- Age: 6-14 y
- Written informed consent

plasma
erythrocytes

- Glycemia and insulinemia
- Lipid profile
- Inflammation markers

Metabolomics workflow

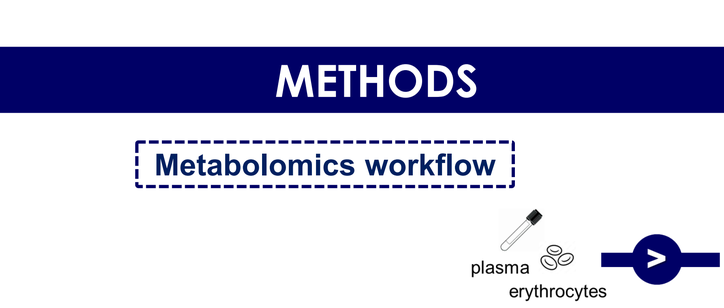


RESULTS

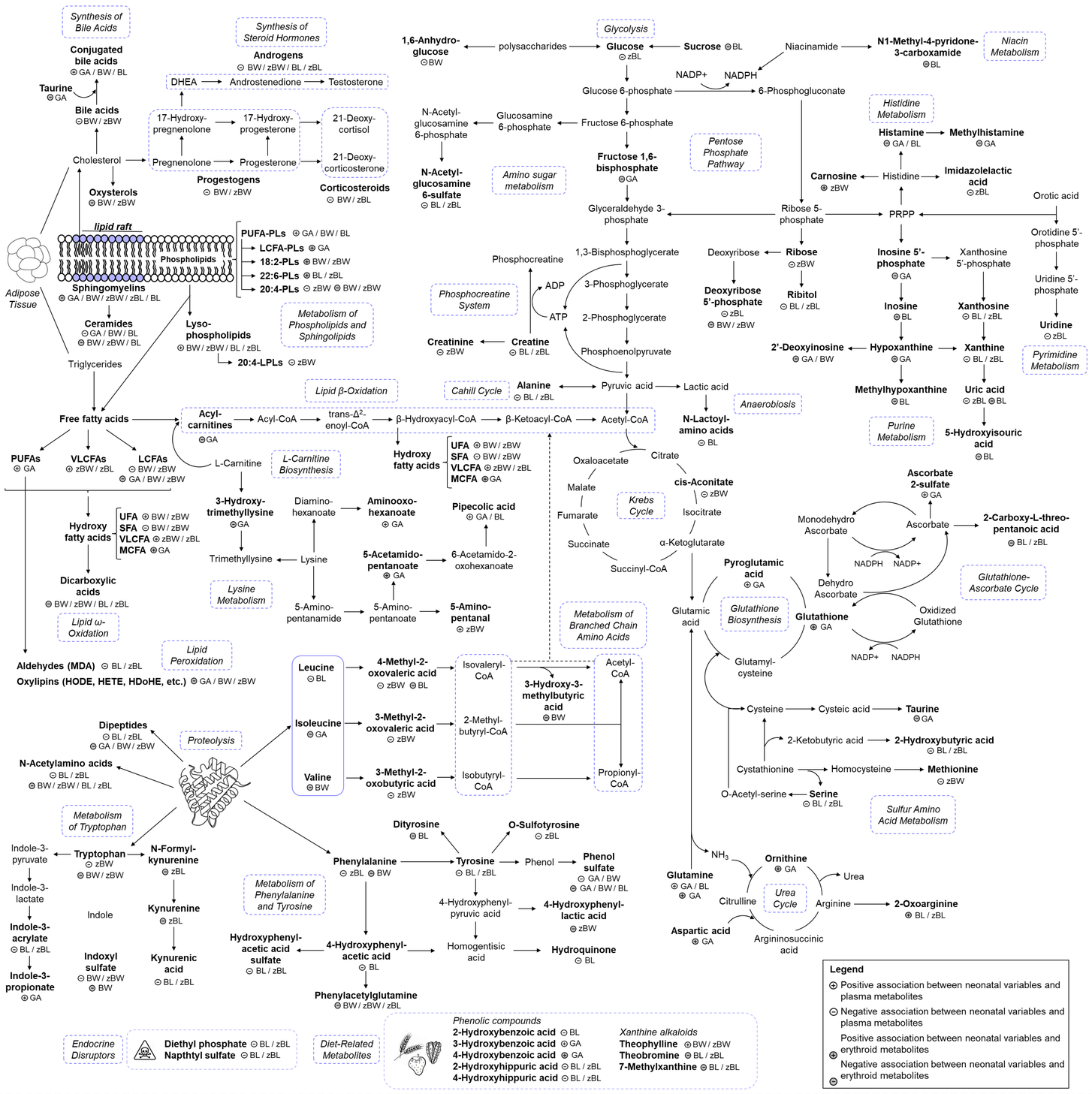
1 Association study between neonatal and clinical variables

Neonatal variables	
GA (weeks)	39.3 ± 1.9
BW (kg)	3.2 ± 0.5
zBW	0.5 ± 4.6
BL (cm)	50.4 ± 2.6
zBL	0.5 ± 1.4

Anthropometry	
Weight (kg)	67.7 ± 19.7
Weight Z-score	4.9 ± 2.1
BMI (kg/m^2)	30.0 ± 5.2
BMI Z-score	4.4 ± 2.0
WC (cm)	96.7 ± 12.9



2 Association study between neonatal variables and metabolomics data



CONCLUSIONS

- ✓ Adverse neonatal outcomes (i.e., low gestational age, weight, and length at birth) may predispose to an **unhealthier metabolic status**, as reflected in negative associations with anthropometric parameters (e.g., waist circumference) and biochemical markers of insulin resistance (e.g., HOMA-IR) and inflammation (e.g., CRP, inflammatory indices).
- ✓ This was accompanied by exacerbations in a multitude of central **metabolic pathways** which play a crucial role in obesity pathophysiology, such as energy metabolism, homeostasis of branched chain and aromatic amino acids, regulation of oxidative stress, and biosynthesis of steroid hormones and bile acids.
- ✓ Accordingly, we hypothesize that even minor variations in neonatal conditions may provoke **deleterious molecular programming mechanisms** with strong impact on later metabolic risk.

References

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