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NMR Metabolomics Profiling Reveals Distinctive Signatures of an Obesogenic Diet in Mice

Uncovering Metabolite Signatures in Six Organs During a High-Fat, High-Sucrose Diet: A Cross-Sectional NMR Metabolomics Study

Drevet Mulard E.¹; Guibert S.²; Lefevre C.^{3,4}; Chauvin M.A.^{3,4}; Pinteur C.^{3,4}; Monet M.A.^{3,4}; Godet M.^{3,4}; Madec A.M.^{3,4}; Morio B.^{3,4}; Rieusset J.^{3,4}; Mey A.^{3,4}; Rautureau G.J.P.²; Panthu B.^{3,4}

¹ University of Lyon, ICBMS UMR CNRS 5246, Bâtiment Raulin, 43 Bd du 11 novembre 1918, 69622 Villeurbanne Cedex, France
² Centre de Résonance Magnétique Nucléaire à Très Hauts Champs, UMR 5082 CNRS / Ecole Normale Supérieure de Lyon / Université Claude Bernard Lyon 1, 69100, Villeurbanne, France
³ CarMeN Laboratory, INSERM, INRA, INSA Lyon, Université Claude Bernard Lyon 1, 69921, Oullins Cedex, France
⁴ Hospices Civils de Lyon, Faculté de Médecine, Hôpital Lyon Sud, 69921, Oullins Cedex, France

Intro

Obesity is a significant risk factor for diseases like type 2 diabetes and cardiovascular disorders. Identifying biomarkers for early obesity-related disorders is crucial for precision medicine. We used NMR to analyze metabolomic profiles of key organs and serum in male C57Bl/6J mice fed a high-fat, high-sucrose diet (HFHSD, 36 % w/w fat, 16.6 % w/w sucrose, Envigo, France) or standard diet (STD, Rhod16A, Genobio) for 6, 10, and 14 weeks. Our study reveals organ-specific metabolite concentrations, highlighting age and diet effects and their interaction.

Results

- 12 mice for each data point (72 total)
- Insulin resistance was observed after 13 weeks of feeding
- Organ weight was not impacted by the diet except for liver weight
- 43 metabolites were quantified
- The heart and the liver are the most impacted by the diet while the brain is not impacted by the diet
- Betaine, dimethyl-glycine, and myo-inositol were impacted by the diet in 5 organs and the serum
- ANOVA reveals diet-time interactions in the liver and the lungs

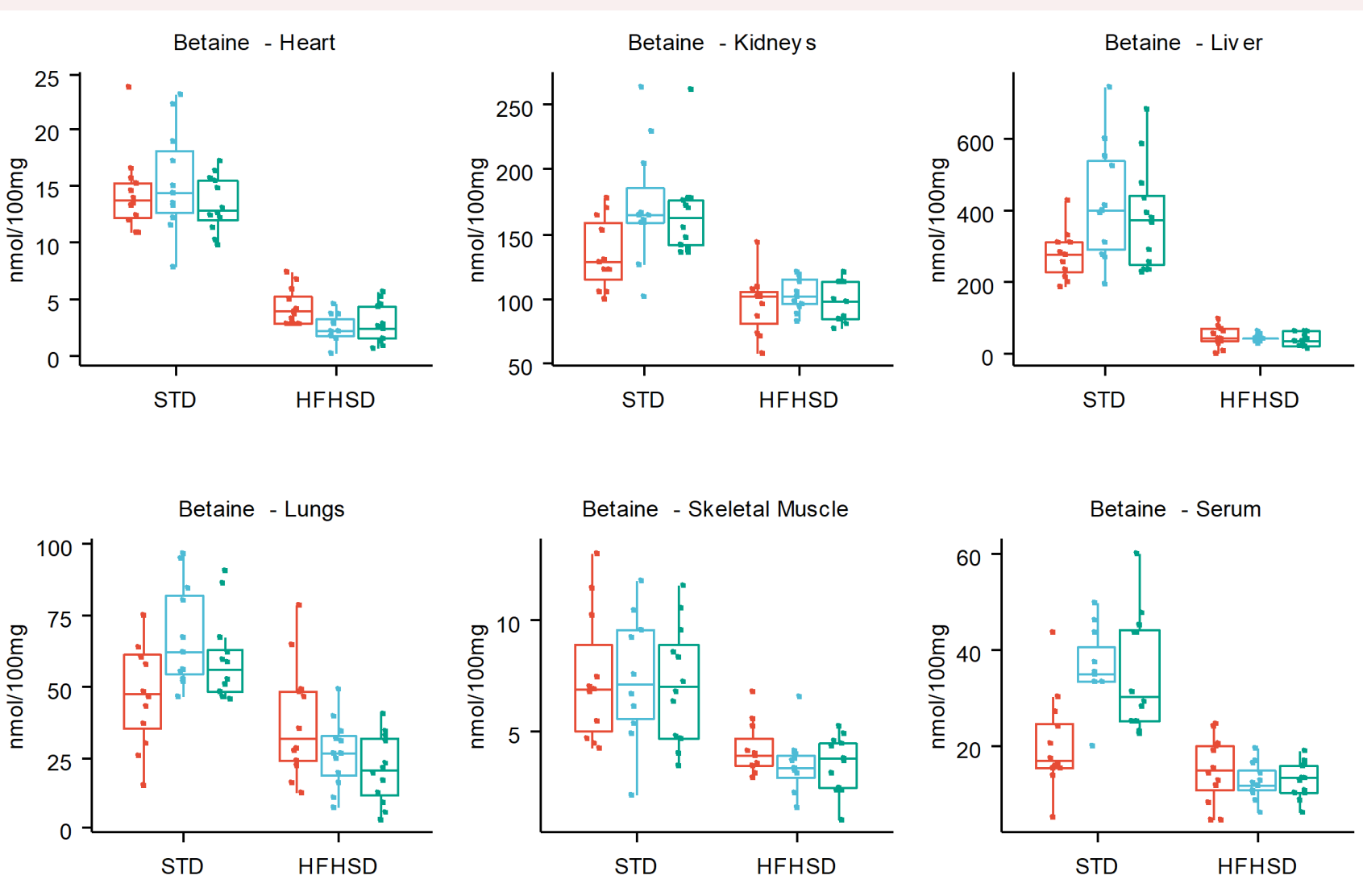
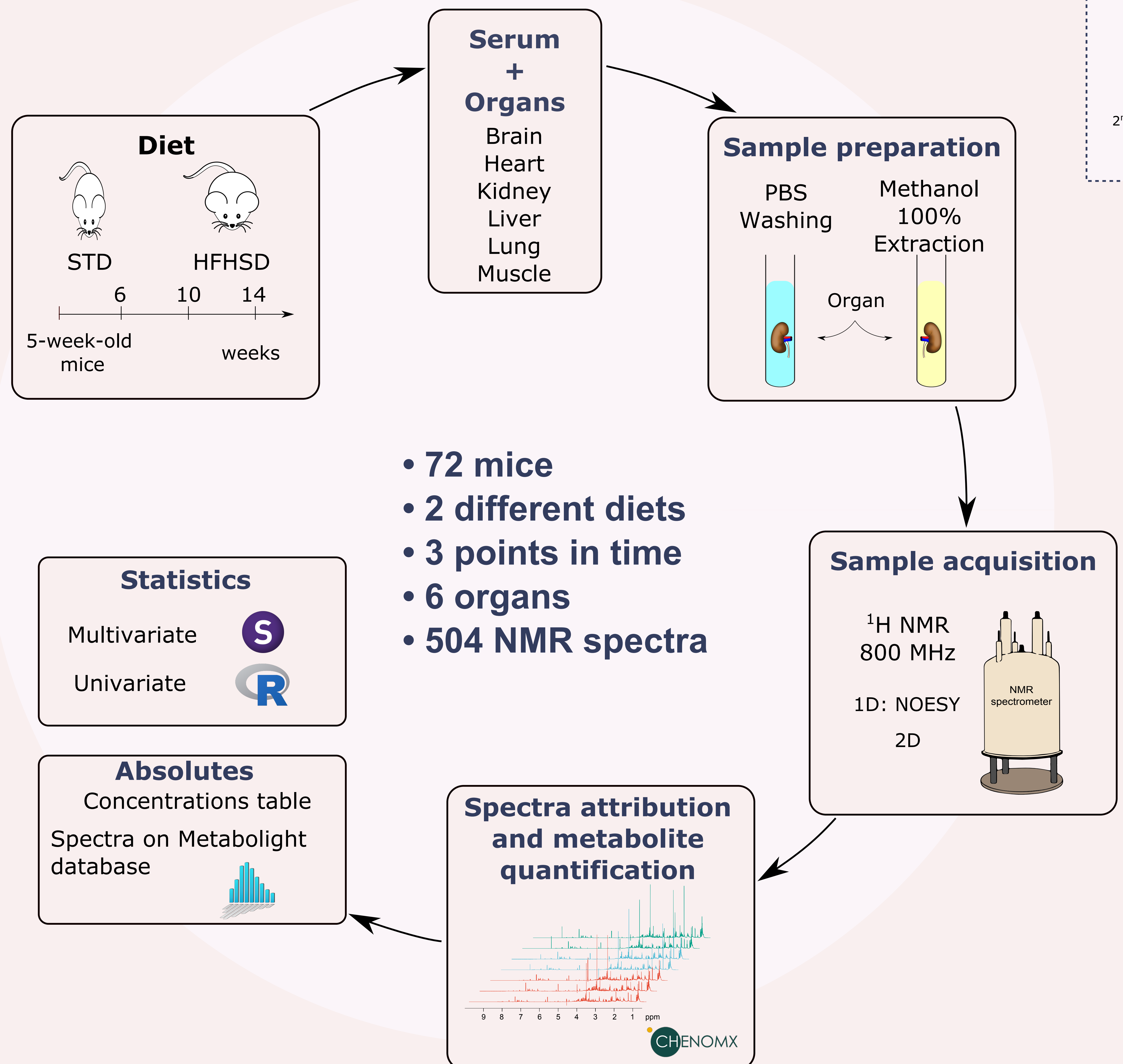


Figure 1: Betaine concentration in nmol/100mg of organ, depending on the diet (STD and HFHSD) and over time (6, 10, and 14 weeks respectively in red, blue, and green), for each organ except the brain. The 3 horizontal bars represent the median, the first, and the third quartile of the boxplots.

Discussion

This research of diet-related metabolic impairments in mice focuses on the effects of aging and a high-fat, high-sucrose diet.

- Aging significantly impacts all organs with different metabolite signatures for each organ
- The brain is not impacted by the diet, while others organs and the serum are significantly impacted (up to 80% in concentration variation)
- Some effects appear as soon as 6 weeks, while others were delayed to 10 or 14 weeks
- Diet decreases metabolite concentrations corresponding to the one-carbon metabolism: betaine, dimethyl-glycine and sarcosine
- Diet-time interaction evidences the need to evaluate carefully the influence of confounding factors over metabolite signatures



- 72 mice
- 2 different diets
- 3 points in time
- 6 organs
- 504 NMR spectra

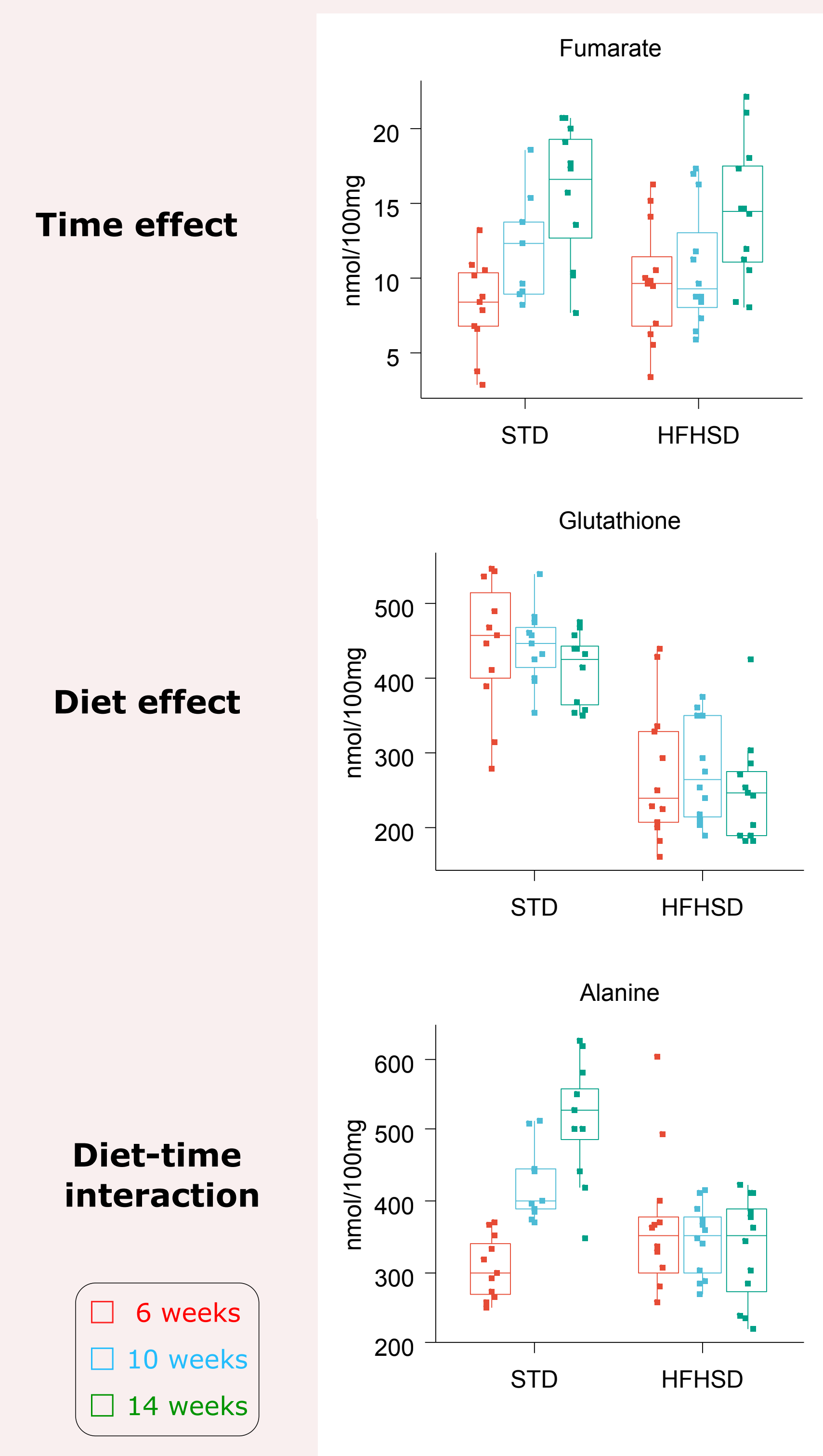
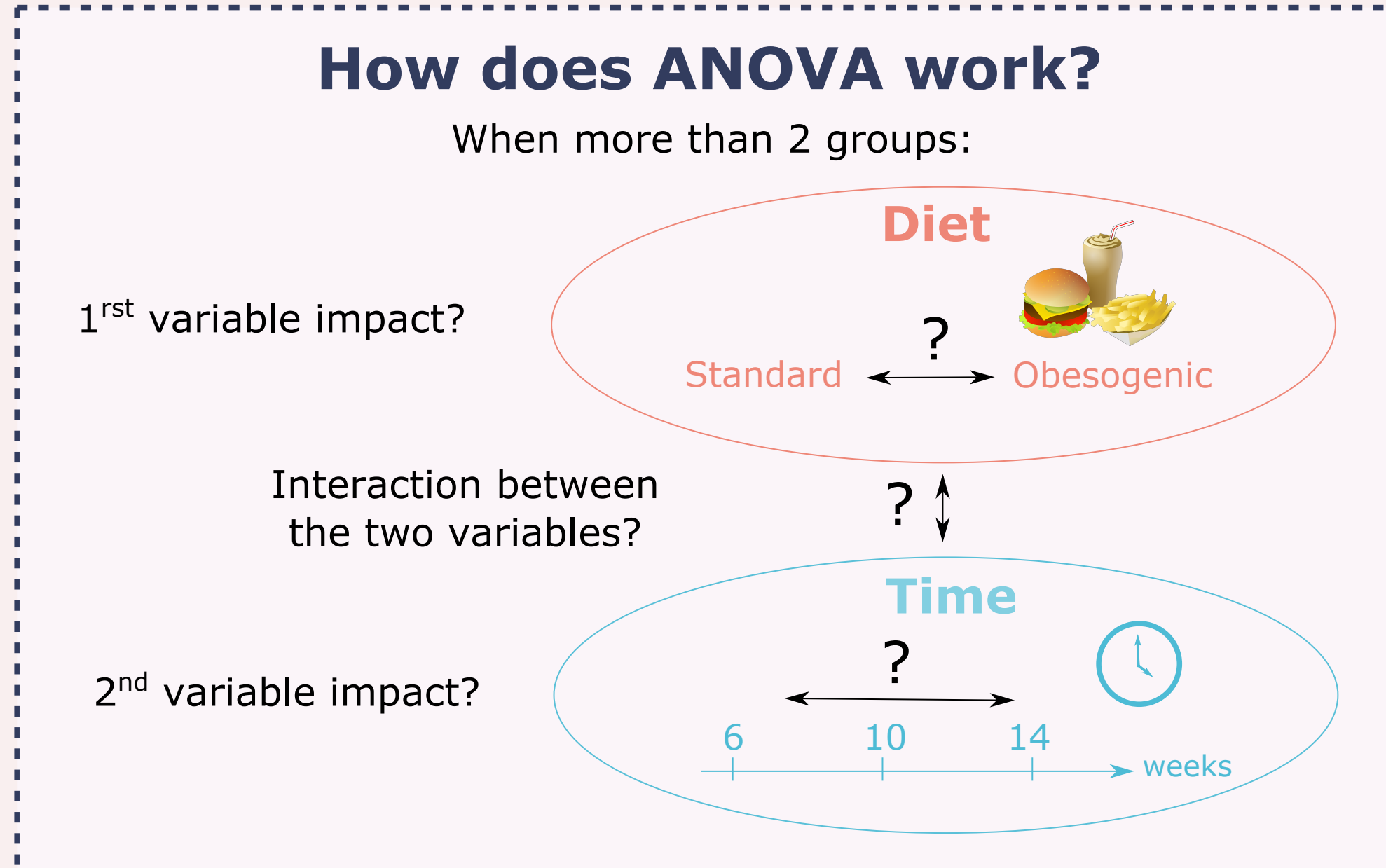


Figure 2: Boxplots of 3 metabolites evolution in liver, each one representing the 3 effect detected by the Analysis of Variance (ANOVA): diet, time and diet-time interaction effect.