Gut-Brain Communication:
How do Microbes and Sex Differences Shape Eating Behavior in 0besity?

Sri Sundaram[1,2], Yee Teng Lee[1,2] Meghedi Vartanian [1,2], Frauke Beyer [1,2], Arno Villringer [1,2,3], Daria Jensen [1,2], Veronica Witte[1,2,3]

[1]Department of Neurology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany
[2]University of Leipzig Medical Center, Leipzig, Germany, [3]University Clinic of Cognitive Neurology, Leipzig, Germany

srividya@cbs.mpg.de

Delving into Dining

- Global rise in obesity is linked to a shift towards pleasure-based eating habits, leading to increased consumption of high-energy foods.

- While weight loss interventions address unhealthy eating patterns and sedentary lifestyles, their long-term success varies among individuals.

- Recent studies emphasize the gut-brain axis's role in unhealthy eating patterns, as well as altered changes observed in various weight loss interventions.

- However, these changes particularly considering the involvement of gut-brain axis remains less explored.
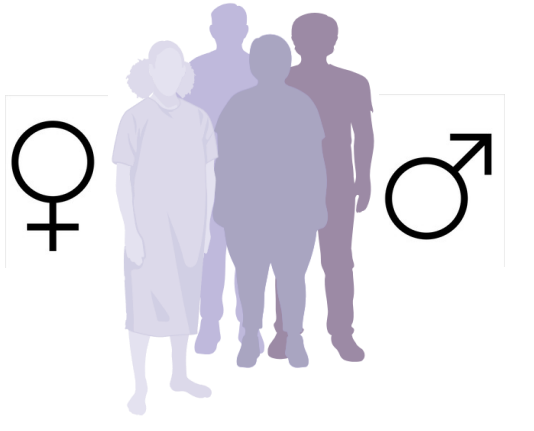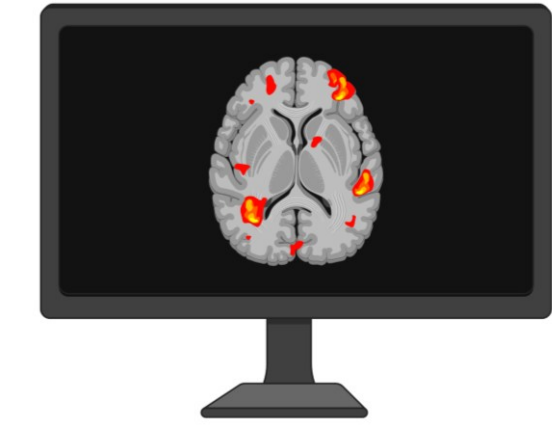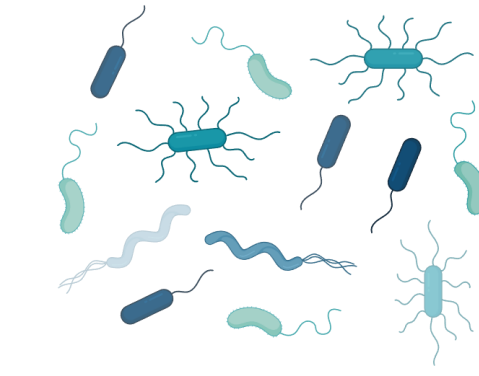
Project Overview

Gut-Brain Axis
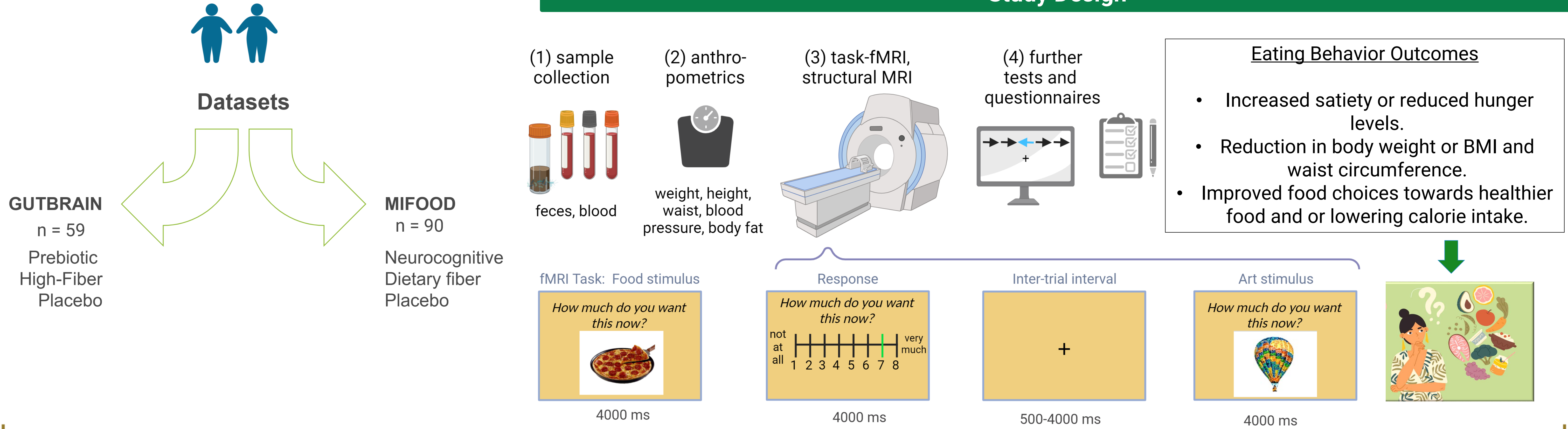
Eating Behaviour & Weight Loss
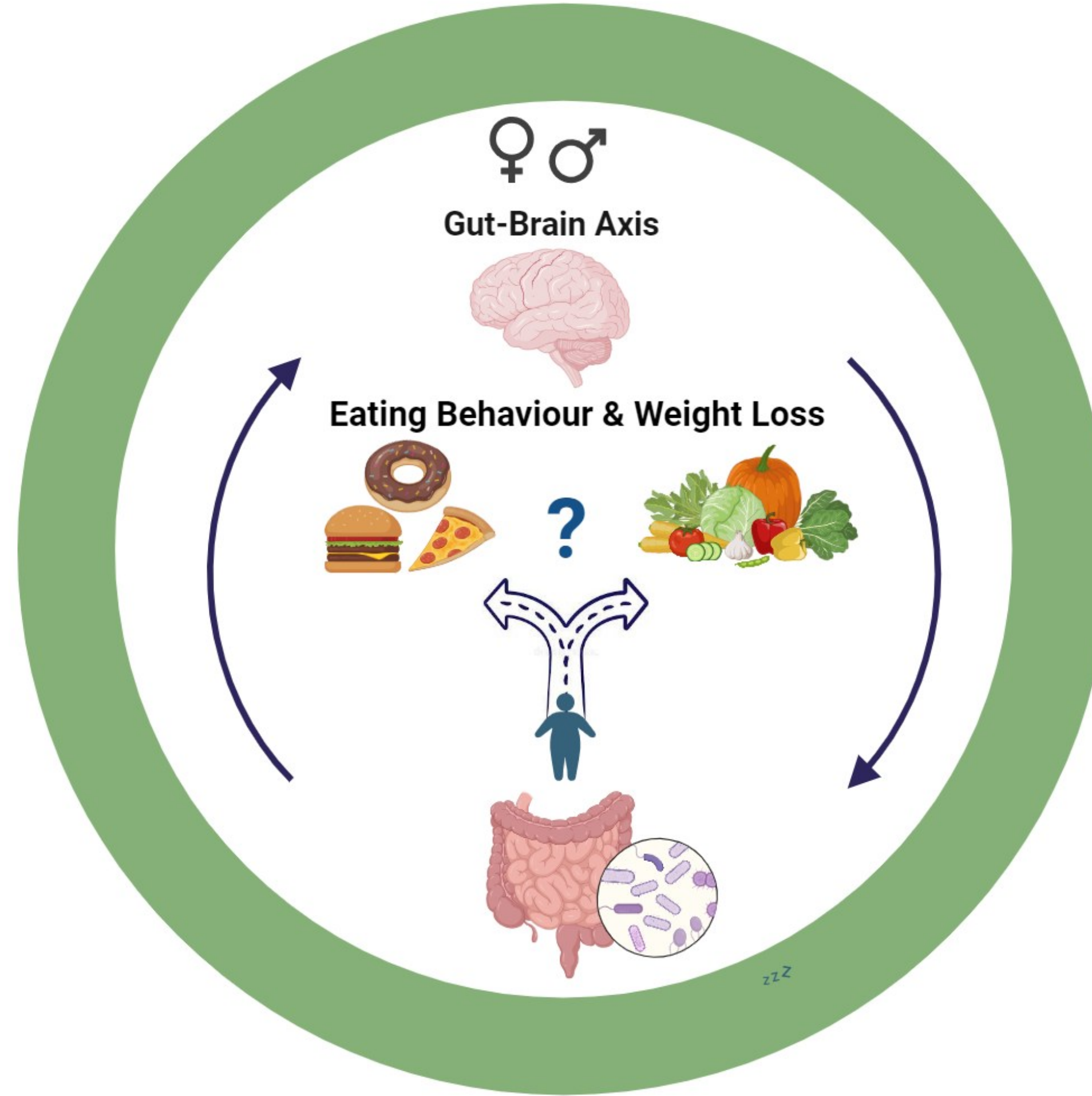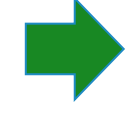
Aims:

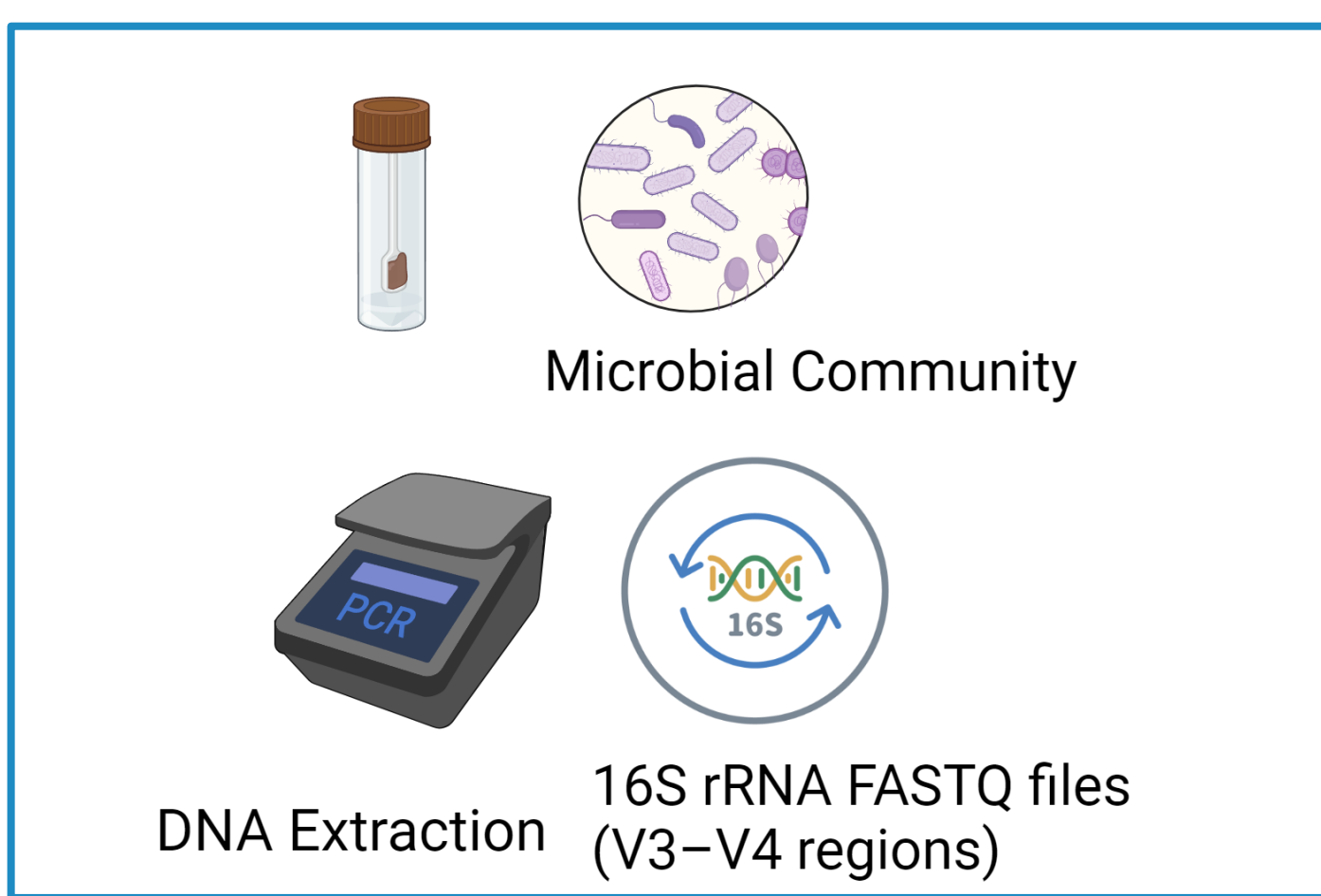By analysing pre-existing datasets, **this project aims to:**

1) Identify gut microbiota profiles associated to improved eating behaviour outcomes.

2) Examine how these microbiota profiles link to neural correlates of food decision-making.

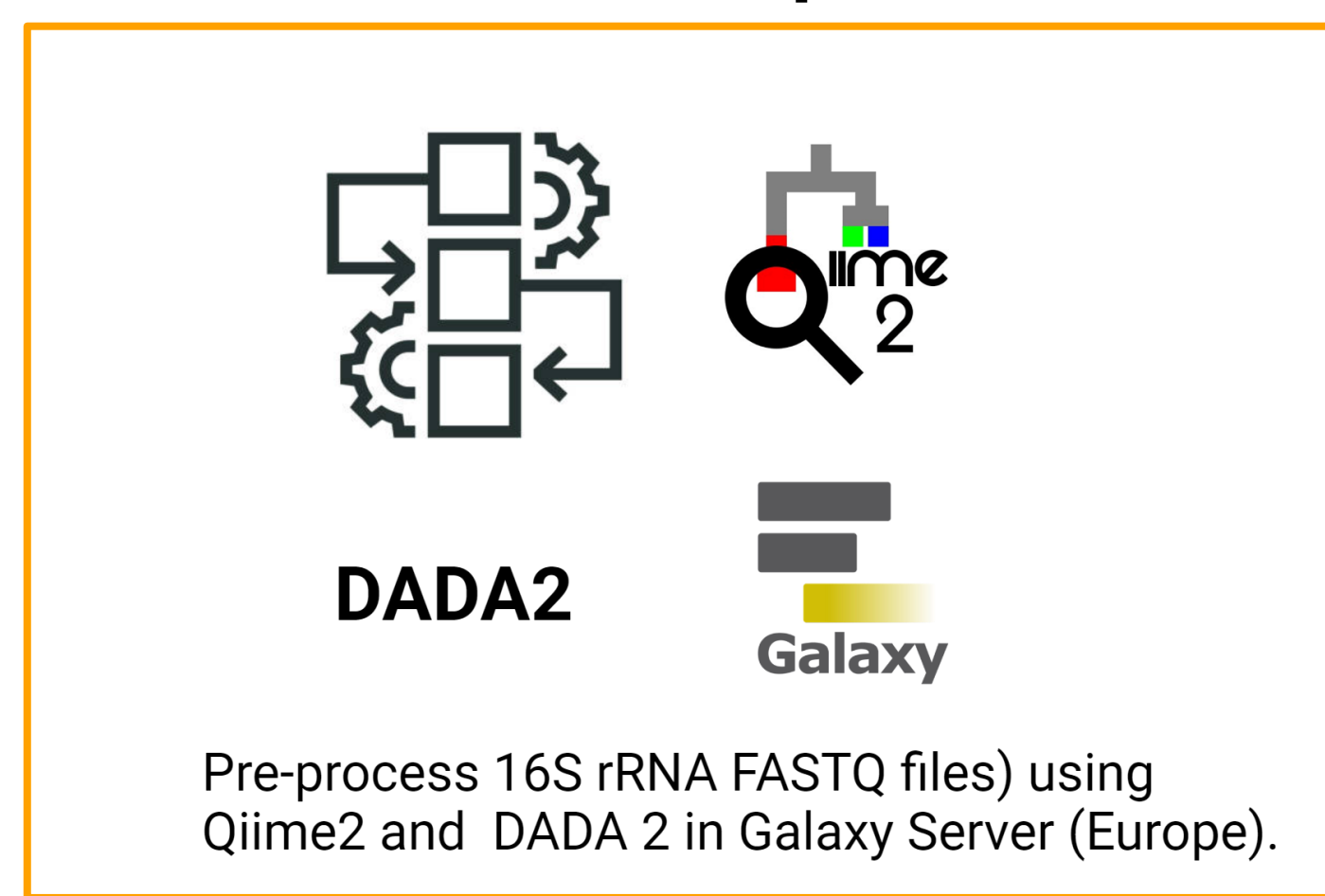3) Assess sex specific differences in weight loss outcomes pre and post interventions.
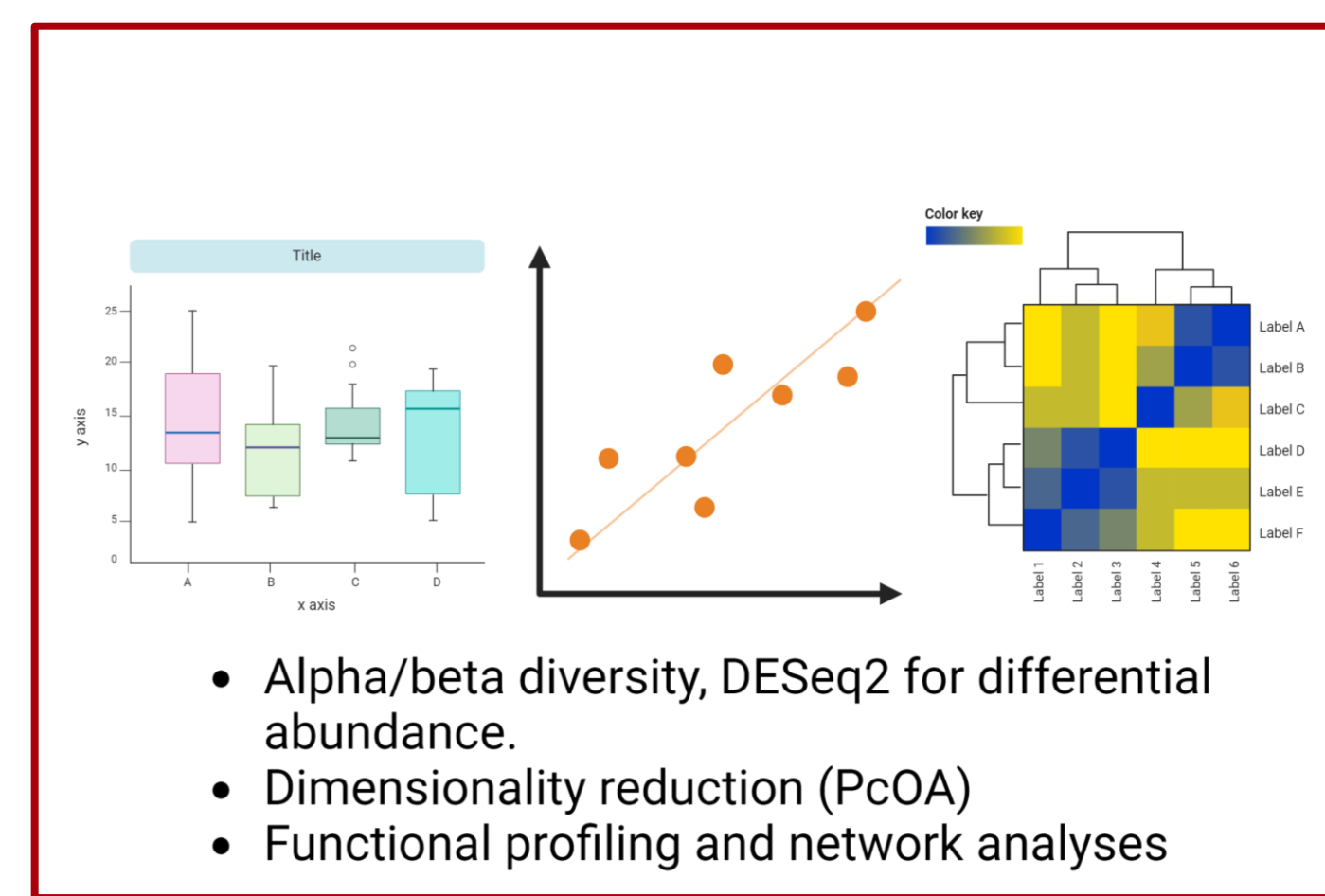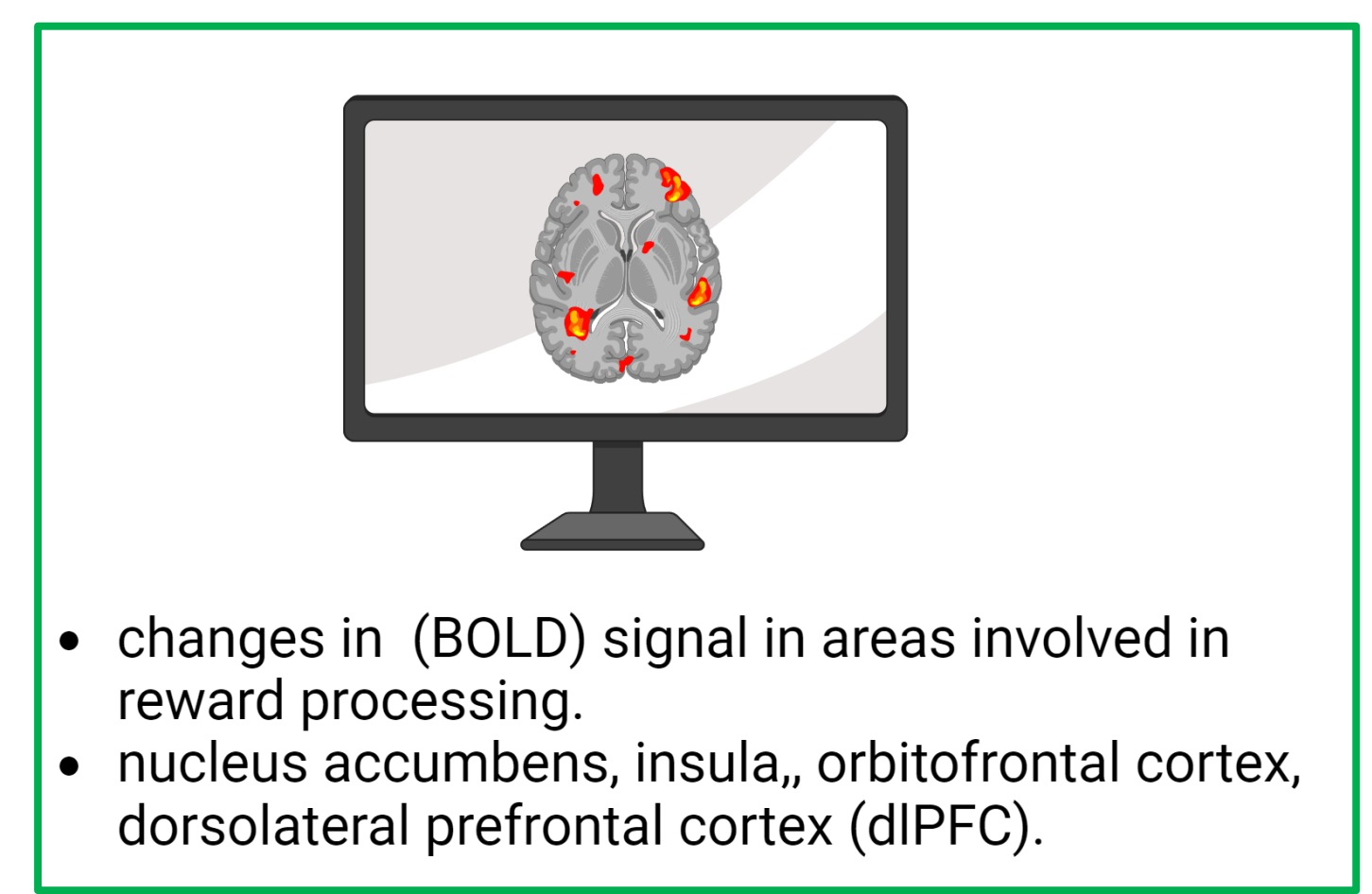
Study Design

Datasets

GUTBRAIN
n = 59
Prebiotic
High-Fiber
Placebo

MIFOOD
n = 90
Neurocognitive
Dietary fiber
Placebo

(1) sample collection — feces, blood

(2) anthro-pometrics — weight, height, waist, blood pressure, body fat

(3) task-fMRI, structural MRI

(4) further tests and questionnaires

Eating Behavior Outcomes

- Increased satiety or reduced hunger levels.
- Reduction in body weight or BMI and waist circumference.
- Improved food choices towards healthier food and or lowering calorie intake.

fMRI Task: Food stimulus
How much do you want this now?
4000 ms

Response
How much do you want this now?
not at all 1 2 3 4 5 6 7 8 very much
4000 ms

Inter-trial interval
+
500-4000 ms

Art stimulus
How much do you want this now?
4000 ms

1. Sample processing

Microbial Community

DNA Extraction

16S rRNA FASTQ files (V3–V4 regions)

2. Bioinformatics Pipeline

DADA2

Galaxy

Pre-process 16S rRNA FASTQ files) using Qiime2 and DADA 2 in Galaxy Server (Europe).

3. Microbiome Analysis

Color Key

- Alpha/beta diversity, DESeq2 for differential abundance.
- Dimensionality reduction (PcOA)
- Functional profiling and network analyses

4. fMRI Analysis

- changes in (BOLD) signal in areas involved in reward processing.
- nucleus accumbens, insula,, orbitofrontal cortex, dorsolateral prefrontal cortex (dlPFC).

Data Integration Considerations

- Use tools like ComBat to correct scanner differences and **harmonize neuroimaging data**.
- Address **compositionality, sequencing depth, and batch effects** in microbiome analysis with DESeq2, rarefaction, and normalization.
- Apply **dimensionality reduction** techniques like PCA to fMRI and microbiome data.
- Apply **FDR correction** methods to prevent false positives in brain region and microbiota analyses.

Analysis Plan

■ Perform quality control, filtering, taxonomic assignment, and quantify bacterial taxa in the gut microbiome.

■ Specific microbial taxas that differ between sexes and correlate with eating behavior scales

■ Linear mixed models to assess microbiota's influence on neuronal activity, with sex as an interaction term.

■ Confounders like age, diet, activity, medications, and hormones will be controlled as covariates, with sensitivity and subgroup analyses for robust findings.

Projected Outcomes

- Understanding how different interventions alter eating behaviors and gut microbiota in obese/overweight individuals.

- Identify specific microbiota profiles linked to improved eating behavior across interventions.

- Explore how microbiota profiles identified in the study impact neural areas associated with eating behavior across weight loss interventions.

- Detailed understanding of sex-specific differences.

References

1. Al-Najim, W., Docherty, N. G. & le Roux, C. W. Food Intake and Eating Behavior After Bariatric Surgery. Physiological Reviews 98, 1113–1141 (2018).
2. Gupta, A., Osadchiy, V. & Mayer, E. A. Brain-gut-microbiome interactions in obesity and food addiction. Nat Rev Gastroenterol Hepatol 17, 655–672 (2020).
3. Beyer, F. et al. Neuroanatomical correlates of food addiction symptoms and body mass index in the general population. Hum Brain Mapp 40, 2747–2758 (2019).
4. Beyer, F. et al. Weight loss reduces head motion: Revisiting a major confound in neuroimaging. Hum Brain Mapp 41, 2490–2494 (2020).
5. Bolyen, E. et al. Reproducible, interactive, scalable and extensible microbiome data science using QIIME 2. Nat Biotechnol 37, 852–857 (2019).
6. Medawar, E., Beyer, F., Thieleking, R., Haange, S. B., Rolle-Kampczyk, U., Reinicke, M., Chakaroun, R., von Bergen, M., Stumvoll, M., Villringer, A., & Witte, A. V. (2024). Prebiotic diet changes neural correlates of food decision-making in overweight adults: a randomised controlled within-subject cross-over trial
7. Medawar, E. et al. Gut microbiota link dietary fiber intake and short-chain fatty acid metabolism with eating behavior. Transl Psychiatry 11, 1–11 (2021).
8. Martinou, E., Stefanova, I., Iosif, E. & Angelidi, A. M. Neurohormonal Changes in the Gut–Brain Axis and Underlying Neuroendocrine Mechanisms following Bariatric Surgery. Int J Mol Sci 23, 3339 (2022).
9. Vartanian, M., Endres, K. J., Lee, Y. T., Friedrich, S., Meemken, M.-T., Schamarek, I., Witte, A. V. (2024). Investigating the Impact of Microbiome-Changing Interventions on Food Decision-Making: MIFOOD Study Protocol
10. WHO European Regional Obesity Report 2022. (WHO European OrganizatiWorld Health Organization. Regional Office for Europeon. Regional Office for Europe, 2022).