EXPLORING ENVIRONMENTAL EFFECTS ON MOLECULAR OUTPUTS IN PRECLINICAL AND CLINICAL SETTING OF ANOREXIA NERVOSA AND OBESITY

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Introduction and Aims

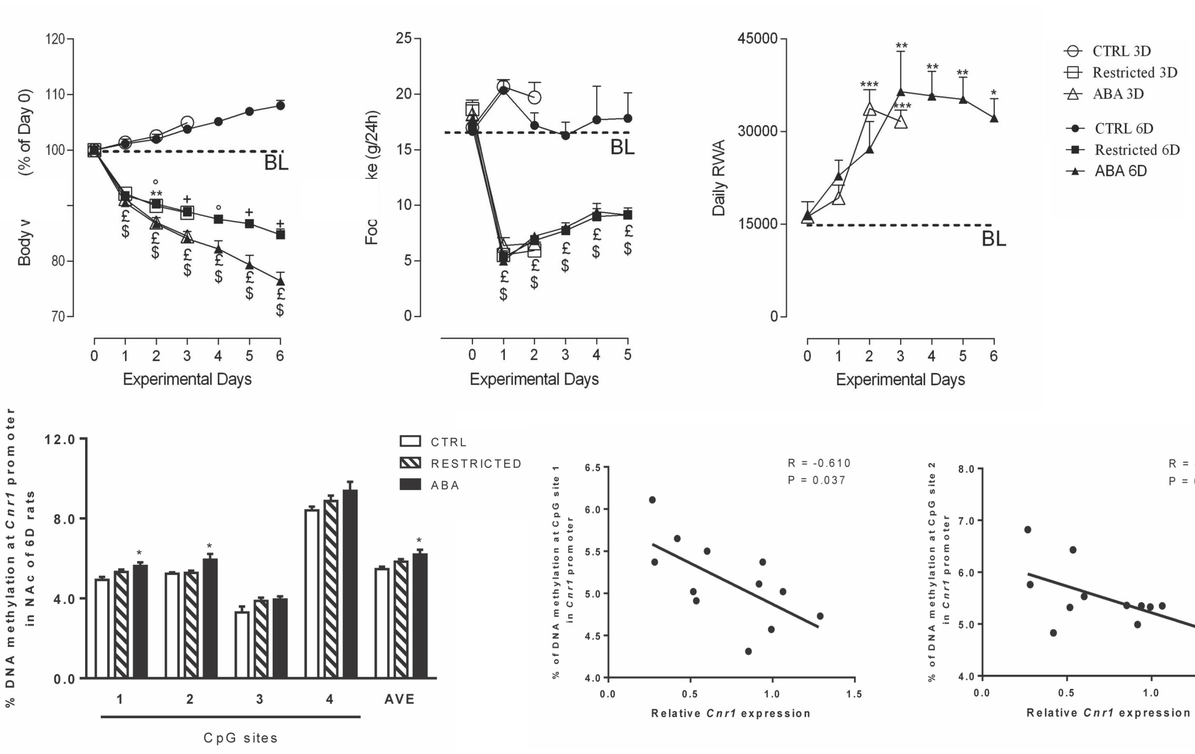
Anorexia nervosa (AN) is a psychiatric disorder characterized by dieting-induced reduced caloric intake and fears of gaining weight, often accompained by over-exercise [1]. On the other side of the scale, another disease characterized by imbalance between energy intake and expenditure is obesity, where disturbance of eating habits and inability to control body weight lead to excess body fat [2]. Both of these conditions are complex neurological disorders of homeostatic and rewarding mechanisms with widespread metabolic consequences. Environment and heritability factors contribute to individual´s vulnerability for development of these conditions, and due to the lack of existing effective therapeutic strategies, a therapeutic approach based on environmental factors is emerging [3].

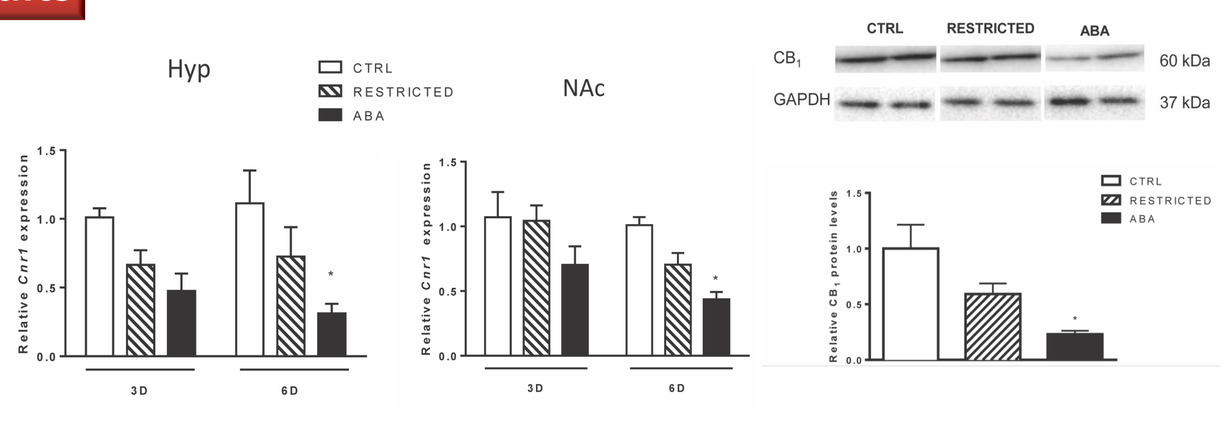
Conclusions

- ✓ preclinical and clinical evidence of a ***selective, opposite and time-dependent regulation of Cnr1*** expression in anorexia nervosa and obesity via epigenetic mechanisms
- ✓ differences in behavioral and genetic contribution to anorexia nervosa onset and development
- ✓ central role played by ***Cnr1 in food intake and its possible relevance as biomarker***
- ✓ ***new avenue for environmental strategies of intervention*** due to the reversible nature of the epigenetic hallmark

Results

Anorexia nervosa: ABA rat model





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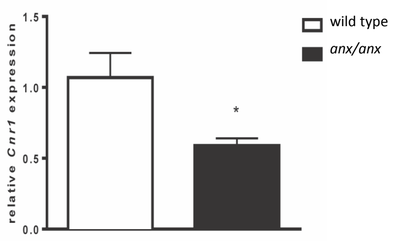
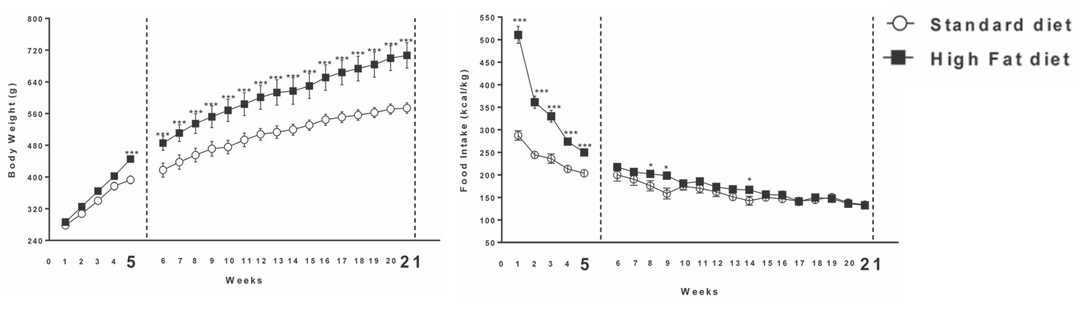
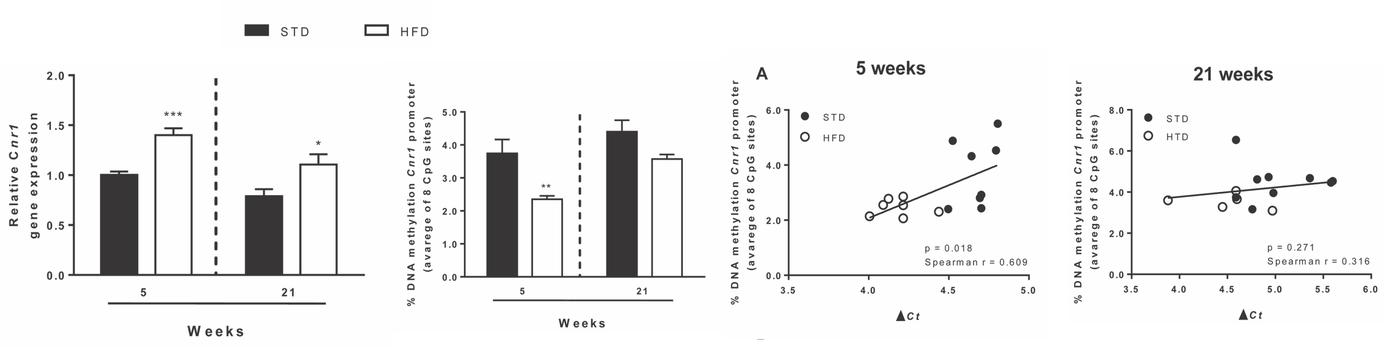
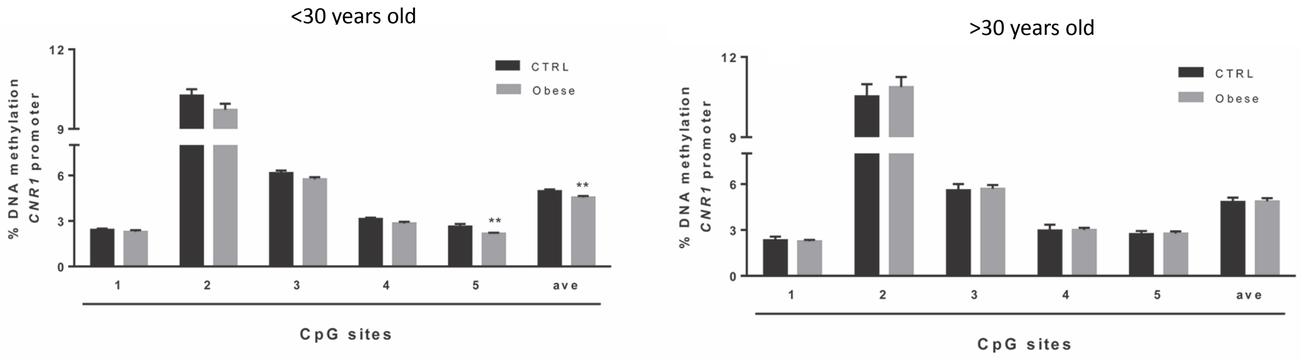


Obesity: DIO rat model and human PBMCs







Methods

Animal experiments or collection of human samples

- Activity-based anorexia (ABA) rat model
- Diet-induced (DIO) obesity rat model
- Collection of PBMCs from obese human subjects

Sample preparation

- RNA and DNA extraction
- Isolated nucleic acids quality control

Gene expression studies

- Retrotranscription (cDNA synthesis)
- Quantitative real-time PCR
- Statistical analysis

DNA methylation analysis

- Bisulfite conversion of DNA
- PCR amplification and biotinylation of DNA
- Pyrosequencing
- Statistical analysis

References

1. Zipfel, S. *et al.* (2015) 'Anorexia nervosa: aetiology, assessment, and treatment.', *The Lancet. Psychiatry*. England, 2(12), pp. 1099–1111. doi: 10.1016/S2215-0366(15)00356-9.
2. Gonzalez-Muniesa, P. *et al.* (2017) 'Obesity.', *Nature reviews. Disease primers*. England, 3, p. 17034. doi: 10.1038/nrdp.2017.34.
3. Hubel, C. *et al.* (2019) 'Epigenetics in eating disorders: a systematic review.', *Molecular psychiatry*. England, 24(6), pp. 901–915. doi: 10.1038/s41380-018-0254-7.

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