The effect of diet-induced obesity on serotonergic enteric neurons in zebrafish

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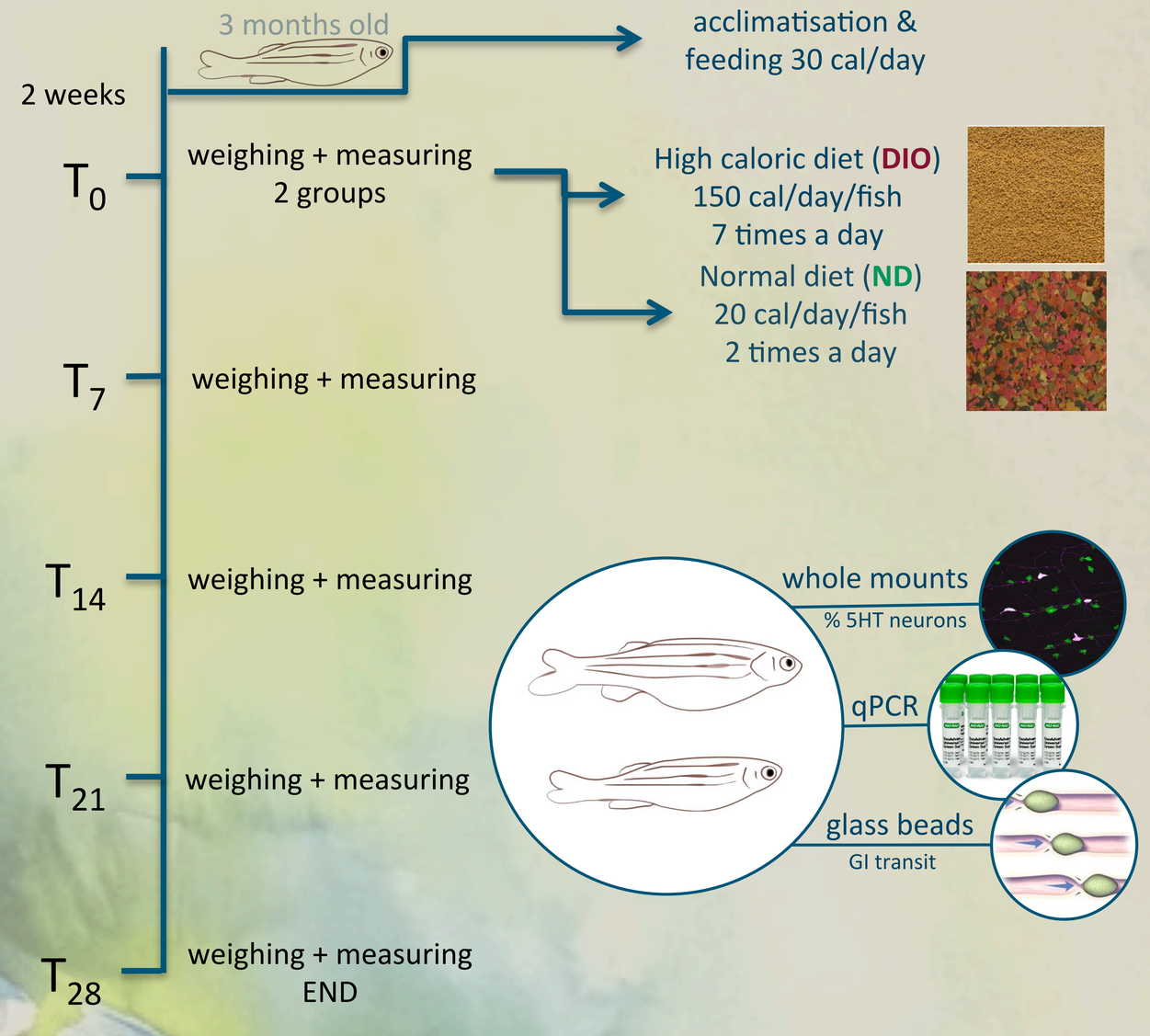
INTRODUCTION

Obesity is a worldwide epidemic and a major risk factor for numerous diseases including cardiac failure, diabetes and cancer. Obesity shows an increasing prevalence demanding for new treatment options and prevention measures. The regulation of feeding behavior and body weight depends on a wide range of neuronal pathways influencing satiety and hunger. Serotonin is one of those players identified to have a profound effect on the energy homeostasis. In the enteric nervous system, serotonin initiates peristalsis and is involved in secretion. At present, biomedical research is predominantly based upon experimental animal models. Recently also zebrafish swam into the spotlights. These fish are characterized by rapid development, easy handling and a high degree of genetic and molecular resemblances for the majority of diseases, including obesity.

AIM

The aim of the present study was to investigate the effect of diet-induced obesity on gastrointestinal (GI) motility and the expression of serotonin in the GI tract.

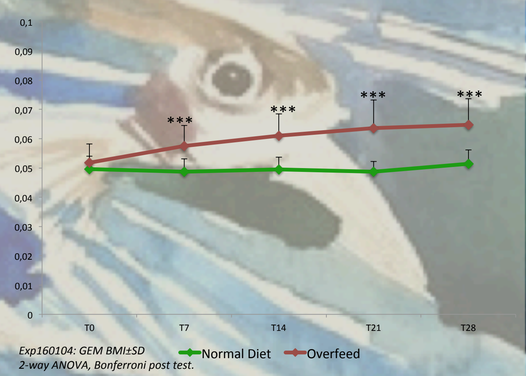
MATERIALS AND METHODS



RESULTS

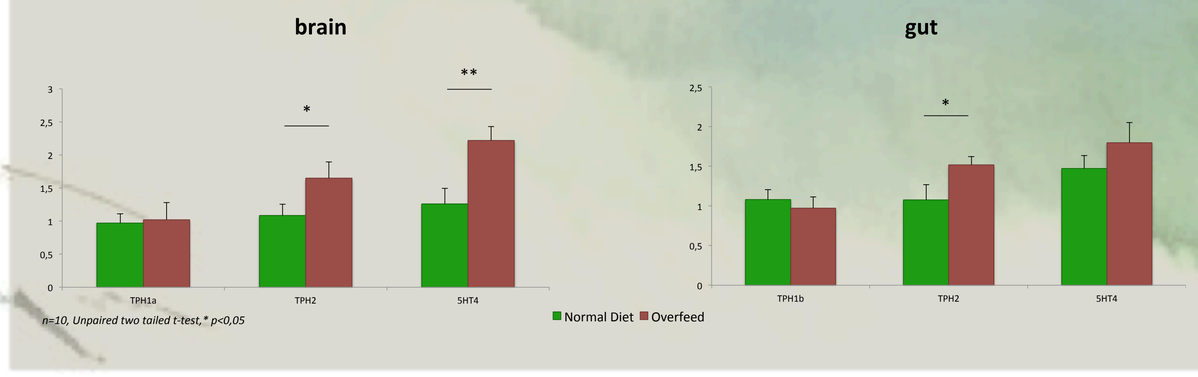
Diet induced obesity

Initially the BMI of OF and ND fish were equal. After 4 weeks overfeeding, the BMI of DIO fish increased significantly, but not of ND fish. The BMI was significantly higher in DIO fish compared to ND fish during the weekly weighing.



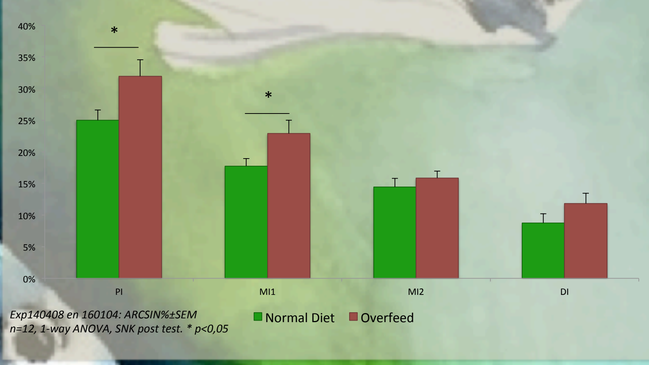
Expression of TPH1a/b, TPH2 and 5HT4R

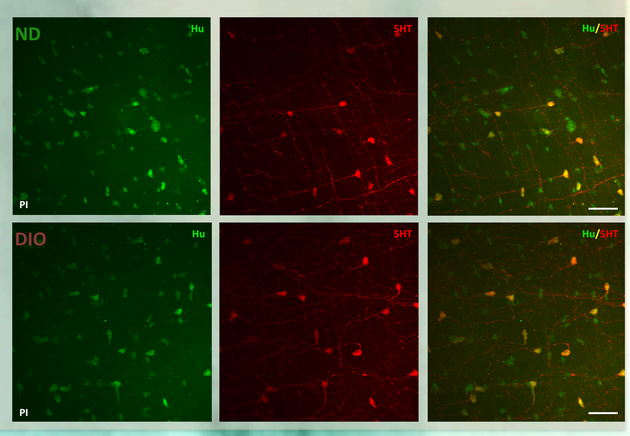
qPCR revealed significant elevated levels for TPH2 in brain and intestine, but not for TPH1a/b. Furthermore, a significant increase in the expression of the 5-HT_4 receptor was observed in brain, but not in the intestine.



Serotonergic neurons

Overfeeding increased the proportion of serotonergic neurons in the PI and MI1, but not in MI2 and DI.



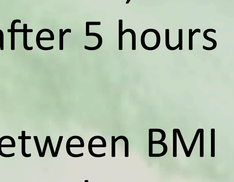


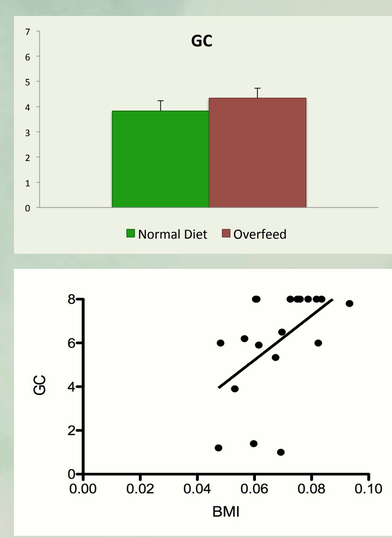
GI transit

GI transit was calculated as the geometric center (GC) for 6 different intestinal regions and the faeces.

Preliminary experiment showed a small, but not significant, increase in the GC after 5 hours in DIO fish compared to ND.

There was a positive correlation between BMI and DIO fish for the GC after 5 hours, but not for the ND.





CONCLUSION

In the present study, analysis of the GI tract of DIO fish revealed an increase of 5-HT expression in enteric neurons in the proximal part of the intestine, which is probably due to an increased TPH2 expression in the intestine, resulting in increased GI transit. Furthermore, DIO revealed increased expression of 5-HT4 receptor in the brain but not in the gut, suggesting other receptors to be involved. These data obtained from zebrafish are in line with earlier findings in (some) mammalian models. Given the faster developmental features, the zebrafish offers additional perspectives for obesity research.

List of abbreviations:
5-HT: serotonin; 5-HTR: 5-HT receptor; BMI: body mass index; DI: distal intestine; DIO: diet induced obesity; ENS: enteric nervous system; F: feces; FL: flexura; GC: geometric centre; GI: gastrointestinal; IR: immunoeactivity; MI: mid intestine; ND: normal diet; PI: proximal intestine, TPH: tryptophan hydroxylase

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