Petrelintide (ZP8396) selectively reduces intake of high fat diet in DIO rats

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Introduction & Objective

- The obesity pandemic is a major health crisis and there is a need for effective pharmacotherapies.
- Overconsumption of highly palatable food is associated with obesity.
- Petrelintide (ZP8396), a novel once-weekly amylin analog currently in phase 1 clinical testing, has shown to induce meaningful reductions in body weight in lean and overweight subjects.
- Here we investigate the effect of petrelintide on food preference in diet-induced obese (DIO) rats to determine whether petrelintide holds the potential to address overconsumption of highly palatable food in humans.

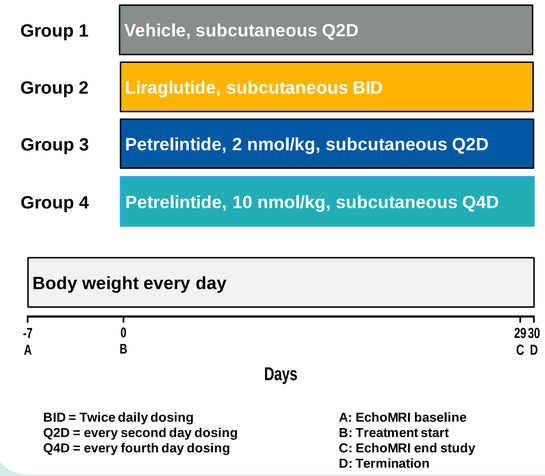
Methods

- DIO rats were given *ad libitum* access to both standard rodent chow diet and high fat diet during a 30-day treatment period.
- Animals (n=10 per group) were treated with either vehicle (every second day), liraglutide (5 nmol/kg twice daily) or petrelintide (2 nmol/kg every second day or 10 nmol/kg every fourth day).
- Body weight, chow intake and high fat diet intake were measured daily.

Results

- Treatment with liraglutide and petrelintide resulted in significant lower relative body weight compared to vehicle (3.3 % ± 0.7 vehicle, -0.1 % ± 1.1 liraglutide, -4.1 % ±0.6 petrelintide 2 nmol/kg, -7.8 % ± 0.7 petrelintide 10 nmol/kg; relative to initial body weights ± SEM).
- Treatment with petrelintide resulted in significant reduction of total cumulative intake of high fat diet compared to vehicle, in contrast to liraglutide (834 g ± 31.1 vehicle, 796 g ± 25.6 liraglutide, 646 g ± 22.3 petrelintide 2 nmol/kg, 576 g ± 17.4 petrelintide 10 nmol/kg; g ± SEM).
- No change in total cumulative intake of chow was observed in any groups compared to vehicle.

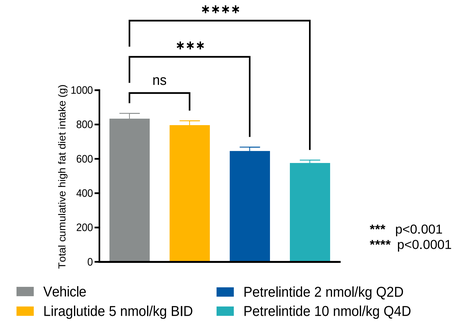
Study design



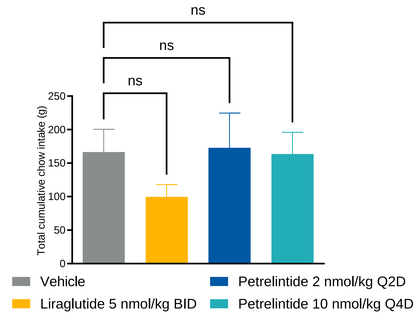
BID = Twice daily dosing
Q2D = every second day dosing
Q4D = every fourth day dosing

A: EchoMRI baseline
B: Treatment start
C: EchoMRI end study
D: Termination

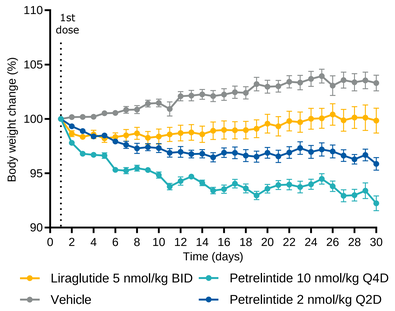
High fat diet intake



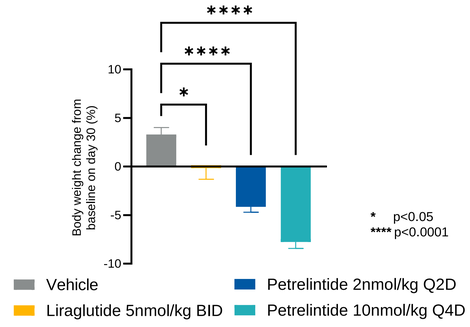
Chow intake



Change in body weight



Change in body weight at day 30



Conclusions

- Petrelintide reduces food intake and body weight in DIO rats primarily by lowering intake of high fat diet.
- Based on these findings, petrelintide might hold the potential to address overconsumption of highly palatable food in humans.
- Petrelintide is currently being explored in a phase 1 trial to assess the potential for the management of obesity.