Semaglutide and exercise synergy in obesity: preserving muscle mass and uncovering organ crosstalk

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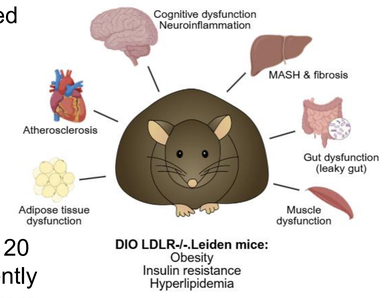
1. Background & aims

Semaglutide, a glucagon-like peptide-1 receptor agonist, is an antidiabetic medication that has recently been approved for treatment of obesity as well. While the benefits of semaglutide for weight management are encouraging, concomitant muscle loss can be a potential drawback.

Here, we evaluated the metabolic effects of semaglutide, exercise and the combination thereof in a translational model of obesity and Metabolic Syndrome to explore associated multi-organ complications.

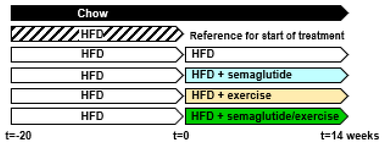
2. Methods & study design

Ldlr-/-.Leiden mice are used as a model for metabolic dysregulation with development of several comorbidities when fed a high fat diet (HFD).

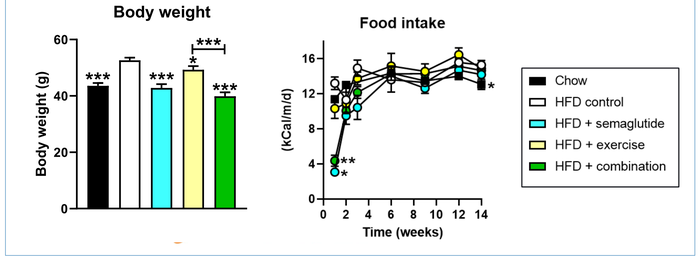


In the current experiment mice were fed the HFD for 20 weeks and were subsequently left untreated (control) or were treated for 14 weeks with semaglutide, exercise (running-wheel) or the combination thereof.

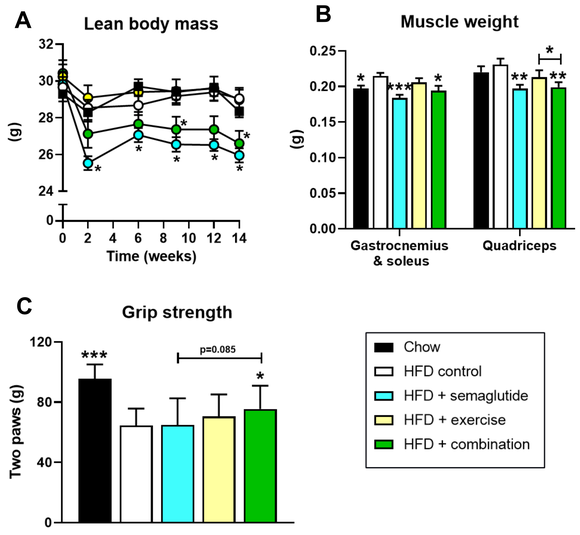
(n=8 chow mice; n=15 HFD mice/group)



3. Semaglutide decreased body weight and transiently decreased food intake

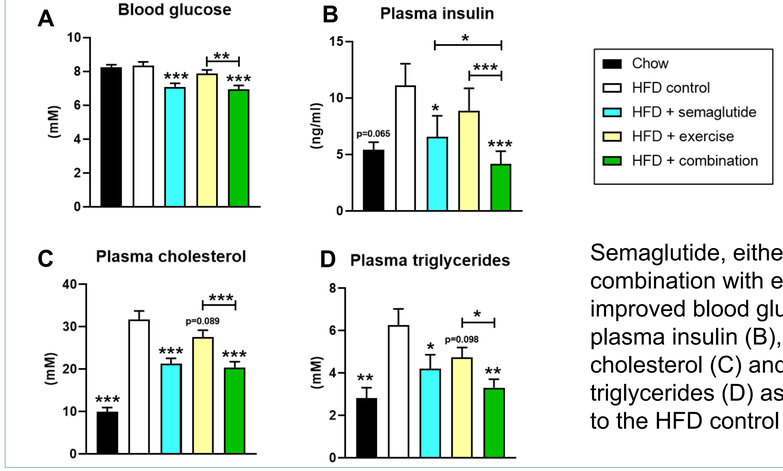


4. Semaglutide, either alone or in combination with exercise, decreased lean body mass and muscle weights



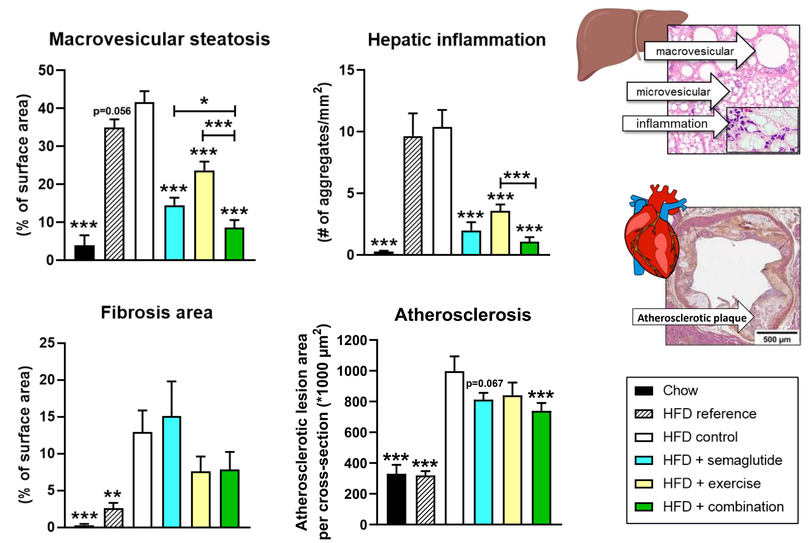
A. Lean body mass was decreased with semaglutide treatment and as well, but to a lesser extent, when combined with exercise.
B. Muscle weights at sacrifice were significantly decreased as compared to HFD control group with semaglutide treatment, and also when combined with exercise.
C. Absolute grip strength was improved as compared to HFD control group in combination treatment group only.

5. Semaglutide, either alone or in combination with exercise, improved metabolic parameters



Semaglutide, either alone or in combination with exercise, improved blood glucose (A), plasma insulin (B), plasma cholesterol (C) and plasma triglycerides (D) as compared to the HFD control group.

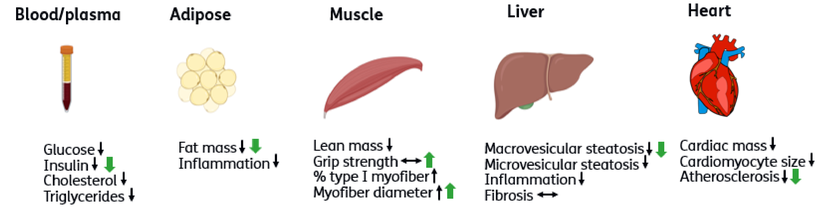
6. Liver steatosis and inflammation improved with all interventions, atherosclerosis in combination group



7. Conclusion

Using a translational model of obesity and the Metabolic Syndrome, we demonstrated that:

- **Semaglutide** has broad beneficial effects on metabolic risk factors, adipose tissue, liver and cardiac parameters.
- Semaglutide decreases lean body mass and muscle mass.
- **Adding exercise** to semaglutide intervention further improved plasma insulin, fat mass, muscle strength, liver steatosis and atherosclerosis.



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