underwent two 2-hours sessions in a hyperbaric chamber of once with application of 100% oxygen (1.4 bar over atmospheric pressure [barO]; HBO) and once with ambient air as placebo (21% oxygen; 1.4 barO; PLC). Tissue-specific insulin sensitivity was assessed by hyperinsulinemic-euglycemic clamps with stabile [$^2H_2$]glucose isotope dilution, while muscle oxygen fluxes were measured with high resolution respirometry. After HBO treatment, hepatic insulin sensitivity was higher (insulin-mediated suppression of glucose production: 71 ± 2% vs. PLC 60 ± 3%, $p < 0.05$), whereas peripheral insulin sensitivity was comparable (2.4 ± 0.6 vs. 3.4 ± 1.7 $mg*kg^{-1}*min^{-1}$, $p = 0.15$). Muscle ROS production markedly increased (+71 ± 3% vs. PLC −29 ± 5%; $p < 0.005$), while mitochondrial oxidative capacity tended to be lower after HBO (n.s.). In conclusion, a single session of HBO treatment already improves hepatic insulin resistance and stimulates muscle ROS release, which could activate antioxidative defense and contribute to improvement of glycemia during chronic treatment.

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Short and Long-Term Effects of High Intensity Interval Training on Intrahepatic Lipid and Visceral Adipose Tissue in Cardiac Rehabilitation Patients

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Introduction: We aimed to compare the effects of high intensity interval training (HIIT) with moderate intensity continuous training (MICT) on intrahepatic lipid (IHL) and visceral adipose tissue (VAT), in cardiac rehabilitation (CR) patients.

Methods: CR patients with coronary artery disease (Age: 63 ± 11; body mass index: 27.3 ± 5.3 kg/m^2; IHL: 5.8 ± 6.4%; VAT volume: 3251 ± 1620 cm^3; 32 males, 8 females) were randomised to three sessions/week of either HIIT (n = 18): 4 x 4 minute high intensity intervals at a rating of perceived exertion (RPE) 15–18/20 interspersed with 3 minute active recovery periods, or, MICT usual care (n = 23): 40 minutes moderate intensity continuous exercise at an RPE 11–13/20, for 4-weeks. Participants then continued with 3 home-based sessions/week for a further 11 months. IHL and VAT were measured via ^{1}H-MRS and MRI, respectively (3T Magnetom Prisma) at baseline, 3- and 12-months. Data are presented as mean (95% CI).

Results: There was a significant ($p < 0.05$) effect of time over 3 months for reductions in IHL [HIIT: −2.8%(−1.6 to −4.1); MICT: −1.4%(−0.3 to −2.5)] and VAT volume [HIIT: −327 cm^3 (−99 to −555); MICT: −456 cm^3 (−248 to −664)]. After 12 months both groups further reduced VAT [HIIT: −545 cm^3 (−322 to −767); MICT: −521 cm^3 (−308 to −734)], however only HIIT maintained improvement in IHL [HIIT: −2.4%(−1.0 to −3.7), MICT: −1.1%(0.1 to −2.3). There were no serious adverse events related to the exercise interventions. No differences were found for energy intake.

Conclusion: HIIT provides long-term clinically meaningful reductions in VAT and IHL in CR patients. MICT provides long-term reductions in VAT but only short-term reductions in IHL.

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Namodenoson Anti-NAFLD/NASH Activity Is Mediated via De-Regulation of the Wnt/β-Catenin Pathway

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Background: The Wnt/β-catenin pathway confers a chain of molecular events in the liver of non-alcoholic steatohepatitis (NASH). Namodenoson is a selective agonist at the A3 adenosine receptor (A3AR), highly expressed in pathological liver cells. Namodenoson induces a robust anti-inflammatory and anti-cancer effects in the liver via de-regulation of the Wnt/β-catenin pathway.

Methods: Hepatic fibrosis model was induced in C57BL/6 mice by CCl4 injections for 6 weeks. Namodenoson 100 μg/kg was administered orally 24 hours after CCl4 injections. At termination, liver enzyme levels were determined and liver tissue was subjected to pathological and western blot (WB) analysis. LX2 cells were incubated with namodenoson (10 nM) and the A3AR antagonist MRS 1523 (50 nM). Proliferation, mRNA and WB analysis assays were performed.

Results: Liver enzymes were markedly increased in the CCl4 group and was markedly decreased and reached normal values following namodenoson treatment (ALT: 8747 ± 1785 vs. 203 ± 66 IU/L; AST: 11,261 ± 2205 vs. 152 ± 93 respectively). De-regulation of the Wnt/β-catenin pathway took place in the namodenoson treated livers, manifested by an increase in GSK-3β, and β-catenin and cyclin D1 decrease. Moreover, mRNA α-SMA levels were decreased upon namodenoson treatment, demonstrating the anti-fibrogenic effect of the drug. Namodenoson inhibited LX-2 proliferation with similar modulation of signaling proteins as demonstrated in the CCL4 liver extracts, supporting the involvement of the Wnt/β-catenin pathway in the anti-NASH effect.

Conclusions: Upstream targeting of the PI3K-Wnt pathways with namodenoson yields an effective anti-NASH effect both in vitro and in vivo, positioning this compound as a drug candidate to combat this liver pathological condition.