Abstracts

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Explaining the association between screen time and overweight in 4-12 year old children

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Objective: Watching TV and computer use are associated with childhood overweight, but it remains unclear whether interventions should focus on these behaviours directly, or on associated determinants that may explain these associations.

Methods: Our cross-sectional study among 4,072 children aged 4-12 years in the city of Zwolle, the Netherlands examined to what extent the associations of watching TV and computer with overweight were explained by other determinants of overweight, by use of logistic regression analyses. Child's body height and weight were measured, and parental questionnaires included socio-demographic characteristics, child's nutrition, physical activity and sedentary behaviour.

Results: Odds ratio for being overweight was 1.4 (95%-CI:1.1-1.8) for watching more than >2 hours per day and reduced to 1.2 (95%-CI:0.9-1.6) after adjusting for socio-economic status, parents' BMI and number of TV's in the household. The odds ratio for being overweight was 1.6 (95%-CI-1.1-2.3) for using the computer >2 hours and reduced to 0.9 (95%-CI:0.5-1.7) after adjusting for parents' BMI, drinking >3 sugared drinks per day, socio-economic status, number of computers in the household and rules on using the computer.

Conclusion: This epidemiologic study confirms suggestions from pedagogic studies. Interventions on reducing TV time in order to reduce obesity should target parents and number of TV's in the household as they explain an important part of the association between viewing TV and childhood overweight. Sugared drinks, number of computers and setting rules on computer use are important targets for prevention as they, with socio-economic status, explained the association between computer use and overweight completely.

Postweaning resistance to fat/sucrose (FS) diet-induced metabolic derangements in mice selectively bred for increased running wheel activity can be overruled by maternal FS overfeeding

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Introduction: Epidemiological surveys and animal studies have shown that feeding a western-type high fat/sugar (FS) diet during the perinatal stage could augment the proneness to FS diet-induced obesity and co-morbidities later in life. In the present study, we investigated whether and how a trait for physical activity might offer resistance to this fetal programming effect.

Methods: Female and male mice from the CD-1 strain, or from two strains originally obtained from the CD-1 ancestral line, but selectively bred for increased wheel running behavior for 52 generations were subjected after weaning to an FS diet or a healthy control diet low in fat and complex carbohydrates until 10 months of age. They were born from mothers, which were feeding during pregnancy and lactation either a FS diet or a C diet.

Results: Compared to controls, activity selected females, but not activity selected males are resistant to perinatal or post-weaning FS diet-induced obesity. However, the combination of these dietary treatments did produce strong (visceral) adiposity in females. With respect to hyperinsulinemia, the opposite effects were found, with activity selected males, but not females, being resistant to perinatal or post-weaning FS diet induced hyperinsulinemia, but not in the combined dietary treatment.

Conclusion: Postweaning resistance to FS-induced adiposity in female mice, and postweaning resistance to FS-induced hyperinsulinemia in male mice as a result of 52 generations of selection for increased running wheel activity can be overruled by maternal FS overfeeding.

Cue induced food craving in obesity: an fMRI study

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Introduction Overeating of high-caloric foods is thought to play a major role in the pathofysiology of obesity. It is of interest that overeating in obesity shares similarities with behavior observed in drug-addicted subjects, e.g. craving, impulsivity, compulsive behavior, and loss of control over intake. Craving for food is a consequence of an increased reactivity to food cues, especially high caloric foods. According to the addiction model of Koob and LeMoal this behavior is a result of dysregulation of the brain reward systems, which results in a hypoactive dopaminergic system and a hyperactive cortico-striato-thalamic (CST)-loop and stress system. There are indications that these mechanisms play a role in obesity and overeating and underlie food craving. This study aims to investigate whether obese people indeed show increased craving for food and a dysregulation of the brain reward systems for food and a dysregulation of the brain reward systems.

Methods 16 obese (BMI >30) and 14 healthy normal-weight (BMI 18-25) subjects were scanned on a 3.0T MRI scanner after a 3 hour fasting period. Gradient-echo echo-planar images were acquired to measure BOLD signal changes for all subjects while performing a cue exposure task with high-caloric food pictures and neutral pictures. Data were analysed in SPM8.

Results Obese subjects showed activation on the high caloric food pictures in the anterior cingulate cortex (ACC), orbitofrontal cortex (OFC), caudate nucleus, amygdala, hippocampus, and superior medial frontal cortex. The control subjects only showed activation in the hippocampus and parahippocampus. The activation on the food pictures was significantly higher in the obese subjects compared to controls in the ACC, OFC, caudate nucleus, and putamen. Moreover, in the obese subjects there were correlations between BMI and activation in the amygdala, hippocampus, thalamus and putamen, while in the control group there were correlations between BMI and activation in the insula and posterior cingulate cortex. Also, the increase change in feeling liking eating before and after the scan was positively correlated with activation in the OFC, insula, thalamus and temporal cortex.

Conclusion Obese subjects show an increased reactivity to food cues and attribute a larger emotional valence to the food pictures than control subjects. This effect is BMI related, i.e. the more obese subjects are more reactive to food cues. Thus, obese subjects show increased craving for food and similar dysregulation of the brain reward systems as in addiction.

PUFA acutely decreases muscle triacylglycerol-derived fatty acid uptake and increases postprandial insulin sensitivity

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Introduction: Increased fat storage in 'nonadipose' tissues such as skeletal muscle is a strong indicator of insulin resistance. There are indirect indications that dietary fat quality may modulate muscle lipid oxidation and accumulation, resulting in a subsequent change in insulin sensitivity (S_I). The study objective was to examine acute effects of meals with various fatty acid (FA) compositions on skeletal muscle FA uptake and storage and postprandial S_I in obese insulin-resistant subjects.

Methods: In a single-blind randomized crossover study, 10 insulin-resistant men consumed 3 high-fat mixed meals (2.6 MJ). The meals were high in saturated FA (SFA) (35.5en% SFA, 18.8en% monounsaturated FA (MUFA) and 1.7en% polyunsaturated FA (PUFA)), high in MUFA (11.6en% SFA, 42.2en% MUFA and 4.6en% PUFA) or high in PUFA; 1:1 mix of n-3 and n-6 (14.4en% SFA, 11.9en% MUFA and 34.8en% PUFA). Fasting and postprandial skeletal muscle FA handling were examined by combining the forearm balance technique with the specific isotope labeling of endogenous and exogenous FA. [²H₂]-palmitate was infused intravenously to label endogenous triacylglycerol (TAG) and FFAs in the circulation and the meals contained [U-¹³C]-palmitate to label chylomicron-TAG. Areas under the curve (AUC) for glucose and insulin, and the product of AUC_{gluc} x AUC_{ins} x 10⁻⁶ (PGI) were used as indices of S₁.

Results: The PGI after the SFA meal was significantly higher as compared to the PUFA meal (p=0.027), with intermediate values for the MUFA meal. The total uptake of TAG-derived FA was significantly lower in the early postprandial phase after the PUFA meal (AUC₆₀₋₁₂₀, p<0.001) and tended to be correlated with PGI (r=0.602, p=0.086). The MUFA meal resulted in higher chylomicron-TAG concentrations (p=0.021), but there were no differences in TAG extraction by the forearm muscle, possibly suggesting a lower clearance by other tissues like adipose tissue.

Conclusion: The reduced uptake of TAG-derived FA by forearm muscle and the higher postprandial S_1 after a high PUFA meal may suggest that a reduced PUFA-induced muscle lipid accumulation might contribute to the higher postprandial S_1 .

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Polyunsaturated fatty acids acutely improve insulin sensitivity and may prevent mitochondrial dysfunction in skeletal muscle

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BACKGROUND: A high-fat, energy dense diet is associated with the development of insulin resistance and type 2 diabetes, however the quality of fat in the diet also plays an important role.

AIM: The aim of the current study was to investigate acute effects of meals with different fatty acid (FA) compositions on insulin sensitivity (IS) and gene expression profiles of skeletal muscle.

DESIGN: In a single-blind randomized cross-over trial, 10 obese insulin resistant men consumed 3 meals (2.6 MJ, 61en% fat), which consisted of saturated FA (SFA, 35.5en%), monounsaturated FA (MUFA, 42.2en%) and a mix (1:1) of n-3 and n-6 polyunsaturated FA (PUFA, 34.8en%). Skeletal muscle biopsies were obtained before and 4h after consuming the meal for whole-genome microarray analysis and plasma samples were collected during this period.

RESULTS: Postprandial glucose and insulin concentrations were significantly lower after the PUFA meal as compared to the SFA meal (iAUC_{gluc} p<0.001 and iAUC_{ins} p=0.005). This may indicate higher postprandial IS after the PUFA meal. The strongest regulated pathways after consumption of the SFA and MUFA meal were ubiquinone biosynthesis, mitochondrial dysfunction and oxidative phosphorylation, which consisted of genes involved in complex I-V of the respiratory chain. Consumption of the SFA meal resulted in significantly decreased expression of 33/96 OXPHOS genes, while 28/96 genes were downregulated after the MUFA meal and only 7/96 after the PUFA meal.

CONCLUSIONS: Replacement of SFA by PUFA in the diet may improve IS. OXPHOS genes were less downregulated after the PUFA meal, which suggests a better mitochondrial function.

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Weight loss-induced disproportional Basal Metabolic Rate reduction is not sustained during weight maintenance

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Introduction: Weight loss due to a negative energy balance is considered to be accompanied by a disproportional reduction of basal metabolic rate (BMR). The aim of this study was to investigate whether the disproportional decrease of BMR is sustained during weight maintenance.

Methods: Subjects were 8 men and 33 women (age: 40 ± 10 years, BMI: 31.7 ± 2.7 kg/m2). The subjects followed a very low energy diet (VLED) for two months, followed by a three-month period of weight maintenance (WM) under free-living conditions. Body composition was assessed using deuterium dilution and the BodPod System (Life Measurement Corporation); BMR was measured (BMRm) with a ventilated hood. Measurements took place before the subjects started the diet, after the diet and after WM. In addition BMR was predicted (BMRp) based on body composition.

Results: Body mass decreased significantly during the VLCD-period (-9.1 ± 4.4 kg, P<0.001) and this reduction was sustained after the three-month WM period (-8.2 ± 4.8 kg, P<0.001). BMRm decreased from 7.11 ± 0.82 MJ/d before the diet to 6.47 ± 0.69 MJ/d after the diet (P<0.001) and restored again after WM to 6.95 ± 0.99 MJ/d (P<0.001). The ratio measured vs. predicted decreased from 0.99 ± 0.08 before the diet to 0.96 ± 0.09 after the diet (P<0.001) and increased to 1.01 ± 0.09 after WM (P<0.001).

Conclusion: Moderate weight loss results in a disproportional reduction of BMR, however this reduction is not sustained for more than three months.

Brown adipose tissue function before and after major weight loss following bariatric surgery

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Introduction: Brown adipose tissue (BAT) can dramatically increase energy expenditure. Therefore, manipulating BAT activity could be a new target to fight obesity and type II diabetes. Morbidly obese subjects report an increased cold sensitivity after weight loss established by bariatric surgery, suggesting adjustments in cold response. Therefore, we hypothesize that BAT activity increases after bariatric surgery.

Methods: Fifteen subjects awaiting bariatric surgery were included (BMI 42.1±3.8 kg/m², body fat 48.5±4.5%). PET-CT-imaging was performed to determine BAT activity by uptake of FDG. Therefore, all subjects underwent an individually attuned cooling protocol. Currently, one year after weight loss, measurements are repeated.

Results: Three morbidly obese, female subjects showed BAT activity after cold stimulation. Combined data from the current and our previous study showed strong correlations between BAT activity and body composition (P<0.001). Cold-induced thermogenesis (CIT) increased significantly within the BAT-positive (n=26) compared to BAT-negative subjects (n=13) (+15.5±8.9% versus +3.6±8.9%, P=0.001). One year after surgery the excess BMI loss (%EBMIL) was 74.3±20.5% (P<0.001). Currently, BAT activity is re-determined to explore if BAT recovers after weight loss. These results will soon be available and presented at the congress.

Conclusion: BAT activity after cold stimulation was only present in 20% of morbidly obese subjects, compared to 96% in our previously studied lean and obese group. BAT is inversely related to body composition (P<0.001). BAT-positive subjects show significant CIT (P=0.001), suggesting BAT is responsible for energy dissipation during cold exposure. Therefore, manipulating BAT activity could be a therapeutic target to burn off excess energy stores in obesity.

Evaluation of an 18-month obesity treatment programme

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Background: The Center for Obesity Europe (CO-EUR) is an obesity treatment center in the Netherlands. CO-EUR uses a multi-disciplinary approach to treat people with obesity. Its 18 months treatment programme consists of psychological counseling, dietary advice and a physical activity programme. Every 3 months a medical check-up is conducted. This study evaluates the 18-month results of the CO-EUR multi-disciplinary treatment programme.

Methods: Subjects with BMI > 30 kg/m² and > 18 years old are included in the programme and the 18-mointh results of the first 132 subjects have been analysed. An intention-to-treat (n= 132) and completers (n=94) analysis was conducted on the three monthly medical check-up data (up to 18 months) with respect to body weight, waist circumference (WC) and blood pressure (BP).

Results: 33.3% of the 132 subjects are male. Mean±SD age was 46.3 ± 12.4 y and mean BMI was 42.1 ± 6.3 kg/m². Males had significantly higher WC (137.3 ± 12.6 vs. 128.7 ± 14.3 cm) and DBP (90.5 ± 11.3 vs. 85.3 ± 9.5 mmHg) at intake compared to females (P < .01). 34 subjects left the programme before month 18 (26%). The completers significantly reduced weight ($7.9\pm8.9\%$), BMI ($10.9\pm14.6\%$), WC ($7.9\pm9.9\%$), and SBP ($7.2\pm18.9\%$) after 18 months of treatment (P at least < .01). Intention-to-treat analysis showed a reduction of weight by $6.4\pm9.9\%$ BMI by $8.9\pm15.4\%$, WC by $7.4\%\pm10.7\%$ and SBP by $5.4\pm21.3\%$ (P at least < .01).

Conclusions: This multi-disciplinary obesity treatment program significantly reduces body weight and waist circumference and improves blood pressure in obese subjects (BMI > 30 kg/m^2) over 18 months.

Socio-cultural determinants of overweight in female Moroccan migrants in the Netherlands and their compatriots in Morocco: a qualitative study

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Introduction: High rates of obesity and related diseases such as type 2 diabetes are common among non-western migrants to western countries and insight into the underlying determinants is necessary for the development of targeted interventions. This qualitative study aimed to explore the socio-cultural determinants of body weight and weight-related behavior in non-western migrant women. We focused on women of Moroccan origin, one of the largest non-western migrant groups in Europe; we aimed to gain insight into the influences underlying overweight in migrants by enriching their perspectives with those of their compatriots in Morocco.

Methods: Eight focus groups were conducted among women: four in Amsterdam, The Netherlands, two in the city of Al Hoceima, Morocco, and two in rural locations in northern Morocco.

Results: Migrant women perceived that overweight arose predominantly because of their intake of traditional foods, while women in Morocco perceived that migration-related changes in eating habits were the culprit. The women appeared to be ambivalent regarding their preferred body size, most expressed a preference for thinness while discussing that, within their communities, this is viewed as a sign of psychological, economic and social problems.

Discussion: Migrants appear to ascribe overweight to their socio-cultural traditions rather than to the obesogenic environment that is a result of migration to a Western society. We discuss how this generates ambivalence regarding body weight and its implications for the development of interventions to prevent or treat overweight.

NPY sensitivity in an animal model of diet induced obesity

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Background Neuropeptide Y (NPY) is a hypothalamic hunger peptide, which is downregulated upon food ingestion. Interestingly, rats on a free choice high-fat high-sugar (fcHFHS) diet for 1 week show increased NPY mRNA levels despite profound hyperphagia. Rats given the choice between fat and chow (fcHF) also overeat, but show decreased NPY levels. After 4 weeks, NPY mRNA levels in both rats on a fcHF or fc HFHS diet are similar to those in rats on chow. However, only rats on fcHFHS diet remain hyperphagic. As mRNA levels do not explain the sustained hyperphagia, we hypothesize that the NPY sensitivity is increased in fcHFHS over the course of 4 weeks.

Methods Rats were subjected to a chow, fcHF or fcHFHS diet for 4 weeks. After 1 and 4 weeks, rats received an intracerebroventricular (ICV) injection of NPY or vehicle. Total caloric intake and individual food components (chow, fat and sugar) were determined 2 hours after ICV injection.

Results After 1 week diet both fcHF and fcHFHS groups overate and showed increased responsiveness to NPY compared to chow. After 4 weeks only fcHFHS remained hyperphagic and showed increased responsiveness to NPY compared to fcHF and chow. Moreover, in rats on fcHFHS, NPY mainly increased the preference for lard and chow, but not sugar after 1 and 4 weeks on the diet.

Conclusion The higher NPY responsiveness in rats on a fcHFHS diet explains their hyperphagic behavior and may result from increased NPY receptor availability since NPYmRNA levels were not increased. Interestingly, NPY increased the hedonic fat component as well as the healthy chow component of the fcHFHS diet.

Hypothalamic neuropeptide Y controls the hepatic secretion of VLDL triglycerides in rats via the sympathetic nervous system

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Introduction: During fasting neuropeptide Y (NPY) neurons in the mediobasal hypothalamus are activated to increase food intake and to conserve energy. Under conditions of food deprivation, lipid metabolism plays an important role in providing fuel for muscle. We investigated whether increased hypothalamic NPY during fasting stimulates hepatic VLDL triglyceride (VLDL-TAG) secretion via the autonomic nervous system.

Methods: We measured VLDL-TAG secretion in Wistar rats after an intravenous bolus of tyloxapol to inhibit uptake of triglycerides by peripheral tissues. In the absence of chylomicrons from the gut, the increase in plasma triglycerides reflects VLDL-TAG secretion by the liver. First, we investigated the effects of overnight fasting (19h fast) in sham, parasympathetic, sympathetic, or total liver-denervated animals.

Results: We report that, in fasted rats, an intact hepatic sympathetic innervation is necessary to maintain VLDL-TAG secretion. Secondly, we demonstrated that in post-prandial animals an intact hepatic sympathetic innervation is necessary to mediate the stimulatory effect of intracerebroventricular administered NPY (1 μ g/ μ L; bolus 5 μ L/5 min, followed by 5 μ L/h) on VLDL-TAG secretion. Finally, rats with a diminished hypothalamic NPY release, due to neonatal monosodium glutamate (MSG) treatment, cannot maintain VLDL-TAG secretion during fasting. Exogenous NPY, however, is still able to increase VLDL-TAG secretion in these animals.

Conclusions: Our findings show that the increased release of NPY during fasting stimulates the sympathetic nervous system to promote VLDL-TAG secretion by the liver. By inference, inappropriately high levels of hypothalamic NPY seen in animal models of obesity may contribute to hypertriglyceridemia by an overstimulation of the sympathetic nervous system.