Abstract book

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Abstracts

Title:	**The effect of development, body weight and body weight change on brain responses during food choice in children.**
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Abstract:	**Introduction:** Childhood obesity is a rising problem mainly caused by unhealthy food choices. Food choices are based on a value signal encoded in the ventromedial prefrontal cortex (vmPFC), and self-control involves modulation of this signal by the dorsolateral prefrontal cortex (dlPFC). This study aimed to examine the effect of development, body weight and body weight change on the neural correlates of healthy food choice in children. **Methods:** 141 children from the I.Family/Idefics cohort (aged 10-17y) from Germany, Hungary and Sweden performed a food choice task while being scanned with fMRI and provided health and taste ratings of the foods. During the choice task participants considered either the healthiness or tastiness of the food or chose naturally. **Results:** Overall children made healthier choices when asked to consider the healthiness. However, for children in earlier stages of pubertal development and children who gained more weight this effect was smaller. There was a positive correlation between pubertal development (Tanner stage) and dlPFC activation during food choice, and a negative correlation with BMI Cole score. There was a positive correlation between weight change and visual processing activation. When asked to consider the healthiness there was a positive correlation between cerebellum activation and BMI Cole score and a negative correlation in this area with pubertal stage. There was a positive correlation between weight change and activation in the inferior parietal gyrus. **Conclusion:** Children in earlier stages of pubertal development and children with a higher body weight have less activation in an area important for self-control during food choice. Furthermore, development, body weight and body weight change influence neural responses to a health cue in areas involved in emotion and decision making. This suggests that effectiveness of health cues or interventions that rely on self-control in children may depend on their developmental stage and weight status. **1. Conflict of interest: -** **2. Funding:** This work was financially supported by the European Union Seventh Framework Program (FP7/2007–2013) under grant agreement nr. 266044, as part of the I.Family project http://www.ifamilystudy.eu). The authors were financially supported by the European Union Seventh Framework Programme (FP7/2007-2013) under Grant Agreements 266408 (Full4Health), 266044 (I.Family) and 607310 (Nudge-It).

Title:	**Timing of Feeding Behavior Affects Rhythms in the Muscle Molecular Clock and Glucose Tolerance**
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Abstract:	**Introduction:** Muscle is the most important tissue for glucose uptake and accumulating evidence indicates that targeting muscle functioning could prevent and treat type 2 diabetes mellitus (T2DM). Glucose metabolism also appears to be under control of the biological clock. Night-shift workers have an increased risk of T2DM, suggesting that disturbing normal sleep/wake patterns could affect glucose metabolism. **Methods:** To examine the effects of timing of feeding on glucose metabolism, rats were subjected to *ad libitum* (AL) or time-restricted feeding (TRF) during the light or dark period. Whole body metabolism was evaluated using calorimetric cages. Expression patterns of molecular clock genes and genes associated with glucose metabolism in muscle, collected at 3h intervals throughout a 24h period, were investigated using qPCR. Glucose tolerance was tested during both the light and dark period using an intravenous glucose tolerance test (ivGTT). **Results:** The amplitude of the respiratory exchange ratio (RER) was increased for all TRF groups, especially due to a stronger decrease during the fasting period. In the light fed groups rhythmic expression of all molecular clock genes tested, including Bmal1 and Per2, was abolished. Conversely, genes associated with glucose metabolism like Pdk4 and Ucp3 showed shifted rhythms during light period TRF. Additionally, TRF dampened the normal day/night difference in glucose tolerance seen in AL fed animals (day/night difference in ivGTT area under the curve (AUC) for AL $p=0.0015$; $p>0.05$ for Light and Dark fed groups; unpaired t-test). **Conclusion:** These data indicate that the muscle molecular clock is altered by TRF and that these changes are accompanied by altered whole body metabolism and glucose tolerance. **1. Conflict of interest:** The authors declare no conflict of interest. **2. Funding:** This project is funded by a TOP grant from ZonMw and is part of a collaboration between the university of Amsterdam (AMC) and Maastricht (MUMC).

Title:	**Dietary patterns and physical activity in the metabolically (un)healthy obese: The Dutch Lifelines Cohort Study**
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Abstract:	**Introduction:** The diversity in the reported prevalence of metabolically healthy obesity (MHO), suggests that modifiable factors, such as diet and physical activity, may contribute to metabolic health. We evaluated differences in dietary patterns and physical activity between MHO and metabolically unhealthy obesity (MUO). **Methods:** Cross-sectional data was used of 9,270 obese individuals, aged 30-69 years, of the Lifelines Cohort Study. Diet, using a 110 item Food Frequency Questionnaire, and physical activity were self-reported. MHO, intermediate obesity and MUO were defined according to the presence of obesity, number of MetS risk factors and history of cardiovascular disease. Sex-specific associations of dietary patterns (identified by principal component analysis) and physical activity with MHO were assessed by multivariable logistic regression (reference group: MUO). Analysis were adjusted for among others demographic characteristics, smoking and alcohol use. **Results:** Among 3,442 men and 5,828 women, 10.2% and 24.4% was MHO and 56.9% and 35.3% MUO, respectively. We generated four obesity-specific dietary patterns. Two were related to MHO, and in women only. In the highest quartile (Q) of the *'bread, potatoes and sweet snacks'* pattern, adjusted odds ratio (OR) (95% confidence interval) for MHO was 0.60 (0.44-0.81). A positive association with MHO was found for the healthier pattern *'fruit, vegetables and fish'*, with OR 1.31 (1.04-1.64) in Q3 and 1.46 (1.15-1.87) in Q4. For physical activity, only in men adjusted analysis showed that vigorous physical activity in the highest tirtile was associated with MHO (OR 1.96 (1.45-2.64)). Non-smoking and ≤2 alcoholic consumptions were positively associated with MHO, in both men and women. **Conclusion:** Our results suggest that a healthier diet and vigorous physical activity is associated with MHO in women and men, respectively. Identification of behavioural lifestyle patterns in the obese population may help in pinpointing vulnerable subgroups and to develop strategies for improving metabolic health. **1. Conflict of interest:** None **2. Funding:** NWO, the European Union's Seventh Framework program, the National Consortium for Healthy Ageing.

Title:	**The Belly Fat study - A dietary intervention to improve metabolic health in subjects with abdominal obesity**
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Abstract:	**Introduction:** Abdominal obesity increases the risk of chronic metabolic diseases. Energy restriction (ER) has shown to induce weight loss and improve metabolic parameters in obese individuals. However, enhancing the nutrient quality of an ER-diet might further benefit metabolic health and the metabolic capacity of the body to respond to dietary challenges. **Methods:** We conducted a parallel-designed randomized 12wk intervention study in which participants with abdominal obesity (BMI >27 kg/m^2 or waist circumference >88cm for females, >102cm for males) were randomized over three groups; a Western-type diet (WD *n*=40) or Targeted diet (TD *n*=40) 25%ER group or control group (*n*=30). The TD aimed to improve metabolic health by including a higher percentage of beneficial nutrients such as MUFA, *n-3* PUFAs, soy protein and fiber. Metabolic health was assessed by determining fasting plasma parameters as well as postprandial responses to a mixed meal test (MMT, 76g carbohydrates, 18g protein, 60g fat). Furthermore, we assessed subcutaneous (SAT) and visceral (VAT) adipose tissue mass as well as intrahepatic triglyceride (IHTG) accumulation by MRI/MRS. **Results:** Both ER-diets induced significantly different weight loss of -6.3±3.9kg in WD and -8.4±3.2kg in TD. Furthermore, both diets significantly reduced IHTG, VAT/SAT ratio and lowered fasting plasma glucose, insulin, HbA1c, HOMA-IR, and QUICKI as well as postprandial responses of insulin and glucose after the MMT. Only TD lowered fasting total cholesterol. No effects were observed in the control group. **Conclusion:** Any 25%ER-diet can induce clinically relevant weight loss, reduce VAT/SAT ratio and IHTG and improves insulin sensitivity and glucose homeostasis. However, enhancing nutrient quality by adding MUFA, *n-3* PUFAs, soy protein and fiber results in greater weight loss and a significant reduction in total cholesterol and can thus be considered as a superior diet in improving metabolic health of abdominally obese subjects. **1. Conflict of interest:** None **2. Funding:** Division of Human Nutrition, Graduate school VLAG

Title:	**Body fat distribution, in particular visceral fat, is associated with cardiometabolic risk factors in obese women**
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Abstract:	**Introduction:** Body fat distribution is, next to overall obesity, an important risk factor for cardiometabolic outcomes in the general population. In particular, visceral adipose tissue(VAT) is strongly associated with cardiometabolic risk factors. It is unclear whether body fat distribution is also important in obese individuals. We aimed to investigate the associations between measures of body fat distribution and cardiometabolic risk factors in obese men and women. **Methods:** In this cross-sectional analysis of obese men and women (BMI≥30 kg/m^2) included in the Netherlands Epidemiology of Obesity Study, waist circumference and waist hip ratio(WHR) were determined, in addition to the amount of abdominal subcutaneous adipose tissue(aSAT) and VAT by MRI. Associations between these adiposity measures and the presence of at least one of the risk factors hypertension, hypertriglyceridemia, low HDL-cholesterol concentrations and hyperglycemia were examined using logistic regression analysis. The analyses were stratified by sex and adjusted for age, ethnicity, education, tobacco smoking, alcohol consumption, physical activity and depending on the association additionally for total body fat or VAT. **Results:** We included 2,981 obese individuals (57%women) with a mean(SD) age of 56(6) years and BMI of 34.0(4.0) kg/m^2, after excluding individuals with missing values of cardiometabolic risk factors(n=33). VAT and aSAT measurements were available in 1,071 participants. There were 241 obese individuals without any other cardiometabolic risk factors. In obese women, all measures of body fat distribution except aSAT (OR per SD:0.76, 95%CI:0.53,1.10) were associated with having at least one cardiometabolic risk factor, of which VAT most strongly associated. One SD higher VAT (64.0cm^2) was associated with an OR of 5.77 (95%CI: 3.02,11.01) of having at least one cardiometabolic risk factor. In obese men, associations showed a similar, but weaker pattern. **Conclusion:** In obese women, but less so in men, measures of body fat distribution, of which VAT most strongly, are associated with cardiometabolic risk factors. **1. Conflict of interest:** none **2. Funding:** The NEO study is funded by the participating Departments, the Division and the Board of Directors of the LUMC, and by the Leiden University, Research Profile Area 'Vascular and Regenerative Medicine'.

Title:	Is parents' perceived neighbourhood physical activity environment related to direct measurement of physical activity of preschool children? The GECKO Drenthe study.
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Abstract:	Introduction: To design effective interventions to stimulate physical activity (PA) in children, it is important to understand the impact of built environmental determinants. This study examined whether neighbourhood characteristics are related to PA patterns, objectively measured by accelerometry in preschool children. Methods: The study included 505 child-parent pairs, children aged 4-7 years, who participated in the GECKO Drenthe birth cohort study. Sedentary behaviours (SB), light PA (LPA), and moderate-to-vigorous PA (MVPA) of children were directly measured by ActiGraph accelerometry (at least 3 wearing days, more than 10 hours per day). Environmental determinants were collected using a questionnaire, including household characteristics (e.g. type of housing), parental behaviours (e.g. accompanying children cycling), children's PA behaviours (e.g. playing outside), and neighbourhood environment (e.g. traffic safety, road network and presence of PA facilities). Potential determinants were identified using linear regression analysis, adjusted by age, gender, siblings, and maternal age and education level. MVPA was ln-transformed. Results: Univariate regression showed 'parents accompanying children doing sports' more often was related to less SB, more LPA and MVPA in children, and more outside play was also related to less SB and more LPA, but not MVPA. Besides, 'more neighbourhood PA facilities' was negatively associated with SB (β=-3.6, [95%CI:-6.7; -0.5] min/day), and positively with MVPA in children (β=0.027, [95%CI: 0.004; 0.050]). If these determinants were stratified by gender and assessed in one model, 'more PA facilities' was only related to less SB and more MVPA in boys, whereas 'more parental support' was related to more MVPA in girls. No other determinants were found to be related to children's PA patterns. Conclusion: Convenient neighbourhood PA facilities (e.g. park, playground) might be positive to stimulate children's PA through parental support, which may depend on the gender of children. This finding should be considered in future interventions and health promotion strategies. 1. Conflict of interest: The authors declare that they have no competing interests. 2. Funding: This work was supported by the University Medical Center Groningen.

Title:	**Short term high fat feeding impacts on mitochondrial function in brown adipose tissue**
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Abstract:	**Introduction:** Mitochondria in brown adipose tissue (BAT) burn fatty acids to produce heat, thereby contributing to energy expenditure. In diet-induced obese (DIO) mice, less and dysfunctional mitochondria are present in BAT accompanied by reduced cold tolerance. The aim of the current project is to unravel the rate and mechanism by which high fat diet (HFD) induces BAT mitochondrial dysfunction in the course of DIO development. **Methods and results:** 12-week-old C57Bl/6J mice were fed a HFD (45% of calories derived from fat) for 0, 1, 3 or 7 days (n = 10 per group). The HFD increased body fat mass reaching significance at 7 days. Of note, 1 day of HFD already increased BAT weight and lipid droplet content. This was accompanied by reduced uptake of [^{3}H]oleate derived from glycerol tri[^{3}H]oleate-labeled lipoprotein-like particles by BAT, suggesting that reduced mitochondrial activity rather than enhanced fatty acid uptake underlies the increased lipid content in BAT. Accordingly, HFD decreased mRNA expression of the mitochondrial biogenesis master regulator *Pgc1α*. In addition, HFD increased mRNA expression of mitochondrial dynamics markers *Opa1*, *Mfn2* and *Fis1* in BAT as well as Opa1 and p-Drp (S637) protein content in BAT, both involved in mitochondrial fusion. **Conclusion:** Short term HFD rapidly reduced BAT function as reflected by rapidly increased BAT weight and reduced uptake of fatty acids, accompanied by a marked reduction in *Pgc1α* and a gene and protein expression profile consistent with increased mitochondrial fusion. **1. Conflict of interest:** The authors declare no conflict of interest. **2. Funding:** This work was supported by a research grant from the Rembrandt Institute of Cardiovascular Science to M.R. Boon and R.H.L. Houtkooper. We acknowledge the support from the Netherlands Cardiovascular Research Initiative: an initiative with support of the Dutch Heart Foundation (CVON2014-02 ENERGISE).

Title:	**Unravelling the cause of the type 2 diabetes epidemic in South Asians: role for the endocannabinoid system?**
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Abstract:	**Background:** South Asians are at higher risk for development of obesity and related disorders including type 2 diabetes (T2D) as compared to white Caucasians. This may in part be due to their lower energy expenditure which coincides with lower activity of energy-combusting brown adipose tissue (BAT). The endocannabinoid system is known to play a pivotal role in energy metabolism and over-activation of the endocannabinoid system leads to obesity. The aim of this study was to investigate if South Asians have higher plasma endocannabinoid levels compared to white Caucasians and whether plasma endocannabinoid levels correlate with energy expenditure, BAT volume/activity and plasma lipid levels. **Methods:** Lean adolescent males of white Caucasian (n=10) and South Asian (n=10) origin were exposed to an individualized cooling protocol to determine BAT volume/ activity by [^{18}F]fluorodeoxyglucose scan. Before and after cooling, energy expenditure was assessed (Oxycon) and plasma samples were collected. In pre and post-cooling samples, endocannabinoids, their congeners (LC-MS/MS), and plasma lipids were quantified. **Results:** Compared to white Caucasians, South Asians had higher plasma levels of 2-arachidonoylglycerol (2-AG; 11.36 vs 8.19 pmol/ml, $p<0.05$), N-arachidonylethanolamine (AEA; 1.04 vs 0.89 pmol/ml, $p=0.05$), and their metabolite arachidonic acid (AA; 23.24 vs 18.22 nmol/ml, $p<0.001$). After pooling of both ethnicities, plasma 2-AG but not AEA an AA positively correlated with plasma triglyceride concentration ($R^2=0.32$, $p<0.05$) and body fat percentage ($R^2=0.18$, $p<0.05$). Interestingly, AA robustly negative correlated with energy expenditure ($R^2=0.46$, $p=0.001$) and positively with total percentage ($R^2=0.33$, $p<0.01$). **Conclusion:** Healthy lean South Asian men have higher endocannabinoid tone as compared to white Caucasians which, at least in part, may underlie their disadvantageous metabolic phenotype later in life. **1. Conflict of interest:** None. **2. Funding:** This study is supported by the Netherlands CardioVascular Research Initiative, GENIUS project (CVON2011-9). MR Boon is supported by a Dutch Diabetes Research Foundation Fellowship (2015.81.1808).

Title:	**No difference in musculoskeletal consultations in general practice between overweight and normal weight children.**
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Abstract:	**Introduction**: Childhood overweight and obesity are associated with self-reported musculoskeletal complaints. We investigated the association between frequency and type of musculoskeletal consultations at the general practice (GP) and weight status of children during a two year follow-up. **Methods:** Data from a prospective longitudinal cohort study including n=733 children aged 2-18 years presenting in general practices in the Netherlands were used. Height and weight were measured at baseline, 6 months, 1 and 2 year follow-up. At those moments children and parents filled out questionnaires about complaints, health related topics and general demographics. Electronic medical files were available for 617 children and were used to collect information on frequency and type of consultations of the children at the GP during the two-year follow-up period. Poisson regression and logistic regression were used to calculate the associations between weight status and the frequency and type of GP consultations. **Results:** Of the 617 included children, 111 (18%) were overweight or obese and 506 (82%) were non-overweight. Overweight children were significantly older (mean age 9.8 years sd (3.6) versus 7.8 (4.0), p=0.004). Overweight children consulted the GP for any type of complaint significantly more often during the 2-year follow up than non-overweight children (mean 7.3 (5.7) vs 6.7 (5.4), OR 1.09, 95%CI 1.01-1.18). No significant difference was seen in the number of musculoskeletal consultations during two year follow-up between overweight and non-overweight children (OR 1.20, 95%CI 0.86 – 1.68). Additionally, no significant difference between overweight and non-overweight children was seen for the number of consultations for any of the further specified musculoskeletal disorder. **Conclusion:** No association was found between childhood weight status and frequency and type of musculoskeletal consultations in GP during a two year follow-up. It therefore seems that musculoskeletal complaints caused by excessive weight do not present in general practice at such a young age. **1. Conflict of interest:** None disclosed **2. Funding:** None

Title:	**Multidimensional web tool intervention to improve cardiometabolic health in patients with a severe mental illness: LION, a cluster randomized controlled trial**
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Abstract:	**Introduction:** Unhealthy lifestyle behaviours play a large role in the alarming cardiometabolic health of severe mentally ill (SMI) patients with obesity rates of 45-55% and diabetes type 2 rates of 10-15%. Most mental health professionals have limited lifestyle-related knowledge and skills, and lifestyle treatment protocols are lacking. Evidence-based practical lifestyle tools may support both patients and staff in improving patients' lifestyle. The 12-months Lifestyle Interventions for severe mentally ill Outpatients in the Netherlands (LION) trial tests whether a multidimensional lifestyle intervention using a web tool improves cardiometabolic health in SMI patients. **Methods:** Twenty-seven community-care and sheltered living teams were randomised into intervention (N=17) or control (N=10) arm. In the intervention group, mental health nurses were trained in motivational interviewing and coached patients using the web tool 'Traffic Light'. First, patient and nurse mapped out patient's lifestyle behaviours, created a risk profile and made a lifestyle plan with attainable lifestyle goals. Hereafter, lifestyle goals were discussed biweekly during regular care visits. This process was repeated after six months until end of the trial. The control group received care-as-usual. Data on waist circumference (WC) and BMI were assessed during routine monitoring of somatic and mental health at baseline, and six and twelve months of intervention. Data of 244 patients (140 intervention, 104 control; 49.2% male, 46.1±10.8 years) were analysed using multi-level linear mixed models. **Preliminary results:** Intention-to-treat analyses showed that the intervention did not improve WC and BMI after six (WC: -1.40 cm; 95%CI=-5.58;2.78; BMI: 0.33 kg/m^2; 95%CI=-0.52;1.19) and twelve months (WC: -0.98 cm; 95%CI=-3.82;1.87; BMI: 0.50 kg/m^2; 95%CI=-0.29;1.29) intervention compared to care-as-usual. **Conclusion:** A multidimensional web tool intervention aiming to increase awareness of unhealthy behaviours by setting lifestyle goals, did not improve cardiometabolic health in most SMI patients. Perhaps, lifestyle coaching should be the main responsibility of an appointed lifestyle expert. **1. Conflict of interest:** The authors declare no conflicts of interest **2. Funding:** Funding for this study is provided by ZonMw, Grant 837001006.

Title:	**Supplementation of Diet With Galacto-oligosaccharides Increases Bifidobacteria, but not Insulin Sensitivity, in Obese Prediabetic Individuals**
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Abstract:	**Introduction:** The gut microbiota affects host lipid and glucose metabolism, satiety, and chronic low-grade inflammation to contribute to obesity and type 2 diabetes. Fermentation end products, in particular the short-chain fatty acid (SCFA) acetate, are believed to be involved in these processes. We investigate the long-term effects of supplementation with galacto-oligosaccharides (GOS), an acetogenic fiber, on the composition of the human gut microbiota and human metabolism. **Methods**: We performed a double-blinded, placebo-controlled, parallel intervention study of 44 overweight or obese (body mass index, 28-40 kg/m2) prediabetic men and women (ages, 45–70 years) from October 2014 through October 2015 in Maastricht, The Netherlands. The participants were randomly assigned to groups who ingested 15 g GOS or isocaloric placebo (maltodextrin) daily with their regular meals for 12 weeks. Before and after this period, we collected data on peripheral and adipose tissue insulin sensitivity, fecal microbiota composition, plasma and fecal SCFA, energy expenditure and substrate oxidation, body composition, and hormonal and inflammatory responses. The primary outcome was the effect of GOS on peripheral insulin sensitivity, measured by the hyperinsulinemic-euglycemic clamp method. **Results**: Supplementation of diets with GOS, but not placebo, increased by 5-fold the abundance of *Bifidobacterium spp.* in feces (*P*=.009, q=0.144). Microbial richness or diversity in fecal samples were not affected. We did not observe any differences in fecal or fasting plasma SCFA concentrations or in systemic concentrations of gut-derived hormones, incretins, lipopolysaccharide-binding protein, other markers of inflammation. In addition, no significant alterations in peripheral and adipose tissue insulin sensitivity, body composition, and energy and substrate metabolism, were found. **Conclusions:** Twelve-week supplementation of GOS selectively increased fecal *Bifidobacterium spp.* abundance, but this did not produce significant changes in insulin sensitivity or related substrate and energy metabolism in overweight or obese prediabetic men and women. **1. Conflict of interest:** none **2. Funding:** The research is funded by TI Food and Nutrition (project GH003), a public-private partnership on pre-competitive research in food and nutrition. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript