

POSTER PRESENTATIONS

8th Fribourg Obesity Research Conference (FORC-2015)

Nutrition, Movement & Sleep Behaviors:

their interactions in pathways to Obesity and Cardiometabolic diseases

P1. Mobile health information system tailored for obesity prevention & treatment (*PathMate*) in teenagers

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P2. Does a Health Information Technology System developed by Children and their Parents improve Obesity Therapy? *

Büchter D¹, Kowatsch T², Brogler B¹, Dintheer-ter-Velde A¹, Wiegand D¹, Pletikosa I³, Durrer D⁴, Schutz Y⁵, Maass W⁶, Laimbacher J¹, Allemand D¹
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P3. Individual modelling for personalisation in m-health interventions for obesity prevention among adolescents

Tabozzi SA, Caramenti M, Carrino S, Caon M, Abou Khaled O, Mugellini E, Rizzo G, Lafortuna CL
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P4. Drinking water for weight control: Is there a role for water-induced thermogenesis?

Nathalie Charrière, Jennifer L Miles-Chan, Jean-Pierre Montani, Abdul G Dulloo.
 Department of Medicine / Physiology, University of Fribourg, Switzerland

P5. How the reduced consumption of sugar-sweetened beverages impacts food intake behavior and brain responses to food viewing

Camille Crézé, Marie-Laure Bielser, Jean-François Knebel, Vanessa Campos, Luc Tappy, Micah Murray, Ulrike Toepel.
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P6. Does my brain want what my eyes like? How food liking influences choice and impacts spatiotemporal brain dynamics of food viewing

Marie-Laure Bielser^{1*}, Camille Crézé^{2*}, Micah M. Murray^{1,3,4}, & Ulrike Toepel¹
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P7. Energy expenditure phenotyping in response to low-intensity physical activity: Validation & application during low power cycling in Sedentary subjects and Athletes

Fares EJ, Isacco L, Charrière N, Miles-Chan JL, Montani JP, Schutz Y, Chenevière X, Dulloo AG
 Department of Medicine / Physiology, University of Fribourg, Fribourg, Switzerland.

P8. An approach to study human variability in isometric thermogenesis in fasted and post-prandial states

Delphine Sarafian, Jennifer L Miles-Chan, Gayathri Yepuri, Jean-Pierre Montani, Yves Schutz, Abdul G Dulloo.
 Department of Medicine / Physiology, University of Fribourg, Switzerland.

P9. Vasoactive properties of HDL improve after early ROUX-EN-Y gastric bypass but not after diet treatment: the superior cardiometabolic benefits of RYGB.

Osto E, McLoughlin E, Doytcheva P, Manz J, Charakida M, Finer N, Van Gaal L, Deanfield J, Lüscher TF
Center for Molecular Cardiology, University of Zurich, Switzerland

P10. Red Bull, Sugar-free Red Bull & caffeine in habitual caffeine consumers: Inter-relationship between thermogenic and blood pressure responses.

Jennifer L Miles-Chan, Nathalie Charrière, Erik K Grasser, Jean-Pierre Montani, Abdul G Dulloo.
Department of Medicine / Physiology, University of Fribourg, Fribourg, Switzerland.

P11. Muscle size, composition and architecture: effects on leg specific strength in obese older women.

Lafortuna CL, Rastelli F, Caramenti M, Orgiu S, Capodaglio P, Falini A, Rizzo G.
Istituto di Bioimmagini e Fisiologia Molecolare del CNR, Segrate, Milano, Italy.

P12. Core temperature in obese versus lean: An exploratory analysis using ingestible telemetry sensor

Cathriona R Loonam¹, Elie-Jacques Fares¹, Julie Calonne¹, Jennifer Miles-Chan, Natalie Charrière¹, Jean-Pierre Montani¹, Yves Schutz^{1,2}, Dominique Durrer-Schutz², Abdul G Dulloo¹

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P13. Influence of dietary fat quality on the obesogenic effect of high fat diet

Raffaella Crescenzo, Francesca Bianco, Arianna Mazzoli, Antonia Giacco, Rosa Cancelliere, Giovanna Liverini, Susanna Iossa

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P14. Impact of dietary fat quality on high-fat induced hepatic steatosis

Raffaella Crescenzo, Francesca Bianco, Arianna Mazzoli, Antonia Giacco, Rosa Cancelliere, Giovanni Di Fabio, Armando Zarrelli, Giovanna Liverini, Susanna Iossa.

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P15. Dietary modulation of body composition and ectopic (liver) lipids during catch-up growth: effects of oils varying in n-6 to n-3 polyunsaturated fatty acids

Julie Calonne, Jennifer Miles-Chan, Jean-Pierre Montani and Abdul G. Dulloo

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P16. Cortical circuits regulating energy homeostasis

Isabel De Araujo Salgado, Romain Migliorini and Christophe Lamy

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P17. Circadian clocks and depression: Molecular pathway of bright light therapy

Laureen Strittmatter, Federica Sandrelli and Urs Albrecht

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P18. Liver-derived ketone bodies are necessary for food anticipation.

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8th Fribourg Obesity Research Conference (FORC-2015)‘Nutrition, Movement & Sleep Behaviors: *their interactions in pathways to Obesity and Cardiometabolic diseases*

P1

Mobile health information system tailored for obesity prevention and treatment (PathMate) in teenagers¹Durrer-Schutz D, ²Kowatsch T, ³Allemand-Jander D, ³Büchter D, ⁴Pletikosa Cvijikj I, ⁵Maass W, ^{1,6}Schutz Y¹Eurobesitas Center (COMS), Vevey, Switzerland; ²University of St.Gallen, Switzerland; ³Children's Hospital of Eastern Switzerland, St.Gallen, Switzerland; ⁴ETH Zurich, Switzerland; ⁵Saarland University, Germany; ⁶University of Fribourg, Switzerland

Introduction: Multi-professional programs for the management of obesity in teenagers, which combine physical activity, nutritional and psychological components, are well established today. However, due to limited resources available, only limited number of patients can be included in these programs, considering the high needs resulting from the generally high prevalence of obesity.

Objective: The objective was to develop a technical platform with a number of innovative, tailored and interactive health services via a tablet PC.

Methods: Six adolescents (13-17 years, BMI percentile > 97 for age & gender) participated in an exploratory longitudinal field study. The following measurements were made at baseline, month 1, 3 and 4: 1. well-being, mental health, mood, eating disorders, and motivational interview all by validated questionnaires; 2. change in body weight and BMI SDS, blood pressure, speed of eating (by sequential photogrametry), daily physical activity (PA by accelerometer, Fitbit), and degree of relaxation (by skin conductance and heart rate), all by objective measurements.

Results: Body weight loss at 4 months average 6.2 kg (range: 3.8 to 8.0 kg). Although the health services were developed together with the teenagers, a large inter-individual variability of the platform usage (inconspicuously measured) was observed. The mood monitoring, relaxing exercise and PA tracking services were perceived most useful.

Conclusions: For the MD's, it appears that this new tool can provide a useful aid to work, communicate and keep in touch with (pre)obese teenagers during and outside the on-site consultation.

P2

Does a Health Information Technology System developed by Children and their Parents improve Obesity Therapy? *Büchter D¹, Kowatsch T², Brogler B¹, Dintheer-ter-Velde A¹, Wiegand D¹, Pletikosa P, Durrer D⁴, Schutz Y⁵, Maass W⁶, Laimbacher J¹, Allemand D¹¹ Children's Hospital of Eastern Switzerland, St. Gallen, ² University of St. Gallen; ³ ETH Zurich; ⁴ Eurobesitas Centre (COMS) Vevey, Switzerland; ⁵ University of Fribourg, Switzerland; ⁶ Saarland University, Germany

Introduction: Existing treatment programs for obese children prove limited effectiveness and sustainability. Health Information System (HIS) enhanced interventions have the potential for higher accessibility and cost-effectiveness of multi professional family based obesity therapy. They aim was not only to modify the patient's behavior but also to positively influence their family system.

Methods: In cooperation with therapists, extremely obese children, their parents, computer scientists and information systems researcher, a mobile HIS was developed, consisting of a tablet PC with photo and patient's privacy services, relaxation tools and the ability to measure speed of eating by electronic stop watch, emotional parameters by self- assessment manikin mood scale and physical activity by 3-axes accelerometer, Fitbit, combined with telephone interviews.. Three groups of each six extremely obese children (BMI > 99.5, median BMI z-score 3.0, age 13.2 ± 2.3 years) were assigned to therapy in either an (1) individual or (2) group setting with HIS, or (3) individual care without HIS. Physical activity, speed of eating and physical and emotional parameters were evaluated before and after 12 months of therapy. All patients and parents gave informed consent for adherence to therapy, monitoring and the use of tablet PC's.

Results: 25% of extremely obese children with HIS and 60% without HIS decreased their BMI-SDS. Children using HIS did not reduce their obesity more than the control group without HIS, if parents did not support their children at home. Those children with parental support did use HIS for activity, mood and nutrition monitoring regularly.

Conclusion: In extremely obese children, home support with HIS is only effective, when children are guided by their parents while using HIS. To select appropriate families for HIS home support, careful examination of the family system including their motivation & psychosocial factors is needed.

P3

Individual modelling for personalisation in m-health interventions for obesity prevention among adolescents

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Evidence-based recommendations, with a particular focus on health-related mobile applications, stress the role played by personalisation in augmenting the usability, the acceptance, the motivation of users and, finally, the efficacy of the health interventions devoted to manage specific medical conditions or improving life quality. The EC funded project PEGASO points to the creation of a personalised technological platform for raising adolescents' awareness and motivation towards active life style and healthful nutrition, as a means to prevent obesity and related health risks. To this aim, a "virtual individual" model (the PEGASO VIM), based on users' body attributes, physiological traits and daily behaviours, has been developed to empower the personalisation of the intervention tailored on single individuals' functional needs and preferences. The PEGASO VIM can thus identify specific behaviours related to overall physical activity and diet quality, which are set as the individual's target in the PEGASO interaction. In particular, the system tracks user's daily behaviours and provides feedback offering educational contents and multiple behaviour change techniques, via a "Companion" app running on smartphone. The dynamic interaction between the user and the system allows selecting customised target behaviours, upon which the persuasive intervention is exerted. To this end, the Companion app implements multiple behaviour change techniques using different means and opportune user interfaces (such as games, gamification, physical activity monitoring, food intake tracking, challenges, social networking). A regular update of the user's profile through smartphone and dedicated wearable sensors allows the system to dynamically adapt to individual characteristics, to user changes and also to assess its own effectiveness.

Project PEGASO is co-funded by European Commission under 7th Framework Programme.

P4

Drinking water for weight control: Is there a role for water-induced thermogenesis?

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Introduction: Drinking large amounts of water is often recommended for weight control. Whether water intake stimulates energy and fat metabolism is, however, controversial with some studies reporting that drinking half-a-litre of water increases resting energy expenditure (REE) by 10-30% and decreases respiratory quotient (RQ), while others report no changes in REE or RQ. The aim here was to reassess the concept of water-induced thermogenesis and fat oxidation in humans, with particular focus on inter-individual variability in REE and RQ responses and on the comparison with a time-control Sham drink.

Methods: REE and RQ were measured in healthy young adults (n=27; BMI range: 18.5–33.9 kg/m²), by ventilated hood indirect calorimetry for at least 30 min before and 130 min after ingesting 500 ml of distilled (21°C) water or after sham drinking, in a randomized cross-over design.

Results: Drinking 500 ml of distilled water led to marginal increases in REE (<3% above baseline), independently of gender, but which were not significantly different from Sham drinking. RQ was found to fall after the water drink, independently of gender, but it also diminished to a similar extent in response to Sham drinking.

Conclusions: This study conducted in young men and women varying widely in adiposity suggest that ingestion of purified water per se does not result in stimulation of thermogenesis.

P5

How the reduced consumption of sugar-sweetened beverages impacts food intake behavior and brain responses to food viewing

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Obesity is increasingly considered as a brain disease in which homeostatic mechanisms regulating food intake are overridden by hedonic drives towards consumption of palatable foods. How consumption of added sugars from sugar-sweetened beverages (SSBs) impact hedonic drives to foods remains unknown.

We studied 14 high SSB consumers before and after 3 months of SSB replacement by artificially sweetened equivalents. Participants performed behavioral pleasantness ratings on a 5-point scale when presented with colour images of solid foods differing in fat content (high- vs. low-fat) and taste quality (savory vs. sweet). Moreover, the spatio-temporal brain dynamics while viewing the food types were assessed using high-density electroencephalography (EEG) and electrical neuroimaging analyses. Behavioural results show a significantly greater appreciation of savory foods, but decreased appreciation of sweet foods post-SSB replacement.

The 3-month SSB replacement modified the initial stages of visual processing as well, in particular in response to low-fat foods. Therein, the neural activity when viewing low-fat/savory foods was reduced in the right inferior temporal gyrus and insula, i.e. brain areas involved in food categorization and valuation. Responses to high-fat foods seem less susceptible to (dietary) modulations, likely due to their greater salience and reward valuation.

Our results show that the replacement of liquid sugars by artificially sweetened equivalents differentially influences responsiveness to solid calories differing in taste quality and fat content, likely explaining changes in behaviour towards food intake.

P7

Energy expenditure phenotyping in response to low-intensity physical activity: Validation & application during low power cycling in Sedentary subjects and Athletes

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Introduction: Standardized approaches to study human energy expenditure (EE) are well defined *at rest* (as basal metabolic rate and thermic effect of feeding), but not in relation to low-intensity physical activities compatible with daily life. Our aim was to develop, validate and to apply a standardized test, using the bicycle ergometer, for assessing the energy cost of low-intensity dynamic work by linear regression across the range of low power output cycling.

Methods: EE was assessed by face-mask indirect calorimetry during cycling for 5 min each at no-load, 5W, 10W, 15W, 20W, 30W, 40W, 50W, and the steady-state EE were then plotted against power load; the slope is used to calculate delta efficiency. A first study was conducted in overnight fasted young healthy untrained men and women (n=15) of normal BMI, and repeatability assessed in 6 subjects on 3 separate days for each subject. A second study compared delta efficiency assessed across the low power output cycling range (10-50W) in Athletes (men, n=8) *versus* sedentary subjects (men, n=20; women, n=27).

Results: Within the low power range of cycling, a strong linearity of the EE vs power relationship was observed between 10-50W; the slope and its reciprocal (delta efficiency 28.3% \pm 2.3) showing low intra-individual variability, with the coefficient of variability (CV) being ~ 6%, independently of gender; inter-individual CV being about 11%. No significant differences in delta efficiency were seen between athletes and sedentary subjects. Inter-individual variability in delta efficiency is not explained by anthropometric and body composition measures.

Conclusions: This standardized and validated approach to study human delta efficiency in response to low-intensity cycling open up new avenues for research in human EE phenotyping with implications for research in metabolic predisposition to leanness and fatness.

P6

Does my brain want what my eyes like? How food liking influences choice and impacts spatiotemporal brain dynamics of food viewing.

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The influence of valuation on food-related decision-making and their impact on visual food perception remains poorly understood, although being of great interest for body weight management. Our study investigated behavioral aspects and spatio-temporal brain dynamics related to the viewing of pairs of food images in twenty-two normal-weight participants. Participants were asked to rate their liking for each food item (valuation phase) and to further choose between the two alternatives (choice phase). Further, visual evoked potentials (VEPs) were assessed.

Behaviorally, highly liked foods were chosen most often, and also rated faster than mildly liked or disliked foods. At the brain level, the level of liking as well as the subsequent choice modulated VEPs as early as 135-180ms after food image onset. Estimation of neural source activity patterns over this time period showed an interaction between liking and choice within the insula, the dorsal frontal and the superior parietal regions. Yet, modulations by liking were apparent only when the viewed food had been chosen over an alternative. Therein, neural responses to disliked foods were found to be stronger than those to food images that were liked more, showing that the spatio-temporal brain dynamics to food viewing are immediately modulated by both the liking of foods and subsequent choices.

These valuation and choice processes occur in brain regions involved in salience and reward attribution as well as in decision-making processes, thus likely influencing daily food choices.

P8

An approach to study human variability in isometric thermogenesis in fasted and post-prandial states

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The assessment of human variability in energy expenditure (EE) under standardized conditions is well defined at rest, and currently under validation for assessing the energy cost of low-intensity dynamic work. However, because physical activities of daily-life consist of a combination of both dynamic and isometric work, there is a need to develop standardized tests for assessing human variability in energy cost of low-intensity isometric work. The first aim was to assess in the fasted state, the feasibility and the repeatability of a standardized leg press isometric exercise by assessing the energy cost of isometric contraction-induced thermogenesis. The second aim was to evaluate whether isometric thermogenesis was altered in response to a 600 kcal mixed meal.

EE was measured after an overnight fast by indirect calorimetry with the subject sitting at rest or while pressing during 8 min intermittently (8 x 30 s press / 30 s rest) with both legs against a press-platform at 5 low-intensity isometric loads (+5, +10, +15, +20 and +25 kg force). EE integrated over each press level increased linearly across the 5 loads (correlation coefficient (r) > 0.9 in each subject). The slope of this EE-Load relationship showed good repeatability when the protocol was repeated on 3 separate days. In response to the 600 kcal mixed meal, the results revealed no significant differences in PPEE between 32-144 min post-ingestion, thereby supporting relative stability of PPEE for about 2h. When the isometric exercise was performed in the post-prandial state, comparison of the slopes of the EE-Load relationship showed no significant difference relative to that in the fasted state, suggesting no impact of meal on the energy cost of isometric exercise.

In conclusion, this standardized intermittent isometric test increases EE at levels comparable with low-level of daily life activities (< 2 METs), and is applicable to both fasted and fed states. The test extends the capacity of human metabolic phenotyping, and opens new avenues for research towards investigating the large human variability in isometric thermogenesis, and its potential role in metabolic predisposition to obesity and chronic diseases.

P9

Vasoactive properties of HDL improve after early ROUX-EN-Y gastric bypass but not after diet treatment: the superior cardiometabolic benefits of RYGB

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Roux-en-Y gastric bypass (RYGB) reduces cardiometabolic risk through different potential mechanisms. High density lipoprotein cholesterol (HDL) changes might explain part of this benefit. We assessed the effect of RYGB on HDL vasoprotective properties in comparison with a hypocaloric diet.

HDL was isolated from serum of obese patients (BMI > 35 kg/m²) before and 6 months after RYGB (n=32) or diet (n=32). In endothelial cells stimulated with HDL, we quantified nitric oxide (NO) production by DAF-2 fluorescence and paraoxonase-1 antioxidant activity (PON-1). Total cholesterol, low density lipoprotein (LDL-C), HDL-C, and triglycerides (TG) were also measured. At baseline there was no significant difference in mean body weight (BW) and BMI between RYGB and diet patients (119.9 Kg; 42kg/m² vs. 110.9 kg; 37.4 kg/m², respectively, p=0.06). At 6 months, BW and BMI were not different (RYGB: 94kg; 33 kg/m²; diet: 99kg; 33.4 kg/m², p=ns). In both groups, mean total cholesterol and TG were reduced; LDL-C decreased only after RYGB. Although total HDL-C increased 6 months after both interventions, only RYGB improved the vasoprotective HDL-stimulated NO production (RYGB: 234.2±178.0 vs diet 98.8±76.4 arbitrary units, p<0.0001) and HDL-associated PON-1 activity (RYGB: 40% vs diet: 9% increase compared to baseline; p<0.0001).

Our study shows that although HDL concentration increased after RYGB or diet-induced BW loss, endothelial protective HDL properties were restored only after RYGB even though patients were still obese. This suggests that BW loss is not sufficient or critical to improve the protective properties of HDL, unless accompanied by yet unknown surgery-specific effects.

P10

Red Bull, Sugar-free Red Bull & caffeine in habitual caffeine consumers: Inter-relationship between thermogenic and blood pressure responses

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Despite increases in the popularity and consumption of energy drinks, and the emergence of “diet” (sugar-free) versions of these beverages, there is still little robust research regarding their acute thermogenic and cardiovascular effects under resting conditions.

We have previously demonstrated that, in habitual caffeine consumers, Red Bull (RB), Sugar-free RB and caffeine (120 mg) enhance thermogenesis. In addition, these three conditions increase blood pressure (4-5 mmHg). However, there is large inter-individual variability in the magnitude of these responses. Here we integrate our data to explore this variability and determine if an inter-relationship exists between energy expenditure (EE) and mean arterial blood pressure (MAP).

Participants attended 4 experimental sessions on separate days according to a placebo-controlled randomized crossover study design. Beat-to-beat haemodynamic measurements were made continuously for 30 min baseline and 2 h following ingestion of 355 mL of either i) RB + placebo; ii) sugar-free RB + placebo; iii) water + 120 mg caffeine or iv) water + placebo.

Overall, across the wide range of individual thermogenic responses measured after ingestion of any of the caffeine-containing beverages/capsules (ΔEE, range: -9 to +15%, average +6%), there was no correlation with pressor response (ΔMAP, range: -4 to +9 mmHg, average +3 mmHg) – with those individuals showing the greatest thermogenic effect not necessarily having the largest change in blood pressure.

P11

Muscle size, composition and architecture: effects on leg specific strength in obese older women

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Muscle impairment and body mass excess are common conditions among older people. Since the impact of obesity on strength production has been scarcely studied in older individuals, we analysed functional and structural characteristics of quadriceps femoris muscle (QF) in obese (OB) and normal weight (NW) well-functioning older women.

In 5 OB (BMI = 36.8 ± 1.9 kg/m², age = 72.4 ± 2.3 yr.) and 6 NW (BMI = 24.3 ± 1.8 kg/m², age = 72.7 ± 1.9 yr.) older women with comparable habitual physical activity, peak knee extension torque (KET) was measured in isometric (90° knee flexion) and isokinetic conditions (240, 180, 120, 60°/sec). Mid-thigh QF cross sectional area (CSA) and muscle tissue fat content (MF%) were determined with MRI (Dixon sequence). Muscle fascicle length (FL) and pennation angle (PA) were assessed with ultrasonography for each muscle belly of the QF (vastus lateralis, vastus intermedius, rectus femoris, vastus intermedius).

Despite similar values in KET, CSA was 17.0% larger in OB than in NW (p<0.05), so that KET/CSA, was significantly lower (p<0.05) in OB. Compared to NW, OB had 28.7% higher MF% (p<0.05) and 24.9% wider average PA (p<0.05), while FL was similar. Overall, isometric KET/CSA was negatively affected by both MF% (p<0.05) and PA (p<0.05), while isokinetic KET/CSA only by MF% (p<0.01).

Muscle composition and architecture thus appear to be important determinants of muscle specific performance in older women. In fact, due to the effect of body mass overload, obese have larger muscle size but unfavourable muscle composition and architecture compared to their normal-weight counterpart, the higher fat content and the wider pennation angle observed in obese being associated with reduced levels of muscle specific strength.

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P12

Core temperature in obese versus lean: An exploratory analysis using ingestible telemetry sensor

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Approximately 40% of total energy expenditure (EE) is used to maintain core body temperature (T_c) in human adults. It has been hypothesized that obese individuals have lower T_c than the lean, and that this difference could underscore a thrifty (energy conservation) mechanism that favours fat storage. The few studies that have tested this hypothesis have, however, yielded conflicting results, ranging from a lower daytime T_c in obese, no difference in T_c between obese and non-obese, to increase mean daily T_c in obese.

To test the hypothesis that obese have lower T_c than the lean, we recruited - in a preliminary study - eight obese (BMI >30 kg/m²) and fifteen lean subjects who had never been overweight (BMI < 25 kg/m²). They ingested a core temperature sensor (HQInc), which recorded temperature at 20 second intervals over 20 h, starting in the late afternoon until 14:00 the next day. In the morning period, EE was measured in the overnight fasted state at rest under basal conditions, followed by low-intensity exercise, involving dynamic exercise (cycling at 50 W) and isometric exercise (intermittent leg press against 25 kg load).

The results indicate no significant differences in T_c profiles between the obese and lean subjects during sleep, under basal (awake) conditions, nor during dynamic or isometric exercise. These preliminary data suggest that obesity may not be associated with a lower core temperature.

P13

Influence of dietary fat quality on the obesogenic effect of high fat diet

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Introduction: In our previous studies, a high fat diet was given to rats to elicit obesity and mimic the feeding style more common in western societies. However, it has pointed out that the obesogenic and diabetogenic effect of high fat diets could be different, depending on the type of fat included in the diet. Therefore, we assessed whether changing the type of fat in the context of a high fat dietary regimen could differently affect whole body homeostasis.

Methods: Adult rats were pair fed with a lard-based (L, mainly monounsaturated and saturated fatty acids) or safflower-linseed based (S-L, polyunsaturated fatty acids of ω -6 and ω -3 series) diets for 2 weeks. Body composition and energy balance were measured. Quantification of uncoupling protein (UCP-1) in interscapular brown adipose tissue (IBAT) was performed.

Results: At the end of the treatment, the percent of body lipid was nearly doubled both in L and in S-L rats, although the final value was significantly lower in S-L than in L rats; conversely the percentage of body protein was maintained constant in S-L rats, while it significantly decreased in L rats. The percent of epididymal and visceral WAT increased, reaching a final value that was significantly lower in S-L rats than in L rats. The percent of body IBAT was significantly higher in S-L than in L rats and its content of UCP-1 was markedly increased in S-L rats compared to L rats. S-L rats exhibit lower lipid gain but higher protein gain compared to L rats. The analysis of fuel oxidation conducted the day before the sacrifice showed that the S-L rats had reduced protein oxidation but higher lipid oxidation compared to L rats.

Conclusions: Here we provide evidence that not only the amount, but also the type of dietary fat, is a primary obesogenic factor. It remains to be assessed whether S-L rats are more exposed to oxidative damage and associated metabolic alterations.

P14

Impact of dietary fat quality on high-fat induced hepatic steatosis

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Introduction: High fat intake is associated with an elevated risk for obesity and chronic disease such as diabetes and cardiovascular diseases. However, it has been pointed out that the obesogenic and diabetogenic effect of high fat diet could be different, depending on the type of fat included in the diet. In the light of the above considerations, we assessed whether changing the type of fat in the context of a high fat dietary regimen could differently affect whole body homeostasis.

Methods: Adult rats were pair fed with a lard-based (L, mainly monounsaturated and saturated fatty acids) or safflower/linseed oil (S-L, polyunsaturated fatty acids of omega-6 and omega-3 series) diets for 2 weeks. Liver composition, as well as respiratory capacity, oxidative status and fatty acid composition of liver mitochondria were measured.

Results: Plasma metabolic characterisation evidenced higher alanine aminotransferase activity in S-L rats compared to L rats. Livers from S-L rats showed higher degree of steatosis and had higher lipids, triglycerides and cholesterol, as well as higher lipid peroxidation, compared to L rats. Liver mitochondria from S-L rats displayed a significant decrease in basal and fatty acid-induced proton leak compared to L rats. Both NAD, FAD and lipid-linked maximal oxidative capacities were significantly higher in isolated liver mitochondria from S-L rats compared to L rats. Evaluation of oxidative status showed that lipid peroxidation was significantly higher in mitochondria from S-L rats compared to L rats.

Conclusions: The results suggest that liver was more affected by the unsaturated fat-rich diet. In conclusion nutritional strategies, aiming at reducing the obesogenic effect of diet, should take precautions in advising high intake of unsaturated fatty acids.

P15

Dietary modulation of body composition and ectopic (liver) lipids during catch-up growth: effects of oils varying in n-6 to n-3 polyunsaturated fatty acids

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Catch-up growth has long been considered to be desirable for health, but achieving this goal often involves nutritional rehabilitation of poorly growing infants and children on an energy-dense high saturated fat diet. This feeding practice is under re-evaluation because catch-up growth is increasingly recognized as a state characterized by a disproportionate recovery of fat mass relative to lean mass (i.e. preferential catch-up fat) associated with hyperinsulinemia and insulin resistance, and a predisposing factor for later obesity, type 2 diabetes and cardiovascular diseases.

In the search for dietary strategies to counter such catch-up fat and associated insulin resistance on an energy dense diet, we previously reported, based upon studies of isocaloric refeeding in previously caloric-restricted rats, that this could be achieved by high fat diets rich in linoleic acid (LA) and/or α -linolenic acid, i.e. the parent n6 and n3 polyunsaturated fatty acids (PUFA), respectively. Here, we investigated the extent to which hepatic steatosis, which generally observed in animals fed or refeed on a high fat diet rich in saturated fatty acids can be modulated by two high PUFA diets providing high amounts of both n6 and n3 PUFA, but also varying in the ratio of n6 and n3 fatty acids.

Our results indicate that whereas the high PUFA diets, independently of n6:n3 ratios, were equally effective in increasing lean mass and preventing excessive total body fat accumulation during refeeding, they nonetheless showed similar induction of hepatic lipid accumulation as observed with the HF-lard (saturated) fat diet. However, the increases in hepatic lipid droplet size were less pronounced in the groups refeed on both high PUFA diets. To what extent such differential effects of these high PUFA diets on liver lipid droplet size may impact upon hepatic steatosis-induced inflammation and liver functions warrant further studies.

P16

Cortical circuits regulating energy homeostasis

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Studies of the neuronal regulation of energy homeostasis have largely focused on autonomic and reward brain circuits. Recent work has highlighted the importance of the cerebral cortex in the control of energy balance and in the pathology of metabolic conditions such as obesity. The insular cortex (IC) in particular is thought to play a key role in orchestrating behavioral responses to body metabolic states. We hypothesized that IC might contain metabolic-responsive circuits, which we aimed at identifying in this study.

We tested IC's responses to metabolic challenges in mice. Fasting and 2DG-induced glucoprivation increased c-fos expression in a subpopulation of IC cells, suggesting the presence of metabolic-responsive, possibly glucose-sensing, neurons. To further investigate this hypothesis, we recorded IC neurons with whole-cell electrophysiology.

Those recordings evidenced a set of neurons showing a cell-autonomous response to glucose with either a glucose-inhibited or glucose-excited phenotype. To better characterize those cells, we established a genetically-encoded activity reporter system that enables the fluorescent tagging of glucose-sensing neurons. In future work, we will use a similar strategy to interrogate the physiological role of IC glucose-sensing circuits with opto and chemogenetics.

P17

Circadian clocks and depression: Molecular pathway of bright light therapy

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Mood disorders are multifactorial and heterogeneous diseases caused by the interplay of several genetic and environmental factors. In humans, these disorders are often accompanied by abnormalities in the organization of the circadian system, which normally synchronizes daily activities and functions of cells and tissues. Bright light therapy (BLT) appears to be effective for several mood disorders including depression. Resetting the circadian system using chronotherapy appears to be an effective treatment for mood disorders.

BLT efficiency is likely rooted in the ability of light to advance clock's phase, which rely on Per1 gene induction. Here we demonstrate, that a light pulse given at the end of the night results in reduced immobility time in the Forced Swim Test (FST). As in humans, the beneficial effects of BLT are transient in mice. These beneficial effects of a light pulse seem to rely, in part on the dopaminergic system.

Our results reveal, Maa gene expression and MAOA activity to be reduced after BLT in WT mice. We also show the influence of the light inducible clock component Per1 in mood related behavior and demonstrate its potential role in relaying the light information for mood improvement. For that, a particular region is of interest : The Lateral Habenula. The fact that light's beneficial effects take 3-4 days to be detected and only last 2 weeks suggests an epigenetic regulation of genes involved in mood related pathways.

P18

Liver-derived ketone bodies are necessary for food anticipation.

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The circadian system in mammals has endowed animals with the ability to anticipate recurring food availability at a particular time of the day. Since daily food anticipation is independent of the suprachiasmatic nuclei (SCN), the central pacemaker of the circadian system, the questions arise of where the food anticipatory signal originates and what role components of the circadian clock may play.

To address these questions we generated tissue specific Per2 knock-out mice. Liver specific deletion of Per2 abolished food anticipation (FA), which was rescued by viral overexpression of Per2 in the liver. RNA sequencing revealed that enzymes of fatty-acid and ketone body metabolism are altered in these animals with Per2 regulating the expression of carnitin-palmitoyl transferase thereby affecting both acetyl-CoA and β -hydroxybutyrate (β OHB) levels. Furthermore, timed release of β OHB alone rescued the FA phenotype in liver Per2 knock-out mice.

We conclude that liver Per2 is necessary for FA and that it regulates FA via modulation of β OHB levels. In contrast to previous belief we show here that FA originates in the liver and not in the brain. However, manifestation of FA involves processing of the liver derived β OHB signal in the brain, indicating that the food entrainable oscillator is not located in a single tissue but is of systemic nature.