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# The effect of the Catechol-O-methyltransferase VAL158Met variant (rs4680) on energy expenditure and weight loss

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ical but also psychological dimensions in metabolic syndrome. Such new concepts require an individualized treatment strategy as well as the close cooperation of different medical specialities.

**Conflict of interest:** B Schau is an employee of Omron Healthcare Europe. M Bieldfeldt and C Schröck, both working at Perleberg Pharma Partner Health Research GmbH, have run the market research in this project.

**Funding:** The research related to this abstract was funded by Omron Healthcare Europe.

## T4:PO.262

## Screen time and metabolic risk factors among adolescents

**Hardy LL**[1], Denney-Wilson E[2], Thrift AP[3], Okely AD[4] and Baur LA[1,5]

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**Introduction:** To examine the association between screen time (ST; i.e., TV/DVD/video, computer use) guidelines and risk factors for cardiovascular disease, type 2 diabetes and fatty liver diseases in mid-adolescence.

**Methods:** Cross-sectional survey of Grade 10 students ($n$ = 496, 58% boys, mean [±SD] age 15.4[±0.4] years) in Sydney, Australia. Measures included BMI, waist circumference, cardio-respiratory endurance, dietary factors, socioeconomic' status (SES) and pubertal status. ST was categorised < or ≥2 hours/day and calculated for weekday, weekend and entire week. Fasting blood was analyzed for HDL and LDL cholesterol, triglycerides, insulin, glucose, homeostasis model assessment of insulin resistance, alanine aminotransferase, gamma glutamyl transferase, high-sensitivity C-reactive protein; and blood pressure. Abnormal results were categorized according to published guidelines.

**Results:** Mean ST for all students was 3.1 hours/day and for weekdays and weekend days 2.6 hours/day and 4.4 hours/day, respectively. Boys were more likely to exceed ST guidelines than girls (OR: 2.71; 95%CI: 1.67–4.38). There were no significant associations between ST guidelines and metabolic risk factors among girls. After adjusting for potential confounders, boys who exceed ST guidelines on weekdays were more likely to have elevated HOMA-IR (AOR: 2.42; 95%CI: 1.11–5.28) and insulin (AOR: 2.73, 95%CI: 1.43–5.23).

**Conclusions:** Adolescent boys with ≥2 hours/day ST on weekdays have twice the risk of abnormal levels of insulin and HOMA-IR compared with peers who spend <2 hours/day on weekdays. These results suggest there is an increased risk of insulin resistance among adolescent boys who do not meet ST guidelines on weekdays.

**Conflict of interest:** None.

**Funding:** Research relating to this abstract was funded by NSW Department of Health.

## T4:PO.263

## Gemini: a UK twin birth cohort with a focus on early childhood weight trajectories, appetite and the family environment

**Van Jaarsveld CHM**, Johnson L, Llewellyn C and Wardle J

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**Introduction:** Gemini is a cohort study of young twins in the UK designed to assess genetic and environmental influences on early childhood weight trajectories with a focus on infant appetite and the family environment.

**Methods:** A total of 2402 families with twins born in England and Wales between March and December 2007 agreed to participate and returned completed baseline questionnaires. The sample includes 1586 same-sex and 816 opposite-sex twins. The study is currently funded for five years of follow-up, but is planned to continue into early adolescence and beyond, pending funding. With current funding of the study, families will be followed up when twins are: 8 months old (baseline), and then at 15, 20, 24, 36 and 48 months of age.

**Results:** Gemini is in its early stages, with baseline and first follow-up data collection completed. The rationale for the Gemini study, its representativeness and the main measures are presented. The two key elements of the Gemini study are that it involves twins and that it is a longitudinal study from birth. The twin design permits estimations of genetic and environmental contributions to appetite, food and activity preferences and weight gain. The longitudinal design from birth permits assessment of very early influences and provides information about causal processes behind excessive early weight gain.

**Conclusion:** This is the first twin cohort to focus on childhood weight gain with detailed and repeated measures of children's appetite, food preferences, activity behaviour and parental feeding styles, alongside detailed and repeated collection of anthropometrics.

**Conflict of interest:** None disclosed.

**Funding:** The research was funded by a grant from Cancer Research UK (C1418/A7974).

## T4:PO.264

## The effect of the Catechol-O-methyltransferase Val158Met variant (rs4680) on energy expenditure and weight loss

**Larsen LH**[1], Ängquist L[2], Larsen TM[1], Holst C[2], Grau K[2], Langin D[3], Saris WHM[4], Pedersen O[5], Sørensen TIA[2] and Astrup A[1]

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**Introduction:** The objective of this study was to examine if the functional Val158Met variant (rs4680) in the Catechol-O-methyltransferase (COMT) is associated with changes in energy expenditure (EE) and weight loss.

**Methods:** Seven hundred and seventy one obese (BMI≥30 kg/m$^2$, 20–51 years, 75% women) participants from the NUGENOB study were included to analyse the association of the rs4680 with (i) baseline BMI, lean body mass (LBM), respiratory quotient (RQ), fat oxidation (FO), free fatty acid (FFA) and energy expenditure (EE); (ii) 3-hour post-prandial iAUC for FO and EE after a high-fat liquid meal (50% of BMR, 95 en% fat); and (iii) weight loss during a 10-week hypo-caloric diet (-600 kcal/day, 20–25% vs. 40-45% fat). Analyses were performed using linear regression models and applying four different genetic models.

**Results:** The minor allele frequency (G-allele) of the rs4680 was 0.48. At baseline, carriers of the G-allele had significantly lower baseline RQ ($P < 0.05$) and higher baseline FO ($P < 0.05$). Post-prandially, there was no significant association of rs4680 with either FO or EE. There was no significant association of rs4680, with or without diet interaction, with weight loss after 10 weeks of dieting.

**Conclusion:** At baseline, the G-allele that reduces the enzymatic activity of COMT was associated with decreased RQ and increased

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FO. However, there was no association of the rs4680 with pre- or postprandial energy expenditure or weight loss.
Conflict of interest: None to declare.
Funding: The study was funded by the European Community (Contact no. QLK1-CT-2000-00618).

## T4:PO.265

## Reducing dietary saturated fat may attenuate genetic susceptibility for high LDL cholesterol (LDL-C) in overweight subjects

**Walker CG**[1], Loos RJF[2], Olson AD[1], Frost GS[3], Griffin BA[4], Lovegrove JA[5], Sanders TAB[6] and Jebb SA[1]
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Introduction: Large-scale genome-wide association studies (GWAS) have identified many SNPs reproducibly associated with dyslipidaemia in cross-sectional studies. Whether these loci affect metabolic responses to dietary changes is unknown. Our aim was to examine how established LDL-C associated SNPs altered the LDL-C response to a dietary intervention to decrease saturated fat (SFA) intake.
Methods: The RISCK study lowered SFA intake by replacement with MUFA or carbohydrate. Following 1 month run-in period on a 'reference' diet (~18%SFA, 38%fat as energy), participants ($n$ = 720) were randomised to (i) reference diet; (ii) MUFA (~10%SFA,38%fat,20%MUFA); or (iii) LF (~10%SFA,28%fat,11%MUFA) diets. Participants who completed the 6 month intervention were genotyped ($n$ = 530) for 12 LDL-C associated SNPs. A cumulative genetic predisposition score (GPS) for each individual was calculated by summing the risk alleles carried (maximum 24).
Results: At baseline, eight out of 12 SNPs, tended to be associated with higher LDL-C, of which two reached significance (rs6756629, $P$ = 0.013; rs4420638, $P$ = 0.007) and the cumulative GPS was positively associated with LDL-C (B = 0.094, $P$ = 0.049). In response to intervention, LDL-C decreased with LF (B = −0.286, $P$ < 0.0001) and MUFA diets (B = −0.293, $P$ < 0.0001) compared to reference. The absolute decrease in LDL-C with intervention was more pronounced the higher the GPS (B = −0.097, $P$ = 0.044) with a trend toward a greater proportional decrease (B = −0.086, $P$ = 0.074). There was no significant interaction effect between MUFA or LF with GPS.
Conclusion: We confirm that SNPs previously identified through GWAS have a cumulative effect on LDL-C levels. More importantly we show, despite having a high genetic susceptibility (high GPS), LDL-C levels can still be lowered by targeted dietary interventions.
Conflict of interest: None.
Funding: The RISCK dietary intervention study was funded by the Food Standards Agency project number NO2031. Genetic analyses were funded by the participating centres.

## T4:PO.266

## Polymorphism in codon 103 of MC4R gene influences abdominal obesity and hypercholesterolemia in a rural population of Tamilnadu, South India

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Overweight and obesity have long been associated with adverse health outcomes such as cardiovascular disease, metabolic syndrome and Type 2 diabetes. The combinations of changes in eating habits and sedentary lifestyles have contributed significantly to the increased prevalence of overweight and obesity worldwide.
The melanocortin receptor gene 4 (MC4R) regulates food intake and energy expenditure. Polymorphisms in the MC4R gene predispose individuals to heritable obesity. The present study was conducted to study the influence of G→A polymorphism in the MC4R gene in a representative population of Tamilnadu, South India.
A cohort of unrelated individuals ($n$ = 62, mean age 33.24 years, Age group 32–48 years) were recruited with informed consent. Demographic factors, dietary pattern, physical activity etc were recorded through a questionnaire based interview. BMI, waist hip ratios, Waist and hip circumference were recorded. Fasting serum lipid profiles were analyzed by photometric method. Genotyping of DNA sequence variation of codon 103 of MC4R gene was done by PCR RFLP method using sequence specific primers and *Hinc II* restriction enzyme.70% ($n$ = 42) of obese subjects in the study cohort were homozygous (G/G) and 30% were heterogygous (G/A) for the G allele.
Hypertriglceridemia (TGL levels above 180 mg/dL) and elevated LDL levels (135 mg/dL) was observed among G allele homozygotes. The mean waist circumference among obese men (G/G homozygote) was 93.5 cms indicating abdominal obesity. The results indicate that the G→ A substitution in codon 103 of MC4R gene predisposes the study cohort to abdominal obesity and hypertriglyceridemia.

## T4:PO.267

## Gene analysis of congenital generalized lipodystrophy in Japan

Sakai T[1], Kusakabe T[1], Ebihara K[1,2], Aotani D[1], Yamamoto-Kataoka S[1], Fujisawa T[1], Yamamoto Y[1], Aizawa-Abe M[2], Miyamoto L[1], Miyazawa T[2], Hosoda K[1,2] and Nakao K[1,2]
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Congenital generalized lipodystrophy (CGL) is a rare disorder characterized by near complete absence of body fat at birth or early infancy. Diabetes mellitus accompanied by insulin resistance, hypertriglyceridemia, fatty liver, cardiomegaly, acromegaloid features and acanthosis nigricans can usually be present. CGL is frequently inherited in an autosomal recessive fashion. *Seipin* and *AGPAT2* have been identified as causative genes for CGL. *Seipin* mutations were found in patients originating from Europe and the Middle East. *AGPAT2* mutations were found predominantly in African ancestry. However, direct estimates for the prevalence rate of CGL and gene analysis of CGL are not fully performed in Japan. At first, we investigated the number of patients with lipodystrophy in Japan by inquiry survey in members of Japan Endocrine Society and found 21 CGL patients. Then, we performed gene analysis in ten CGL patients from different geographical areas of Japan. (Percent body fat, 5.5 ± 0.6%; leptin level, 1.0 ± 0.1 ng/mL) (mean ± SE). We found three different homozygous mutations in *Seipin* gene (Y187C, E189X and R275X) from eight CGL patients. We did not find any mutations of *AGPAT2* genes in these CGL patients. Our results suggest that *Seipin* is a major causative gene for CGL in Japan.

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