Pediatric Endocrinology In Premature Infants

The optimal nutritional balance needed for preventing metabolic syndrome while achieving optimal development for preterm infants

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Student: Mor Frisch



About the study

Longitudinal case control study

- Inclusion criteria: Preterm twins born at SMC between 2008-2015
- **<u>Cases</u>:** SGA twin (<10th%)
- <u>Controls</u>: AGA twin (10th-90th%)
 We chose twins in order to control genetic and life style variables
 - <u>Exclusion</u>: Death prior to discharge, CNS & genetic abnormalities

We identified 1300 pairs of twins born at Sheba Medical Center between 2008-2015

97 sets of AGA/SGA twins qualified for the study

Twins that reached the age of 5 will be included in the study

What's next?

The aims of the study

 To check for <u>early signs</u> of <u>metabolic</u> <u>syndrome</u> at the age of 5-8 years among the small babies (SGAs)



The metabolic syndrome

Metabolic syndrome is a clustering of at least three of five of the following medical conditions:

abdominal (central) obesity
elevated blood pressure
elevated fasting plasma glucose
high serum triglycerides
low HDL

Metabolic syndrome is associated with the risk of developing cardiovascular disease and diabetes.

What's next?

The aims of the study



 To study the risk and additional risk factors for early markers of metabolic syndrome among the above population

 To check if the twins still show a difference in their percentiles today at 5-8 years



The aims of the study

What's next?

- To study weight changes over time
- If there are early signs, we want to be aware of them and therefore prevent or postpone the development of diabetes

What's next?

The aims of the study

 To evaluate neurodevelopment among SGA preterm infants and its correlation to early nutrition and growth



We created a chart that includes more than 50(!) different demographic & clinical parameters in analyzed risk factors

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About the chart :

- <u>Maternal demographic data</u> e.g. mother's age at birth
- <u>Pregnancy data</u> e.g. types of birth (vaginal\CS); spontaneous pregnancy or IVF
- Hospitalization data
- Feeding data e.g. percentage of breast milk; number of days to regain birth weight
- <u>Infant demographic data</u> and clinical course during the NICU stay or initial hospitalization
 Etc...

Reading similar articles in Pubmed

In order to find what is already known and what we can innovate

Full text links Abattatt Mentri Felix Records Mer. 2014 New 27(17) 1795 + doy 10 310 Growth parameters of discordant preterm twins during the first year of Markeven R1, Miron E. Lebovitch L. Kunt J. Strauss T. Maayan-Metzger A Author information OBJECTIVE: To evaluate and compare growth parameters (weight, length and head nce) of discordant preferm twins during the first year of life METHODS: Retrospective data were collected on 78 pairs of >10% discordant preterm twins. Data regarding short-term recorded. Growth param recorded at birth and again at 1 year of age, as collected by phone interview. RESULTS: At 1 year of age, the gap was significantly reduced between the group of smaller twins and the group of larger twins on all the parameters studied. Discordance in weight decreased from a mean of 22% at birth (calculated from the weight of the larger twin) to 8 f in length from 6.5% to 2.5% and in head circumference from 5.5% to 1.3% at 1 year of age While length and head circumference (HC) z-scores improved in both the largo and the sm siblings, weight z-score decreased significantly among the large twins and decreased mi among the small twins CONCLUSIONS: The gaps in growth parameters between the smaller twins of preterm discordant twins and their larger siblings are significantly reduced during the first year of The impact of the differential growth patterns between the two siblings should be further evaluated. KEYWORDS: Growth: praterm, twin discordance PMID 34397374 [PubMed - indexed for MEDLINE] PubMid V 2018 Mar (66.3) 111-21. dai: 10.10165 metabol 2015.10.027.10.02 2015 00 al.

Publios 6

Abdominal obesity and circulating metabolites: A twin study approach. Bag LH*, Keyn SM*, Ramo JT*, Sansas AJ*, Sonnen P*, Hansaramen A*, Lundborn J*, Lundborn N*, Onent-Korso A*, Rissanen A*, Ale-Korsola M*, Kapno J*, Pietineven KH** Author information

OBJECTIVE: To investigate how obesity, insulin resistance and low-grade inflammation link to ulating metabolities, and whether the connections are due to genetic or environmental factors.

SUBJECTS AND METHODS: Circulating serum metabolites were determined by proton NMR spectroscopy. Data from 1368 (531 monozygotic (MZ) and 837 dizygotic (DZ)) twins were used for bivariate twin modeling to derive the genetic (rg) and environmental (re) correlations between waist circumference (VIC) and serum metabolites. Detailed examination of the associations between fat distribution (DEXA) and metabolic health (HOMA-IR, CRP) was performed among 286 twins including 33 BMI-discordant MZ pairs (intrapair BMI difference ≥3kg/m(2)).

RESULTS: Fat, especially in the abdominal area (i.e. WC, android fat % and android to gynoid fat ratio), together with HOMA-IR and CRP correlated significantly with an atherogenic Ipoprotein profile, higher levels of branched-chain (BCAA) and aromatic amino acids, higher levels of glycoprotein, and a more saturated fatty acid profile. In contrast, a higher proportion of gynoid to total fat associated with a favorable metabolite profile. There was a significant genetic overlap between WC and several metabolites, most strongly with phenylalanine (rg=0.40), glycoprotein (rg=0.37), serum triglycerides (rg=0.36), BCAAs (rg=0.30.0.40), HDL particle diameter (rg=-0.33) and HDL cholesterol (rg=-0.30). The effect of acquired obesity within the discordant MZ pairs was particularly strong for atherogenic lipoproteins.

CONCLUSIONS: A wide range of unfavorable alterations in the serum metabolome was associated with abdominal obesity, insulin resistance and low-grade inflammation. Twin modeling and obesity-discordant twin analysis suggest that these associations are partly explained by shared genes but also reflect mechanisms independent of genetic liability.

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KEYWORDS: Bivariate twin model, Genetic correlation, Obesity measures, Serum metabolites; Twi study

MID 26892522 (PubMed - in process)

Europe PMC Funders Group Author Manuscript nt J Obes (Lond). Author manuscript; available in PMC 2015 December 01. Published in final edited form as: Int J Obes (Lond). 2015 June ; 39(6): 899-909. doi:10.1038/ijo.2015.24. Longitudinal weight differences, gene expression, and blood biomarkers in BMI discordant identical twins Jenny van Dongen^{1,2,*}, Gonneke Willemsen^{1,2}, Bastiaan T. Heijmans³, Jacoline Neuteboom⁴, Cornelis Kluft⁴, Rick Jansen⁵, Brenda W.J. Penninx^{2,5}, P. Eline Slagboom³, Eco J.C. de Geus^{1,2}, and Dorret I. Boomsma^{1,2} ¹Department of Biological Psychology, VU University Amsterdam, Amsterdam, The Netherlands ²EMGO institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands ³Department of Molecular Epidemiology, Leiden University Medical Center, Leiden, The Netherlands ⁴Good Biomarker Sciences, Leiden, The Netherlands ⁵Department of

Psychiatry, VU University Medical Center, Amsterdam, The Netherlands

Abstract

Background-BMI discordant monozygotic (MZ) twins allows an examination of the causes and consequences of adiposity in a genetically controlled design. Few studies have examined longitudinal BMI discordance in MZ pairs.

Objectives-To study the development over time of BMI discordance in adolescent and adult MZ twin pairs and to examine lifestyle metabolic inflammatory and gene expression differences associated with concurrent and long-term BMI discordance in MZ pairs.

Subjects/Methods-BMI data from 2775 MZ twin pairs, collected in eight longitudinal survey

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Girls and Boys Born before 28 Weeks Gestation: Risks of Cognitive. Behavioral, and Neurologic Outcomes at Age 10 Years

Karl C. K. Kuban, MD, SMEpi¹, Robert M. Joseph, PhD², Thomas M. O'Shea, MD³, Elizabeth N. Allred, MS^{4,5}, Timothy Heeren, PhD⁶, Laurie Douglass, MD¹, Carl E. Stafstrom, MD, PhD⁷, Hernan Jara, PhD⁸, Jean A. Frazier, MD⁹, Deborah Hirtz, MD¹⁰, and Alan Leviton, MD^{4,5}, on behalf of the Extremely Low Gestational Age Newborn (ELGAN) Study Investigators*

Objectives To compare the prevalence of cognitive, neurologic, and behavioral outcomes at 10 years of age in 428 girls and 446 boys who were born extremely preterm.

Study design A total of 889 of 966 eligible children previously enrolled in the multicenter Extremely Low Gestational Age Newborns Study from 2002-2004 were evaluated at 10 years of age. Children underwent a neuropsychological battery and testing for autism spectrum disorder (ASD), and parents reported on their child's behavior, development, and seizures.

Results Of the children, 28% of boys and 21% of girls exhibited moderate to severe impairment on summary measures of cognitive abilities. Boys had a higher prevalence of impairment than girls in nearly all measures of cognition, were more than twice as likely to have microcephaly (15% in boys, 8% in girls), and require more often assistive devices to ambulate (6% in boys, 4% in girls). In contrast, boys and girls had comparable risk for a history of seizure (identified in 10% of the cohort) or epilepsy (identified in 7% of the cohort). The boy-to-girl ratio of ASD (9% in boys, 5% in girls) was lower than expected compared with the overall US autism population.

Conclusions In this contemporary cohort of children born extremely premature and evaluated at school age.

JAMA & MAL Antibiotic Exposure During the First 6 Months of Life and Weight Gain During Childhood.

Genter, Al¹, Boyan M⁴, Ross RX⁴, Dayment S⁴, Parks EP⁴, Locaio AR³, Guindmeier RX⁴, Stallingt W⁴, Zacute TE¹,

Author information

Assertant apport ANCE: Early-life emission exposure has been associated with increased adjointly in animal models: modulated trought the gut monotions, intent antibiotic exposure is commen and often imporporties: Studies of the association between infant antibiotics and childhood neight gan have reported increases requires.

ORJECTIVE: To assess the association between early-life antibiotic et

DESIGN AND SETTING: Refrospective, longitudinal study of singleton births and matched longitudinal study of twin pairs conducted in a network of 30 pediatric primary care practices enving more than 200.000 children of diverse racial and socioeconomic backgrounds acress nonsylvamis, New Jersey, and Delaware.

RTICIPANTS: Children born between November 1, 2001, and December 31, 2011, at 35 As gestational age or older, with birth weight 2000 g or more and in the fifth percentile given for gestational age, and who had a preventive health visit within 14 days of life and ast 2 additional visits in the first year of life. Chidren with complex chronic conditions and who received long-term antibiotics or multiple systemic contracted period prescriptions, e who received long-term antibiotics or multiple systemic contracted prescriptions, excluded. We included 38,522 singleton children and 92 twins (46 matched pairs)

dant in antibiotic exposure. Final date of follow-up was December 31, 2012.

OSURE: Systemic antibiotic use in the first 6 months of life.

IN OUTCOMES AND MEASURES: Weight, measured at preventive health visits from age months through 7 years.

ESULTS: Of 38,522 singleton children (50% female; mean birth weight, 3.4 kg), 5287 (14%) the exposed to antibiotics during the first 6 months of life (at a mean age of 4.3 months) biotic exposure was not significantly associated with rate of weight change (0.7%; 95% CI, 1% to 1.5%; P = .07, equivalent to approximately 0.05 kg; 95% C1, -0.004 to 0.11 kg of weight gain between age 2 years and 5 years). Among 92 twins (38% female; mean th weight, 2.8 kg), the 46 twins who were exposed to antibiotics during the first 6 months of received them at a mean age of 4.5 months. Antibiotic exposure was not significantly ociated with a weight difference (-0.09 kg; 95% Cl, -0.26 to 0.08 kg; P = .30). NCLUSIONS AND RELEVANCE:



States States

Leptin, insulin, insulin-like growth factors and their binding proteins in cord serum: insight into fetal growth and discordancy. Question S1 Hed M. Merton P. Staat 8 Author Information

Delivery of the second second

DESIGN: Prevalent case-control study.

CONTRACT 1045 2000 New 2010 1805-90

PATIENTS: Twenty pars of discordant twins (5 monozygotic, 15 dizygotic) and 20 pairs of twins (6 motozygotic, 14 dizygotic) matched for gestational age.

MEASUREMENTS: Cord blood levels of IGF-1, IGF-2, IGF8P-1, IGF8P-3, insulin, leptin and EASOREMENTS: Conversions at birth. Intra- and inter-pair differences and correlation intercommentic measurements at birth. Intra- and inter-pair differences and correlation servicinets were traiculated, and the data were fitted to multivariate regression mode

RESULTS: In both discordant and concordant groups, the smaller twins had a significantly lower local of GPU-1 (P<0.03) and significantly higher level of (GPU-1 (P<0.03) han there large course. IGPIB-1 varies revealed correlated with GPU-1 (P<0.03) hand like the significantly higher in the smaller discordant than the smaller concordant twins (P<0.03) and in the larger discontant than the larger concordant twins (P < 0.004). Among the monozygotic twins, the leptin level was significantly higher in the larger discordant than the larger concordant twins ($P \le 0.025$). Percentage birth weight discordancy was statistically e birth weight discordancy was statistically correlated

with twin-pair differences in IGF-1 and IGFBP-1. CONCLUSIONS: Of the six factors studied, IGF-1 appears to be the main indicator of strauterine growth. Twin discordancy may involve compensatory rather than adaptive chanisms or a multihormone relative resistance syndrome.

HAD 17054458 (PubMed - indexed for MEDLINE)

ublication Types, MeSH Terms, Substances

Reading similar articles in Pubmed

In order to find what is already known and what we can innovate

We did not find anything similar to our idea

 The most similar study was a monozygotic twins study in Leiden. They took 2775 pairs of twins and followed up on them over 20 years **Reading similar articles in Pubmed**

In order to find what is already known and what we can innovate

Their goals were:

1.Checking the incidence of discordancy – changes in BMI over 20 years

2.Periodic evaluation of the following: inflammatory, metabolic and other biomarkers (glucose, insulin, total cholesterol, LDL, triglycerides, CRP, IL-6, sIL-6R) in the cohort of the monozygotic twins

What's next?

Recruitment of the participants of the study Invite the twins during their summer vacation

- Running blood tests checking blood markers of the metabolic syndrome (glucose, insulin, total cholesterol, LDL, triglycerides, CRP, IL-6, sIL-6R, and GGT, a lower level of HDL)
- Height evaluation
- Weight evaluation
- BMI
- Cognitive test
- Psychological test
- Parents background questionnaire
- Nutritional assessment

Recruitment of the participants of the study









* Invite the twins during their summer vacation and other school vacations during the year

How does a day in the research look like?



Dr. Iris Morag

 <u>Running blood tests</u> – checking blood markers of the metabolic syndrome (glucose, insulin, total cholesterol, LDL, triglycerides, CRP, IL-6, sIL-6R, and GGT, a lower level of HDL)



- <u>Height evaluation</u>
- Weight evaluation

<u>BMI</u>



<u>Nutritional assessment</u>



<u>Sarit Atia</u> Dietitian

<u>Cognitive test</u> Gabriel Mandel





- Endocrine Evaluation
- Parents background questionnaire



Prof. Orit Hamiel

Visceral fat and adipose tissue





Dr. Orly Stern

Cardiac Echo Dr. Sharon Borik



<u>What's next</u>

- Recruit more twins (hopefully)
- Analyzing the data



Thank You





To Dr. Iris Morag on her acceptance to a special research program in Stanford, USA for a year!!!

