Results: IS and β-cell function decreased over 6-yrs by 14-24.3% (all p<0.001; Fig. A-B); although BMI or WC did not change (<2%). Conversion to dysglycemia was ~12% over 6-yrs, where higher total NEFA increased the risk by 25% (RR=1.25 (1.02-1.52) per SD). While total NEFA were not associated with IS, palmitate predicted declines in HOMA-IS (p=0.037). Higher total NEFA predicted declines in IGI/IR and ISSI-2 (both p<0.02; Fig. C), with higher concentrations of palmitate, oleate, and linoleate predicting declines in ISSI-2 (p=0.003 to 0.043); these three species comprised 74.8% of total NEFA.
Conclusions: Given that palmitate, oleate, and linoleate comprise the majority of the NEFA pool, our findings suggest that *total* NEFA rather than individual species may more strongly influence T2DM risk, primarily through β-cell dysfunction.
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Short Oral Abstract 15 – Increase in angiotensin converting enzyme in response to a high fat diet (Rita Schüler, Germany)

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Objective: In addition to an effective treatment in cardiovascular diseases, inhibition of angiotensin-converting enzyme (ACE) also improves insulin sensitivity. On the contrary, carriage of the D-allele of the ACE insertion/deletion (I/D) polymorphism is associated with increased ACE serum levels and impaired glucose tolerance. We aimed to investigate effects of a high-fat diet (HF) on ACE considering possible nutrigenetic effects.
Methods: In the NUGAT (NUtriGenomic Analysis in Twins) study 46 healthy twin pairs went from a 6-week carbohydrate-rich low-fat diet (LF) to a 6-week HF diet under isocaloric conditions. Clinical investigation days (CIDs) took place after 6 weeks LF and after 1 and 6 weeks of HF. At each CID subcutaneous adipose tissue biopsies were taken for gene expression analysis on Agilent 8x60K microarrays. Serum parameters were analyzed in blood samples using ELISA. To assess insulin sensitivity intravenous glucose tolerance tests (ivGTT) were performed and incremental areas under the curve (AUC) calculated. Genomic DNA extracted from whole blood was genotyped using Illumina HumanOmniExpressExome BeadChips.
Results: After six weeks HF circulating ACE levels increased by 15% (HF6 161±49 ng/ml vs. LF 139±41 ng/ml; p<0.001) paralleled by an increase in adipose tissue gene expression (1.41-fold, p<0.001). Interestingly, in homozygous carriers (GG) of the rs4343 polymorphism, which serves as a surrogate marker for ACE I/D polymorphism, the increase in serum levels was nearly twice as high as compared to non-carriers (AA) or heterozygous carriers (AG) (p<0.001). Whereas no change in glucose tolerance was observed for AA/AG-carriers, glucose tolerance significantly declined in GG-carriers after six weeks of HF ($\Delta AUC_{glucose}$, recessive model: p=0.009).
Conclusions: ACE might constitute a molecular link between dietary fat intake and cardiovascular diseases as well as impaired glucose metabolism. The extent of this relationship seems to be nutrigenetically modulated.
Protocol registration: www.ClinicalTrials.gov, identifier NCT01631123
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