Regulation af Glukagon og GLP-1

- hos mennesker med og uden adipositas

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Clinical Research Article

Altered Glucagon and GLP-1 Responses to Oral Glucose in Children and Adolescents With Obesity and Insulin Resistance

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Baggrund

- Stigende forekomst af adipositas hos børn og unge.
- Øget risiko for type 2-diabetes, fedtlever og hjerte-kar-sygdomme.
- Ikke forudsigeligt hvem der udvikler de kardiometaboliske komplikationer.
  - ofte kædet sammen med glukosestofskiftet, herunder insulinresistens
- Specielt interessante er glukagon, GIP (glucose-dependent insulinotropic polypeptide og GLP-1 (glucagon-like peptide-1).

Glukagon

1. Stimulerer nedbrydningen af glykogen til glukose (glykogenolyse)
2. Stimulerer nydannelse af glukose (glukoneogenesen)
3. Stimulerer nedbrydningen af fedt til frie fedtsyrer (lipolysen).
4. Hæmmer glykolysen (nedbrydningen af glukose).

Inkretiner (GIP og GLP-1)

1. Stimulerer dannelsen af insulin (blandt mange andre funktioner)

Uklart om insulinresistens medierer sin effekt på adipositas-relaterede komplikationer via glukagon og inkretiner samt om dette sker allerede i barndommen…

Formål

- At teste koncentrationerne af **glukagon, GLP-1 og GIP** i blodet under en oral sukkerbelastningstest (OGTT) og se om der er forskel mellem grupperne af børn og unge med
  - obesity and insulin resistance (OIR), N=22
  - obesity and normal insulin sensitivity (OIS), N=22
  - Normal weight (NW), N=36
- Alder: 7-17-årige
- Hypotesen er, at OIR vil have højere faste-koncentrationer af disse hormoner, samt højere glukagon og lavere GLP-1 og GIP respons under OGTT, hvilket vil associere til dårligere insulinfølsomhed, β-celle funktion og højere levertal.

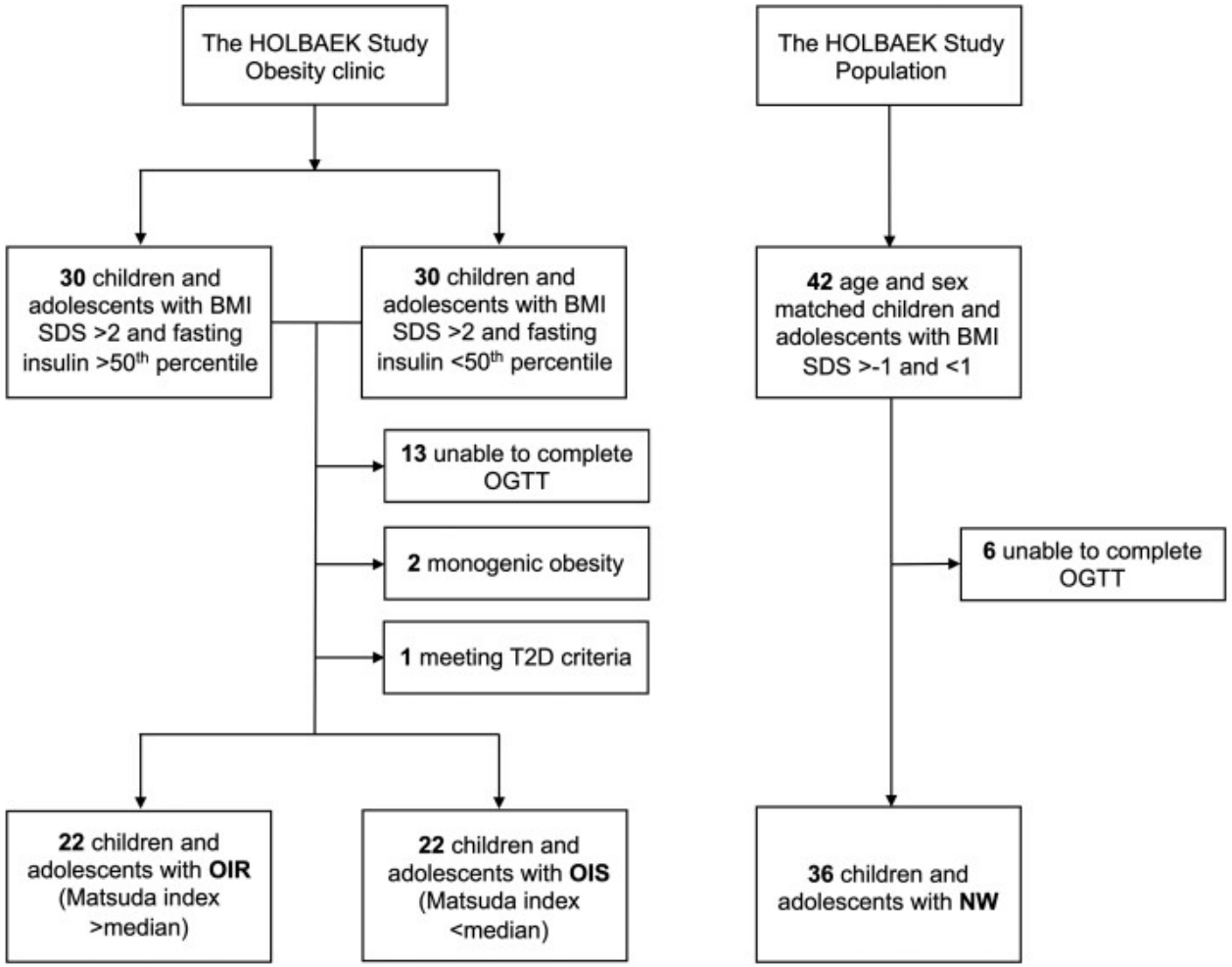
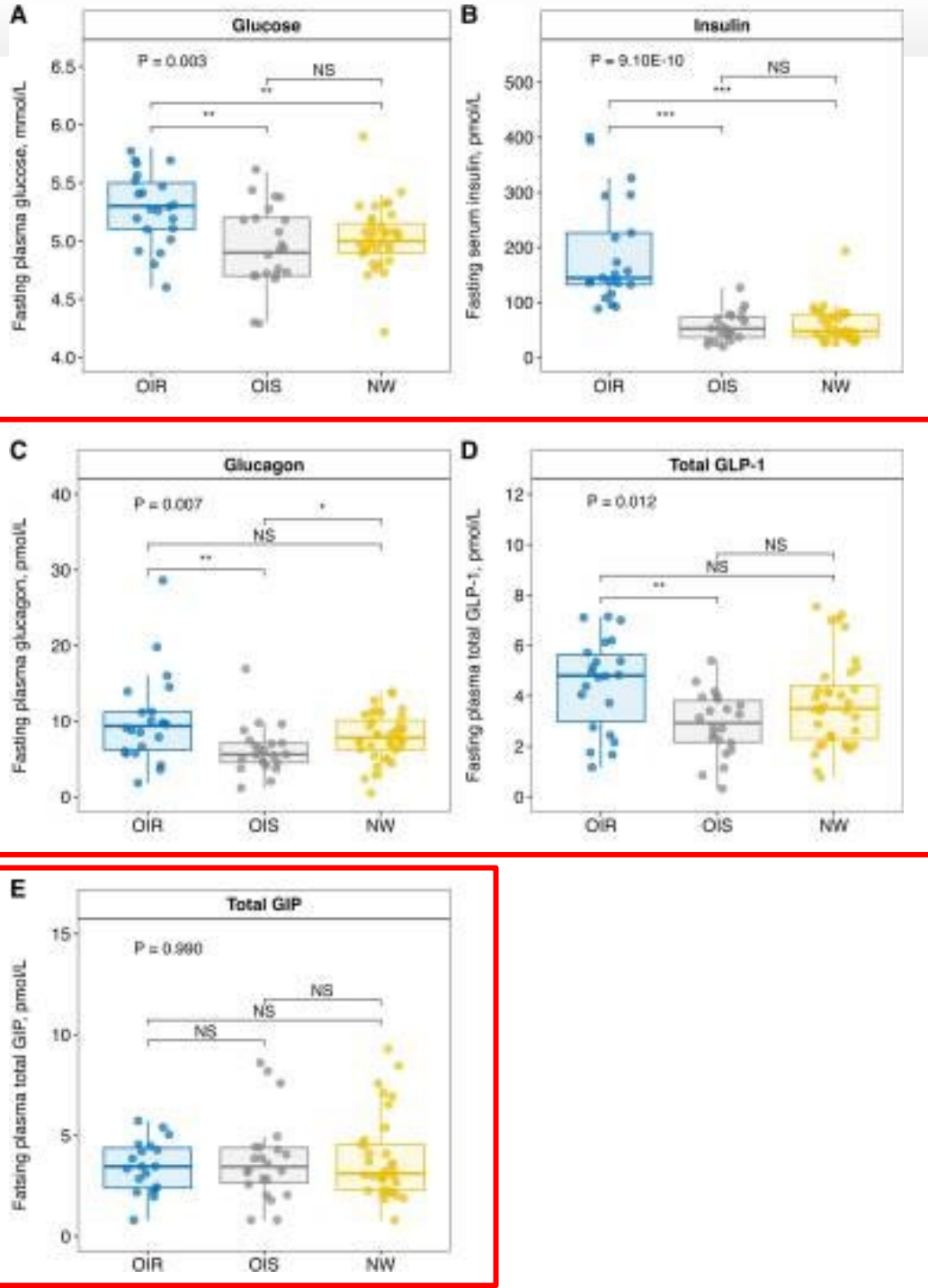

The HOLBAEK Study Obesity clinic
30 children and adolescents with BMI SDS >2 and fasting insulin >50th percentile
30 children and adolescents with BMI SDS >2 and fasting insulin <50th percentile
13 unable to complete OGTT
2 monogenic obesity
1 meeting T2D criteria
22 children and adolescents with OIR (Matsuda index >median)
22 children and adolescents with OIS (Matsuda index <median)
The HOLBAEK Study Population
42 age and sex matched children and adolescents with BMI SDS >-1 and <1
6 unable to complete OGTT
36 children and adolescents with NW

Table 1. Clinical characteristics of the study groups

	OIR	OIS	NW
N	22	22	36
Age, years	13.6 (12.4, 15.3)	11.3 (9.4, 13.0)	11.2 (9.0, 13.3)
Sex (boys vs girls), n	6/16	13/9	15/21
BMI SDS	2.94 (2.73, 3.14)	2.63 (2.42, 3.01)	0.13 (0.01, 0.47)

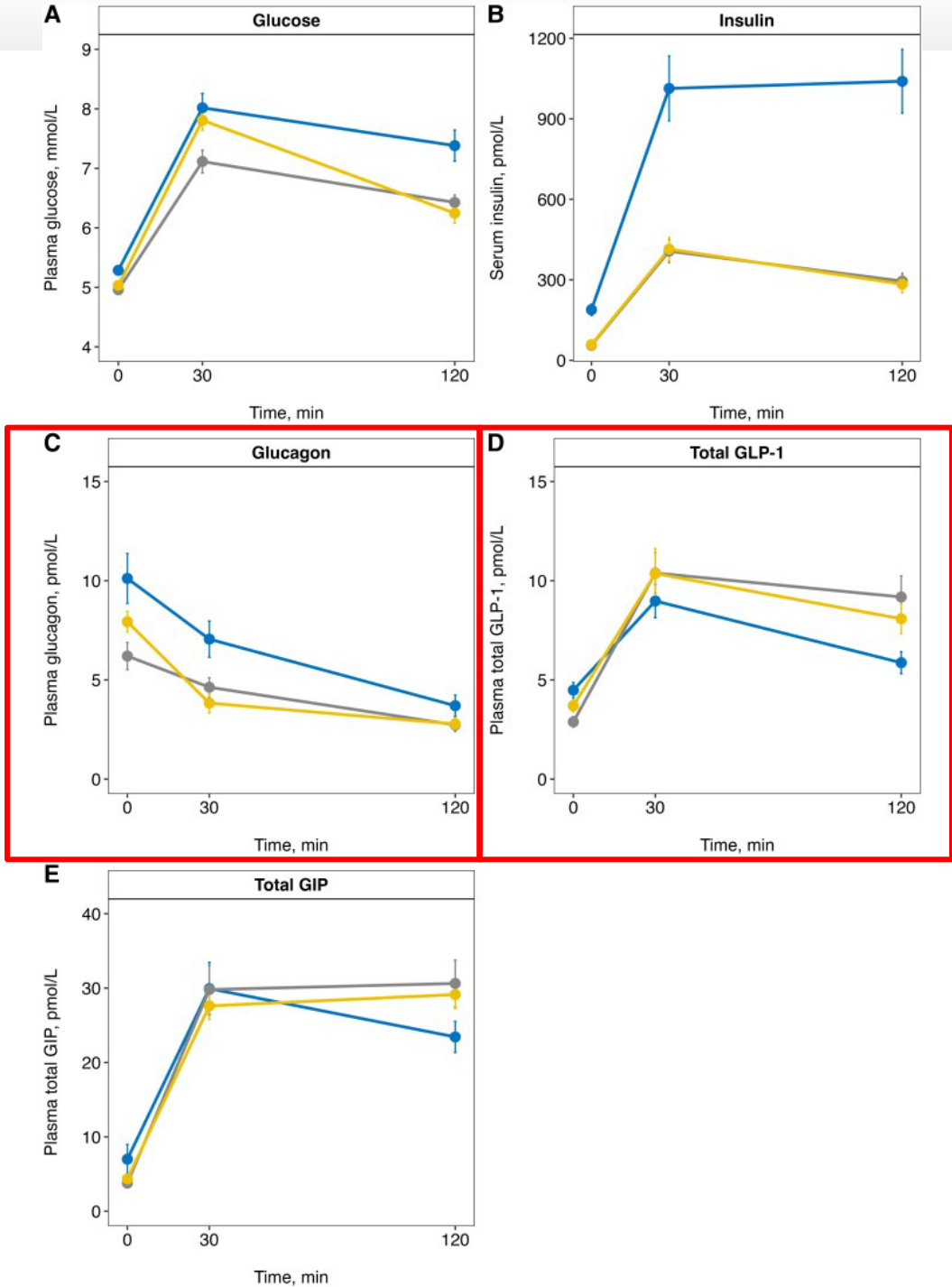
Resultater (fastende – før OGTT)

- Forhøjede fastekoncentrationer af glukagon og GLP-1 i OIR-gruppen sammenlignet med OIS- og NW-grupperne.
- Ingen signifikant forskel i GIP-fastekoncentrationer mellem grupperne.
- Korrelationer mellem fastehormoner, insulinresistens og leverenzymer.



Resultater (OGTT)

- Højere glucagon-AUC i OIR-gruppen sammenlignet med OIS- og NW-grupperne.
- Lavere GLP-1-AUC i OIR-gruppen sammenlignet med OIS- og NW-grupperne.
- Ingen signifikant forskel i GIP-AUC mellem grupperne.
- Korrelationer mellem hormonresponser under OGTT, insulinresistens og leverenzymer.



Konklusion

- Børn og unge med overvægt og insulinresistens (OIR) har forhøjede fastekoncentrationer af glukagon og GLP-1 (ikke GIP).
- OIR har forhøjet glukagon og et svækket GLP-1 respons under en OGTT (sammenlignet med jævnaldrende med OIS og NW.
- I modsætning hertil viste personer med OIS ingen signifikante forskelle i hormonresponser sammenlignet med kontroller med normalvægt.
- Forhøjet glukagon og et svækket GLP-1 respons var associeret med nedsat insulin følsomhed og β-cellefunktion.
- Undersøgelsens resultater tyder på, at insulinresistens er koblet til overvægtsrelaterede ændringer i glukagon- og GLP-1-sekretionen, hvilket kan have betydelige konsekvenser for fremtidig sygdomsrisiko.

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