Title: Longitudinal study of the GLUcagon REsponse to hypoglycemia in children and adolescents with new-onset type 1 DIAbetes (GLUREDIA study): characteristics and predictive biomarkers

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Aims: To longitudinally assess alpha-cell response to hypoglycemia in pediatric patients with new-onset type 1 diabetes (T1D) and compare it with that of healthy subjects.

Methods: Using an insulin-induced hypoglycemia test (IIHT), we assessed 23 T1D patients at 0-, 6-, 12-, and 18-months post-diagnosis and compared them with a control group of eight healthy first-degree relatives (FDR). The IIHT involved a subcutaneous insulin dose calibrated to induce hypoglycemia, with blood samples collected at baseline and during stage 2 hypoglycemia (<54 mg/dL) to evaluate glucagon, cortisol, catecholamines, vasopressin, and growth hormone levels.

Results: In the control group, stage 1 hypoglycemia (<70 mg/dL) was consistently asymptomatic and triggered a significant increase in glucagon secretion (1.92 ± 1.06 pmol/L, p<0.001), followed by spontaneous glycemic correction. In contrast, the T1D group experienced stage 2 hypoglycemia with impaired alpha-cell response throughout the 18-month follow-up (0.64 pmol/L ± 2.43; p=0.15). At 0- and 12 months, glucagon response was nonsignificant, while a transient restoration was observed at 6 months (2.00 pmol/L ± 3.03; p<0.001), followed by a paradoxical suppression at 18 months (-1.63 pmol/L ± 1.43; p<0.001). Basal glucagon levels remained stable across all time points and did not differ between the two groups.

Conclusion: These findings highlight progressively impaired glucagon response in early T1D, with potential implications for hypoglycemia risk and disease management. The IIHT proved safe and reproducible. Ongoing studies, including 82 additional T1D patients (DIATAG cohort), will further refine our understanding of alpha-cell dysfunction in T1D progression. This study showed the dynamics of alpha-cell secretion in response to metabolic changes over time, providing insights into its role in glycemic regulation and disease progression.

SPEAKER BIOSKETCH - Maude BECKERS (UCL)

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CURRENT AND PAST POSITIONS:

- Paediatric Endocrinologist and Diabetologist in the Specialized Paediatrics Unit in Cliniques Universitaires Saint-Luc, Brussels, since 2023.
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EDUCATION:

- Specialization in Paediatrics in Cliniques Universitaires Saint-Luc, UCLouvain, from 2018 to 2023
- Master's in medicine in UCLouvain from 2012 to 2018

AWARDS AND HONORS:

- FNRS SD grant since 2023
- Nestle BVK/SBP Congress 2022 Prize for best long oral presentation: "INSENODIAB Study: Determinants and characteristics of insulin dose requirements in children and adolescent with new-onset type 1 diabetes". Beckers M, Bernard N, Gallo P, Bugli C, Lysy P. A. Société Belge de pédiatrie. Bruxelles. Mars 2022.
- Sandoz Scientific Award 2023 applicant. "Determinants And Characteristics Of Insulin Dose Requirements In Children And Adolescents With New-Onset Type 1 Diabetes : Insights From The INSENODIAB Study". Beckers M, Polle O, Bernard N, Gallo P, Lysy P.
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OTHER RELEVANT PROFESSIONAL ACTIVITIES AND ACCOMPLISHMENTS:

Scientific Committees

- Associated member in BELSPEED, since 2025.

Academic responsibilities

- Pathologies pédiatriques : Endocrinologie in ISEI, Brussels, since 2022
- Anamnèse et examen clinique pédiatrique in UCLouvain Medical School, Brussels, since 2022
- Principe des essais cliniques in UCLouvain (Public Health Master's), in 2022-2023.