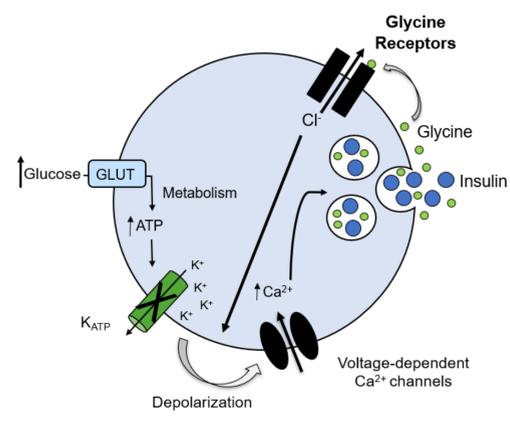


Glycine Receptor Activity in β Cells Is Downregulated in Type 2 Diabetes and After High Glucose Culture

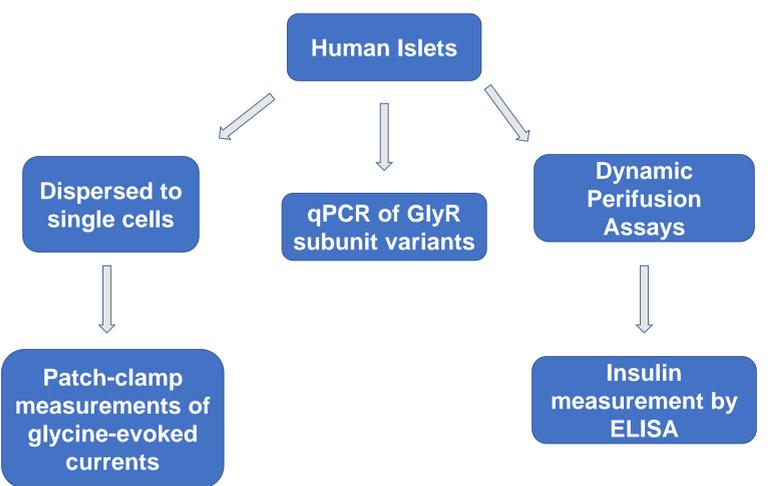
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Introduction



- Glycine receptors (GlyRs) are present in human β cells, and mediate glycine-evoked currents that contribute to cell depolarization, increasing insulin secretion.
- In islets from donors who had type 2 diabetes, GlyR activity is impaired, and the mechanisms that lead to this change are still unknown.
- We aimed to further investigate how the GlyRs can influence islet function, and if the GlyR dysfunction in type 2 diabetes (T2D) is caused by hyperglycemia.

Methods



Results

Glycine-induced currents are reduced in T2D β cells and cells cultivated in high glucose for 48h

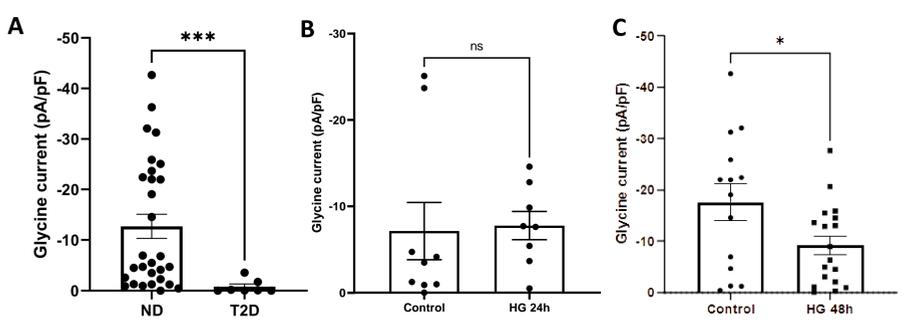


Figure 1. Glycine-evoked currents in human β cells. A: Currents in donors without (control) and with T2D. Cells from donors without diabetes were cultured in 5.5 mM glucose (control) or 15 mM glucose (HG) and glycine-evoked currents were measured after 24 (B) and 48 hours (C). * $P \leq 0.05$ and *** $P \leq 0.001$.

GlyR gene expression is decreased in T2D

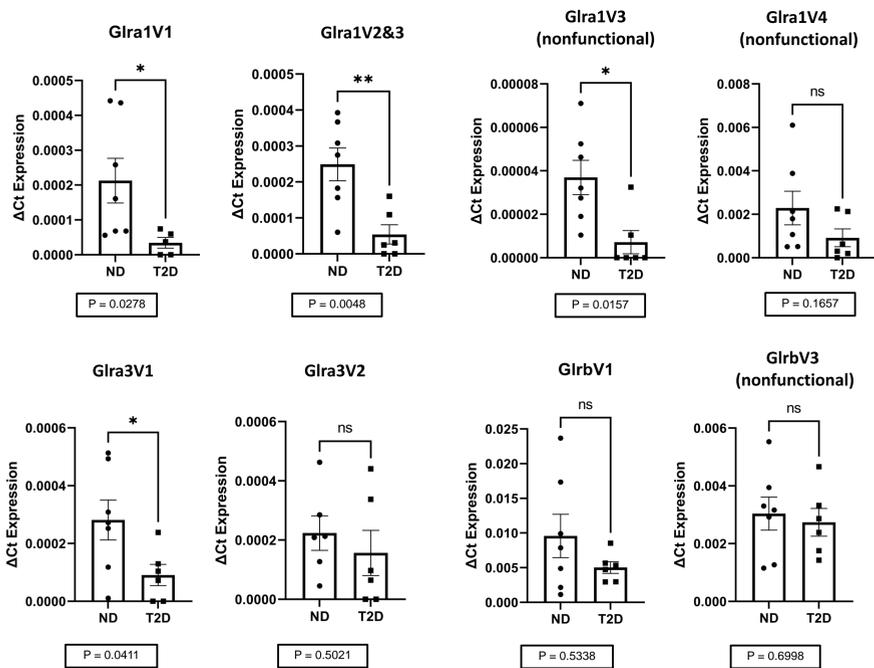


Figure 2. mRNA expression of GlyR subunit variants in human islets of donors with and without T2D. Data is shown as ΔCt expression, calculated using the gene cyclophilin A as housekeeping. * $P \leq 0.05$ and ** $P \leq 0.01$.

Strychnine reduces glucose-stimulated insulin secretion

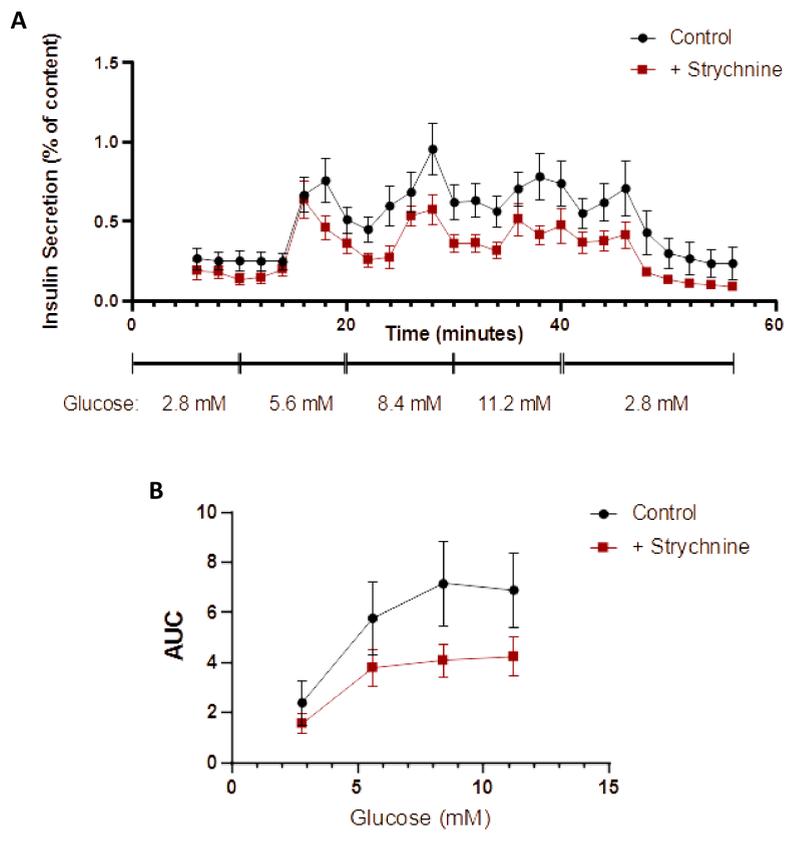


Figure 3. Effect of 10 μM strychnine on insulin secretion. A: Fold increase of insulin secretion in relation to the content ($n = 6$ donors). Perfusion was made according to the following protocol: 10 minutes 2.8 mM glucose, 10 minutes 5.6 mM glucose, 10 minutes 8.4 mM glucose, 10 minutes 11.2 mM glucose and 16 minutes 2.8 mM glucose. B: Area under the curve (AUC) calculated for each condition.

Summary

- Glycine-evoked currents in β cells are decreased in T2D and after 2 days of culture with high glucose;
- GlyR gene expression in T2D is decreased, but there is no shift in subunit splice variant expression;
- Strychnine reduces glucose-stimulated insulin secretion.