

***In Silico* Optimization of Basal Insulin Infusion Rate during Exercise: Implication for Artificial Pancreas**

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Abstract

Background:

Several clinical trials have been performed to assess safety and efficacy of closed-loop control. Some included physical activity (PA), with the goal of challenging the control algorithms with a rapid change in insulin sensitivity while reducing the risk of hypoglycemia. However, the question remains as to the necessity to inform the control algorithm on the imminent PA. The aim here is to assess *in silico* (i) if it is necessary to announce upcoming PA and (ii) if this is the case, what is the safest strategy of basal insulin reduction in the context of the closed-loop control.

Methods:

We modified the University of Virginia/Padova type 1 diabetes simulator to incorporate the effect of PA based on a study in healthy subjects that demonstrated an almost doubling of insulin sensitivity during PA versus rest. Two *in silico* experiments, including a PA session, have been simulated on the virtual adult population: one in the absence of and one with different degrees of reductions and durations of basal insulin infusion rates.

Results:

Most *in silico* subjects experienced hypoglycemia in the absence of basal insulin adjustment. We show that, in the absence of patient-specific information, a safe and effective strategy is to reduce basal insulin by 50% starting 90 min before exercise and by 30% during exercise.

Conclusions:

Our results suggest that control algorithms could benefit by knowing an upcoming PA. Ideally, the control algorithm should be informed about the patient-specific basal insulin reduction pattern. An alternative strategy that has been proposed here has been deemed safe and effective in *in silico* experiments.

J Diabetes Sci Technol 2013;7(6):1461–1469

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Abbreviations: (AP) artificial pancreas, (BG) blood glucose, (CGM) continuous glucose monitoring, (CVGA) control variability grid analysis, (PA) physical activity, (T1DM) type 1 diabetes mellitus, (UVA) University of Virginia

Keywords: physical activity, simulation, type 1 diabetes

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