Simulating clinical studies of the glucoregulatory system: in vivo meets in silico

In this report we use a validated model of the glucoregulatory system including effects of insulin and glucagon for simulation studies in seven type 1 diabetes patients. Using simulations, we replicate the results from a clinical study investigating the effect of micro-doses of glucagon on glucose metabolism at varying ambient insulin levels. The report compares in vivo and in silico results head-to-head, and discusses similarities and differences. We design and simulate simple studies to emphasize the implications of some glucoregulatory dynamics which are ignored in most previous clinical studies: the effect of discontinuing insulin and glucose infusions prior to glucagon administration, the delayed effect of insulin, timing of data sampling, and carryover effects from multiple subcutaneous doses of glucagon. We also use simulations to discuss two hypotheses of how insulin and glucagon might interact in influencing the glucose response. Following the simulations we propose a study design that potentially could explore if the hypotheses are true or false.

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