





Hypoglycaemia Incidence and Recovery During Home Use of Hybrid Closed-Loop in Adults with Type 1 Diabetes

Y. Ruan¹, L. Bally^{3,9}, H. Thabit^{7,8}, J. K. Mader⁵, H. Kojzar⁵, S. Dellweg⁶, C. Benesch⁶, S. Hartnell², L. Leelarathna⁷, M. Tauschmann^{1,4}, M. E. Wilinska^{1,4}, M. L. Evans^{1,2}, S. Arnolds⁶, T. R. Pieber⁵ and R. Hovorka^{1,4}

¹Wellcome Trust–MRC Institute of Metabolic Science, University of Cambridge

²Department of Diabetes & Endocrinology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

³Department of Diabetes, Endocrinology, Clinical Nutrition & Metabolism, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

⁴Department of Paediatrics, University of Cambridge, Cambridge, UK

⁵Department of Internal Medicine, Division of Endocrinology & Diabetology, Medical University of Graz, Graz, Austria

⁶Profil Institut fur Stoffwechselforschung GmbH, Neuss, Germany

⁷Central Manchester University Hospitals NHS foundation, Manchester Academic Health Science Centre, Manchester, UK ⁸Division of Diabetes, Endocrinology and Gastroenterology, Faculty of Biology, Medicine and Health, University of Manchester, UK ⁹Department of General Internal Medicine, Inselspital, Bern University Hospital, University of Bern, Switzerland

Introduction We assessed glucose excursion around hypoglycaemia to increase understanding of hypoglycaemia incidence and recovery during hybrid closed-loop insulin delivery.

Methods We retrospectively analysed data from 60 adults with type 1 diabetes who received in crossover randomised design day-and-night hybrid closed-loop and insulin pump therapy, the latter with or without real-time continuous glucose monitoring. Over 4-week study periods, we identified hypoglycaemic episodes defined as sensor glucose < 3.0mmol/l and analysed sensor glucose relative to the onset of hypoglycaemia.

Results We identified 377 hypoglycaemic episodes during hybrid closed-loop versus 662 during control intervention (P<0.001) with a predominant reduction of nocturnal hypoglycaemia. The slope of sensor glucose prior to hypoglycaemia was steeper during closed-loop than during control intervention (P<0.01), while insulin delivery was reduced (P<0.01). During both daytime and night-time, participants recovered from hypoglycaemia faster when treated by closed-loop. At 120 min post-hypoglycaemia, sensor glucose levels were higher during closed-loop compared to control period (P<0.05).

Conclusion Closed-loop reduces the risk of hypoglycaemia particularly overnight with swift recovery from hypoglycaemia leading to higher 2-hour post-hypoglycaemia glucose levels.

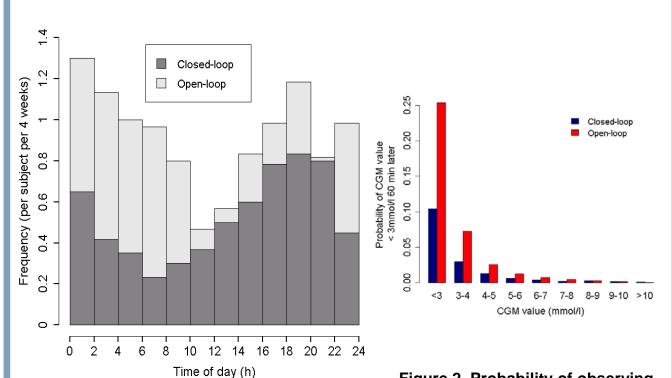
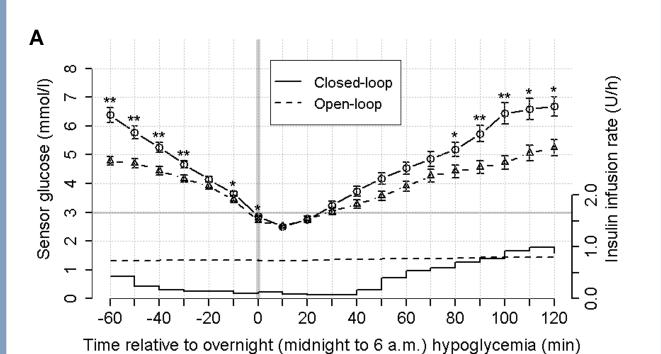


Figure 1. Incidence of hypoglycaemia events (sensor glucose < 3.0 mmol/l for at least 10min) during hybrid closed-loop insulin delivery (dark grey bars) and control periods (light grey bars) (mean; N = 60).

Figure 2. Probability of observing a sensor glucose value < 3mmol/l (y-axis) conditional on the sensor glucose value 60 min earlier (x-axis).

Table 2. Sensor glucose values at 30, 60, 90 and 120 min following the onset of hypoglycaemia (sensor glucose < 3.0 mmol/l for at least 10 min) during hybrid closed-loop insulin delivery and control periods.

Time relative to onset of hypoglycaemia (min)	Sensor glucose (mmol/l) [mean(SD), N = 60]		P value
	Control	Closed-loop insulin delivery	
	Overnight period (midnight to 6 a.m.)		
+30	3.0 (0.9)	3.2 (1.2)	0.80
+60	3.9 (1.3)	4.5 (1.7)	0.53
+90	4.6 (1.8)	5.7 (2.2)	0.003
+120	5.2 (2.2)	6.7 (2.5)	0.010
	Daytime period (6 a	.m. to midnight)	
+30	3.3 (0.9)	3.9 (0.8)	0.006
+60	5.0 (1.8)	6.2 (1.8)	0.007
+90	5.8 (2.0)	7.4 (2.1)	0.001
+120	6.8 (2.0)	8.0 (2.1)	0.020



Sensor glucose (mmol/l) (mol/l) (mol/l

Figure 3. Sensor glucose values from -60 min to 120 min relative to the onset of hypoglycaemia (sensor glucose < 3.0mmol/I; vertical bar) during hybrid closed-loop period (circles connected by solid line; mean ± SEM; N=60; * P < 0.05, ** P < 0.01 compared to control therapy) and during control period (triangles connected by dashed line). Piecewise-constant lines without error bars represent mean insulin infusion rates during closed-loop period and dashed lines without error bars are insulin infusions during control period. Panel A shows glycaemic and insulin infusion data during the night-time period (midnight to 6 a.m.) and panel B shows the daytime period (6 a.m. to midnight).