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**Sensing hypoglycaemia at an earlier stage using an integrated physiological multi-signal data fusion approach**

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**Aims:** Detecting imminent hypoglycaemia reliably at an earlier stage than current continuous glucose monitoring systems (CGMS) can achieve is a major unmet need. In a proof of concept study, we investigated whether monitoring changes in physiological parameters, in tandem with CGMS, could provide earlier warning of hypoglycaemia.

**Methods:** We used a data fusion model to combine vital sign (VS) and CGMS measurements, and to detect aberrant VS dynamics, in eight individuals with Type 1 diabetes experiencing hypoglycaemia during stepped hyperinsulinaemic hypoglycaemic clamps with continuous non-invasive recording of their heart rate, respiratory rate and peripheral arterial oxygen saturation. Two VS 'novelty scores' were calculated based on a kernel density estimate of the joint distribution of VS and derived VS-volatility features. The time course of these novelty scores was compared with the glucose profiles.

**Results:** Aberrant physiological measurements consistently preceded critically low CGMS values, and were later counter-balanced by homeostatic regulation. VS derangement correlated with both low glucose concentrations and sharp changes in glucose levels. Elevated novelty scores identified multiple transient VS derangements which could be observed before glucose levels fell below 4mmol/l. Persistently elevated novelty scores also occurred in some individuals when their glucose levels were below the hypoglycaemic threshold.

**Conclusions:** The VS data fusion model showed multiple plausible early warning signals that could be used to provide earlier warning of imminent hypoglycaemia, and possibly to detect homeostatic mechanisms that are compromised. Further development of this methodology could have substantial clinical impact, especially for children and hypoglycaemia-prone adults with diabetes.