

# A non-invasive, home-based EEG hypoglycaemia warning system for personal monitoring using skin surface electrodes: a single-case feasibility study

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**Aims:** Hypoglycaemia unawareness is a common condition associated with increased risk of severe hypoglycaemia. The purpose of our study was to develop a simple to use, home-based and non-invasive hypoglycaemia warning system based on electroencephalography (EEG), and to demonstrate its use in a single-case feasibility study.

**Methods:** A participant with type 1 diabetes forms a single-person case study where blood sugar levels and EEG were recorded. EEG was recorded using skin surface electrodes placed behind the ear located within the T3 region by the participant in the home. EEG was analysed retrospectively to develop an algorithm which would trigger a warning if EEG changes associated with hypoglycaemia onset were detected.

**Results:** All hypoglycaemia events were detected by the EEG hypoglycaemia warning algorithm. Warnings were triggered with blood glucose concentration levels at or below 4.2 mmol/l in this participant and no warnings were issued when in euglycaemia.

**Conclusion:** The feasibility of a non-invasive EEG-based hypoglycaemia warning system for personal monitoring in the home has been demonstrated in a single case study. The results suggest that further studies are warranted to evaluate the system prospectively in a larger group of participants.

**1. Introduction:** Severe hypoglycaemia is a serious condition which causes significant morbidity and mortality in patients with type 1 and type 2 diabetes [1]. As a precursor to severe hypoglycaemia, mild hypoglycaemia may give rise to a range of symptoms such as fatigue, dizziness, fast heart rate and confusion, but many patients are unaware of the condition, a phenomenon known as hypoglycaemia unawareness [1]. Patients with hypoglycaemia unawareness are at high risk of developing severe hypoglycaemia [2]. Early detection of mild hypoglycaemia could help prevent episodes of severe hypoglycaemia and improve overall glucose control.

The current standard method for self-monitoring is an invasive blood test and there is need for a simple non-invasive monitoring technique which can be performed, as and when required by the person, in the home. Hypoglycaemia has a significant impact on the electrical signals of the brain, particularly in the low frequency bands such as the delta EEG band (0.5-4 Hz) of the electroencephalograph (EEG) signal [3,4]. This suggests the use of EEG for the detection of hypoglycaemic events [5]. A number of clinical studies have demonstrated the potential of EEG monitoring in this context [6, 7]. The purpose of our study was to develop a simple to use, home-based and non-invasive hypoglycaemia warning system based on EEG, and to demonstrate its use in a single-case feasibility study.

**2. Methods – Hypoglycaemia Warning System:** The EEG recording system utilised a bio-potential amplifier, microcontroller and battery power supply (Figure 1).

The bio-potential amplifier (Texas Instruments, ADS1298) was configured to acquire a single differential EEG channel with 24 bit resolution and sample rate of 250 Hz. The microcontroller (XPS, LPC2368) logged the EEG channel to a SD memory card for subsequent analysis. **Additional functionality enables signals also to be sent instantaneously via Bluetooth to compatible devices.**

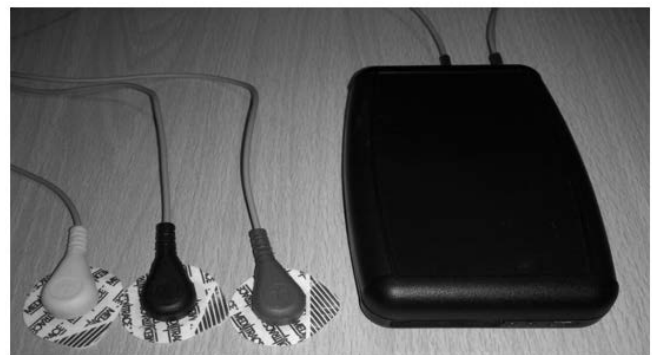
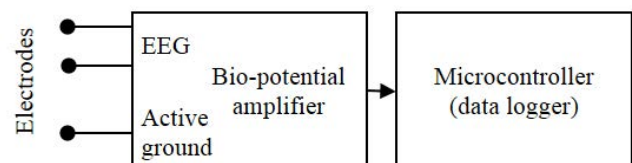


Fig. 1 Portable EEG recording system. Functional block diagram (top) and photograph of the system (below). A single channel differential EEG signal was recorded as the potential difference between two electrodes (T3a-T3b). A further electrode provides the active ground connection to the person.

**3. Methods – Data Collection:** Ethical approval was obtained for the study from the University of Hull's Faculty of Science Ethics Committee and a single participant with type 1 diabetes was recruited. The participant had type 1 diabetes for 8 years, was hypoglycaemia aware and had good glucose control with an HbA1c of 7.1 mmol/L. Following instruction in the use of the system the participant was invited to use the system as a self-monitoring tool in the home over a period of several days. Juhl et al [6] have already demonstrated that

subcutaneous electrodes positioned close to electrode position T3 on the International 10-20 System give a measurable response to hypoglycaemic events, so in this study similar electrode locations were utilised as illustrated in Figure 2. Disposable sticky pad silver/silver chloride electrodes, typically used in electrocardiography, were used since they were easy and fast to apply by the participant. The participant could perform EEG recording as and when they wanted and no strict recording protocol was enforced apart from asking the participant to sample and record routine plasma glucose levels using an Accu-Chek Aviva Nano blood glucose monitor at intervals during EEG monitoring. The participant was also asked to maintain a diary of symptoms during EEG recording.



Fig. 2 Photograph of the electrode positions used in the study. EEG electrodes were positioned at T3a and T3b positions as illustrated. The active ground (Gnd) electrode was positioned on the ear lobe.

**4. Methods – Hypoglycaemia warning algorithm:** EEG recordings were analysed retrospectively with the aim of developing an algorithm to provide a warning of potential hypoglycaemia. The algorithm was implemented and tested in Matlab. First, the EEG was band-pass filtered between 1 to 4 Hz to identify EEG changes principally within the delta band. Amplitude changes in this band have been shown to be a sensitive marker for hypoglycaemia[3,4]. The detection algorithm analysed a 60 second rolling window of filtered EEG. Within this window the number of times the EEG exceeded the amplitude threshold was counted and classed as an EEG event. The algorithm would issue a hypoglycaemia warning if the number of EEG events exceeded the count threshold. The amplitude and count thresholds for this case were 0.1 mV and 50 events respectively. It is anticipated that these thresholds could be optimised for hypoglycaemia detection in specific subjects.

**5. Results:** The participant performed self-monitoring on five occasions and the durations ranged from 20 to 87 minutes. Recordings were commenced in the early evening (recordings 1 to 4) or afternoon

(recording 5) on **five** separate days whilst sitting down. The recordings are summarised in Table 1.

Table 1: Details of the recordings undertaken by the participant.

Recording	Duration (minutes)	Maximum blood glucose (mmol/l)	Minimum blood glucose (mmol/l)	Symptoms	Warning issued by the EEG system
1	87	8.3	4.2	None	Yes
2	79	6.0	4.9	None	No
3	56	7.3	3.4	Shaky	Yes
4	73	13.3	11.1	None	No
5	20	6.0	2.7	Shaky	Yes

From the above EEG recordings; example 10s segments of EEG recorded during euglycaemia (above 4.0 mmol/L) and hypoglycaemia (below 4.0 mmol/L) are illustrated in Figure 3 alongside their respective power spectral densities.

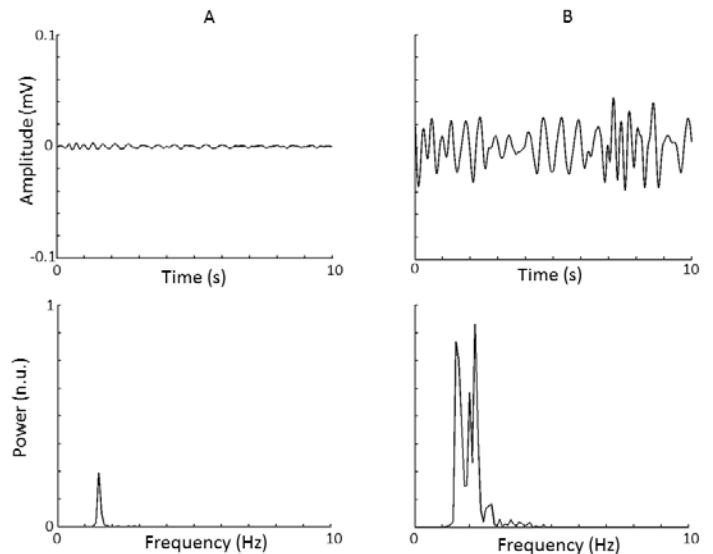


Fig. 3 Delta-band filtered EEG of 10 s duration (top) and corresponding power spectral density (bottom) with normalised units (n.u.) of power during (A) euglycaemia (7.8 mmol/l) and (B) hypoglycaemia (4.2 mmol/l) captured from EEG recording 1 (see Table 1).

Retrospective application of the hypoglycaemia warning algorithm to the recordings resulted in the generation of three warnings by the non-invasive monitoring system (Table 1). All warnings were confirmed to be coincident with low plasma glucose concentration readings.

Figure 4 provides a representative example of the time-course of the monitor output in relation to the measured plasma glucose level during a monitoring period in which low levels of plasma glucose concentration were experienced by the participant.

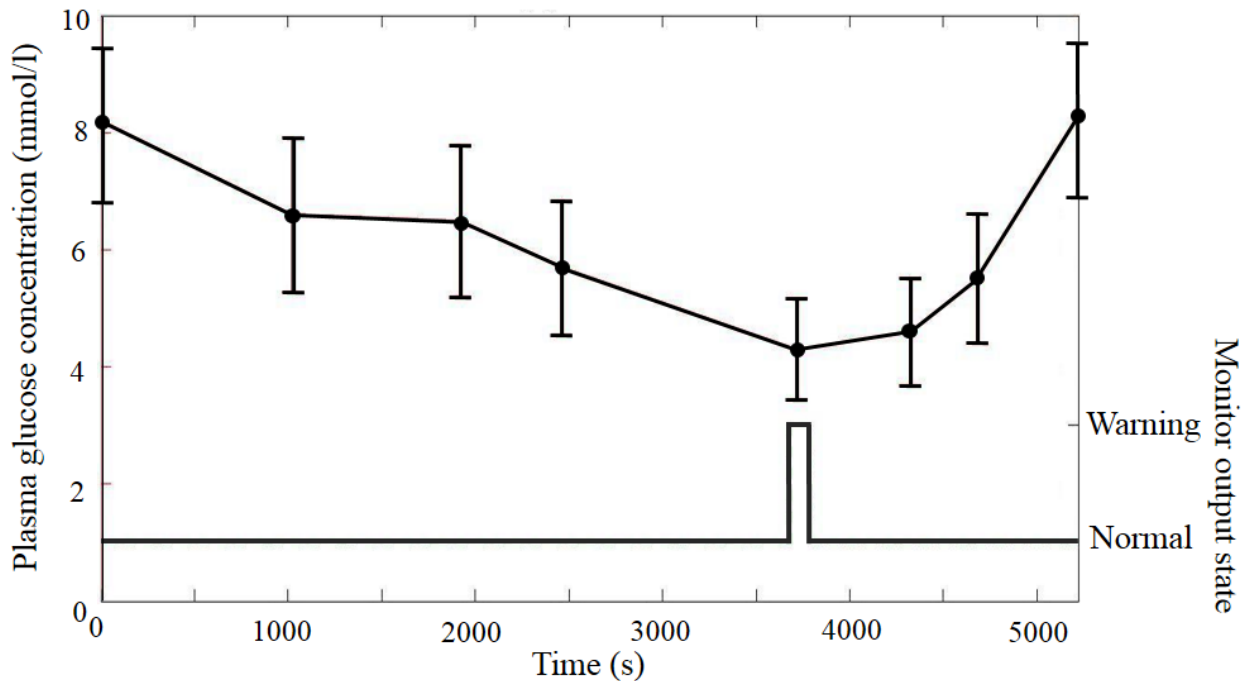


Fig. 4 Retrospective time-course of the hypoglycaemia monitor output state (bottom trace) in relation to measured plasma glucose concentration levels (top trace with error bars indicating accuracy of glucose monitor) during a period of monitoring in which the participant experienced low levels of plasma glucose concentration. The monitor issued a warning coincident with the lowest concentration level (4.2 mmol/l). The error bars on the plasma glucose concentration level indicate the specified accuracy of the blood glucose monitor used within the study ( $\pm 20\%$  at glucose concentrations  $\geq 4.2$  mmol/l and  $\pm 0.83$  mmol/l at glucose concentrations  $< 4.2$  mmol/l) [8].

**6. Discussion:** This study demonstrates the feasibility of an EEG-based non-invasive hypoglycaemia warning system for personal monitoring in the home. We have demonstrated the feasibility of the system to obtain EEG measurements using disposable sticky pad body surface electrodes, with the advantage that such electrodes are easily applied by the user.

Combined with the low number of electrodes and ease of application our device utilised is a low-cost and portable EEG recording system which can either log EEG recordings onto a memory card for later analysis or send the EEG signal instantaneously via Bluetooth to compatible devices with potential use for real-time remote monitoring. The detection algorithm performed no complex mathematical calculations allowing the possibility of use on small portable devices, thus bringing a novel approach to hypoglycaemia alerts using wearable technology within the home with measurements performed by the user.

The use of surface electrodes is in contrast to other similar studies using subcutaneous electrodes during clinical trials [6] which, although may provide EEG recordings with higher quality and fewer artefacts, are inconsistent with the aim of producing a simple and non-invasive warning system which empowers the user to perform monitoring as and when required and with minimal risk of infection. Consistent with previous studies the EEG exhibited high amplitude slow waves during hypoglycaemia [3, 4, 6, 7, 9]. The EEG waveform changes associated with hypoglycaemic events accord with a study

performed by Nguyen et al. which reported a significant increase in waveform power associated with hypoglycaemia within the Delta EEG band [7].

We were able to retrospectively tune the parameters of the hypoglycaemia detection algorithm to provide an early warning of hypoglycaemia before the onset of symptoms (Table 1). Blood glucose levels at or below 4.2 mmol/L were associated with warnings from the algorithm. The simple but effective warning algorithm utilises the changes in EEG amplitude due to hypoglycaemia to count events and subsequently; if a pre-defined threshold is met; trigger the hypoglycaemia warning. The warning algorithm is easily configurable to trigger at different levels by analysing a specified rolling time window, so could be tailored to individual users. The algorithm involves no high end processing or calculation on the EEG signal and therefore could be utilised in portable & low power devices. Hence the results of our study suggest that the home-based monitoring system has the potential to provide an early warning of hypoglycaemia and might be a useful tool to aid glucose control and prevent hypoglycaemia concurring with similar clinical trials of EEG hypoglycaemia detection with subcutaneous electrodes [9-10].

The paper presents an initial feasibility study with a view to expanding the research into full clinical trials across several patients subject to the appropriate Ethical approvals. To complete a full study further analysis of the data would be incorporated including performing a power calculation for the statistically appropriate number of participants and also Such trials would need to consider the specific diabetic cohort to be selected in a full study (e.g. type I and/or type II diabetics) along with diabetic patient history and completing trials across varying environments and patient situations would need to be considered.

Further trials would also test the robustness of the algorithm under a range of conditions which might arise in daily use, for example during talking and movement to gather further evidence beyond that of the initial study. A full study of this type was out with the scope of our preliminary investigation. The results from our initial feasibility case

study will, however, ~~enable support~~ the undertaking of future clinical trials with a cohort of diabetic patients. Further studies would also test the device ~~and developed algorithm~~'s application to home-based monitoring, because the system is based on mobile technologies, it has the functional capability to monitor remotely, away from the home.

Additionally, although the system worked well in this case study it is essential that the results are shown to be repeatable in a large group of subjects and to demonstrate that the system is useful in preventing severe hypoglycaemic events and improves overall glucose control in subsequent clinical trials.

**7. Conclusion:** The feasibility of non-invasive EEG-based hypoglycaemia warning system for personal monitoring in the home has been demonstrated in a single case study. The results suggest that further studies are warranted to evaluate the system in a larger group of subjects.

**8. Declaration of interests:** None.

## 9. References

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