Non-Invasive Wearable Sensors to Detect Onset of Hypoglycemia: 
A Scoping Review

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1. Background

- Almost 460 million people globally live with diabetes.
- Hypoglycemia is a dangerous condition that happens when the blood glucose level drops below 70mg/dL.
- Nocturnal Hypoglycemia is especially dangerous, patients can’t wake up to regulate.

2. Research Aims

Aim 1: Understand what physiological factors have been studied to detect hypoglycemia
Aim 2: Understand if tremors are a good indicator of hypoglycemia
Aim 3: Understand if any studies attempted to innovate a technology to detect hypoglycemic tremors

3. Methods, Results & Discussion

3.1 Scoping Literature Review on Tremors and Hypoglycemia

Methods:
- Used Texas A&M EBSCOHost research databases such as MEDLINE and Compendex on October 18, 2017
- 78 results, using keywords ["hypoglycemia"] and ["tremor" OR "trembling"]
- Inclusion Criteria: Studies looking at non invasive technologies / Only studies published in English
- 7 papers were found fitting the inclusion criteria

Results:

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Muhlhauser et al.</td>
<td>1991</td>
<td>17% of respondents reported tremors as their first symptom</td>
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<tr>
<td>2. Chiarelli et al.</td>
<td>1998</td>
<td>74% of children with diabetes surveyed said a frequent symptom they notice is trembling</td>
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<tr>
<td>3. Berlin et al.</td>
<td>2005</td>
<td>77% of respondents reported tremors as symptoms of hypoglycemia</td>
</tr>
<tr>
<td>4. Heller et al.</td>
<td>1987</td>
<td>Hypoglycemic patients had a noticeable increase in tremor readings (RMS) when BG dropped to 2.5mmol/L</td>
</tr>
<tr>
<td>5. George et al.</td>
<td>1995</td>
<td>Tremors did not become impaired like the responses of sweat and adrenaline</td>
</tr>
<tr>
<td>6. Scheckter et al.</td>
<td>2012</td>
<td>Used a simplified measure of tremors as 1 of 4 symptoms to monitor onset of hypoglycemia</td>
</tr>
<tr>
<td>7. Rana &amp; Chou</td>
<td>2015</td>
<td>Hypoglycemic tremor categorized as a medium frequency enhanced physiological tremor</td>
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</table>

3.2 Non Invasive Technologies

An additional search looked at ["hypoglycemia"] and ["non invasive"] to survey the non invasive methods of detecting hypoglycemia

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<tr>
<td>1. Harris et al.</td>
<td>1996</td>
<td>Used 3 sensors to study the variations of pulse rates, humidity, and skin temperature around the wrist</td>
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<tr>
<td>2. Nguyen &amp; Jones</td>
<td>2010</td>
<td>Alpha frequency of EEG Signals affected during hypoglycemia</td>
</tr>
<tr>
<td>3. Siegel, Lee, &amp; Pikov</td>
<td>2014</td>
<td>Correlation between BG levels and millimeter wave absorption (MMW) was found with hypoglycemia</td>
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<tr>
<td>4. Yadav et al.</td>
<td>2013</td>
<td>Spectroscopy methods require more improvement in order to compete with popular CGMs on the market</td>
</tr>
<tr>
<td>5. Yotha et al.</td>
<td>2016</td>
<td>Monitored pulsatile changes in blood flow, internal pulse, body temp, and skin conductance</td>
</tr>
<tr>
<td>6. San, Ling, &amp; Nguyen</td>
<td>2016</td>
<td>Longer QT intervals of ECG signals analyzed in order to detect hypoglycemic episodes</td>
</tr>
<tr>
<td>7. Zanot et al.</td>
<td>2017</td>
<td>A biosensor that has shown promise when tested on T1DM subjects</td>
</tr>
<tr>
<td>8. Howsmon &amp; Bequette</td>
<td>2015</td>
<td>Exhaustive review of similar methods, concluded that sweat and body temperature are not accurate</td>
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3.3 Commercialized Technologies

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Continuous Glucose Monitoring devices (CGMs) are the most popular devices to monitor blood glucose and detect hypoglycemia:

Pros:
- Provides glycomic control
- Provides continuous monitoring
- Detects hypoglycemia

Cons:
- Expensive
- Accurate during the day, not so much at night
- Invasive
- Not prescribed for people with type 2 diabetes
- Requires frequent calibration and part change

4. Discussion

- Hypoglycemic tremors:
  - Categorized as medium frequency enhanced physiological tremor
  - Not impaired with time
  - Common among diabetics
  - Signal can be analyzed using Actigraphy

- Hypoglycemic tremors seem worth studying.
- Other commercial technologies are very limited and have high false alarms

5. Work in Progress

- Currently, work is in progress to:
  - Design and test a wearable sensor that analyzes the tremor signals in real-time
  - Use Actigraphy to study the tremor signal
  - Develop a mobile application that
    - Communicates with the sensor
    - Provides extra features aimed at helping the patients manage their diabetes.

Most technologies have not been designed for usability and wearability, let alone user engagement.

Common issues to consider in the design:
- Usability and ease of use
- Maintenance and calibration
- Recurring costs
- Wearability and non-obtrusiveness
- Data Processing V.S Battery Life
- Age and type of diabetic patients
- User engagement
- Optimal detection sensitivity

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