Investigating the Efficacy of Using Hand Tremors for Early Detection of Hypoglycemic Events: A Scoping Literature Review

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1. Background
- Around 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
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

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Findings</th>
</tr>
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<tbody>
<tr>
<td>1. Muhlbauer et al.</td>
<td>1991</td>
<td>17% of respondents reported tremors as their first symptom</td>
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<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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<td>3. Berlin et al.</td>
<td>2005</td>
<td>77% of respondents reported tremors as symptoms of hypoglycemia</td>
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<td>4. Hoffer 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>
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<td>5. George et al.</td>
<td>1995</td>
<td>Tremors did not become impaired like the responses of sweat and adrenaline</td>
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<td>6. Schecter et al.</td>
<td>2012</td>
<td>Used a simplified measure of tremors as 1 of 4 symptoms to monitor onset of hypoglycemia</td>
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<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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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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</thead>
<tbody>
<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>Alfa frequency of EEG Signals affected during hypoglycemia</td>
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<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. Yudav et al.</td>
<td>2015</td>
<td>Spectroscopy methods require more improvement in order to compete with popular CGMs on the market</td>
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<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>
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<tr>
<td>7. Zanon et al.</td>
<td>2017</td>
<td>A biosensor that has shown promise when tested on T1DM subjects</td>
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<tr>
<td>8. Howsman &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 Survey of Diabetes Patients (preliminary)

18 diabetes patients at Texas A&M University were surveyed to understand the context in which hypoglycemia events occur.

- Average BG at which Hypoglycemia was reported: 64%
- Average BG at which tremors were reported: 31%
- % of hypoglycemic events involving tremors: 72%
- % of participants that experience Hypoglycemia >Once/week: 64%
- % of Events reported that happened while Sleeping: 72%

4. Discussion
- Hypoglycemic tremors:
  - Are categorized as medium frequency enhanced physiological tremor
  - Are not impaired with time
  - Are common among diabetics
  - Can be analyzed using Actigraphy

- Commercial technologies (e.g., CGMs) 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
  - Develop a mobile application that
    - Communicates with the sensor
    - Provides extra features aimed at helping the patients manage their diabetes
  - Use a patient-centered design to solicit requirements from diabetic patients about their symptoms and opinion regarding such a technology.

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

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