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Evaluation of alcohol intoxication and withdrawal syndromes based on analysis of tremor signals

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ABSTRACT

In this paper, we analyze the relationship between the clinical assessment of tremors caused by alcohol withdrawal (AW) syndrome and the underlying tremor signal as recorded by an accelerometer. The ultimate goal of the study is to find out the relationship between energy of the tremor signal in patients in AW and tremor rating provided by physicians. We have developed an iOS application that calculates the tremor component of the Clinical Institute Withdrawal Assessment, revised (CIWA-Ar) score using accelerometer data. We report on the characteristics of AW tremor, the accuracy of electronic tremor assessment compared to expert clinician assessment. It should be noted that this application is not a replacement for physician's assessment, but it will help physicians to quantify the severity of the tremor which is one of the components of CIWA-Ar protocol.

Our first and key finding is that there is a logarithmic relationship between the CIWA-Ar score and the tremor energy in the [5,15] Hz range. Based on training on 84 recordings from 50 patients with the clinical diagnosis of AWS, and testing on a separate set of 33 patients with AWS, the proposed logarithmic relationship provides a CIWA-Ar Root Mean Square Error (RMSE) of 0.91 (with respect to a consensus rating from 3 expert physicians on a 7 point scale). This compares to a RMSE of 1.04 for junior physicians, 0.94 for junior nurses, 0.94 for senior nurses, and 0.95 for expert physicians.

1. Introduction

Alcohol is the most commonly used mind-altering drug worldwide [1], and between 10–30% of all Emergency Department (ED) visits are related to alcohol consumption [2]. Alcohol Withdrawal Syndrome (AWS) develops in 13–71% of individuals who suddenly stop or reduce their drinking after prolonged/heavy consumption and may be fatal if not treated appropriately [4,5]. Pharmacologically, alcohol acts as a central nervous system (CNS) depressant, and reduced consumption results in the characteristic neuronal hyperexcitability of AWS. Between 5–15% of individuals who develop AWS will subsequently develop the major symptoms of withdrawal, including seizures, hallucinations and delirium [6].

Benzodiazepines, the treatment of choice for AWS, are effective in preventing seizures/delirium and treating symptoms [7,8,17,21,22]. Benzodiazepines pharmacologically mimic alcohol, and their dosing requires careful titration to alleviate symptoms without excessive sedation [9,18,19]. They are also commonly abused recreationally, and patients present to the ED claiming to be in alcohol withdrawal simply to obtain benzodiazepines [3]. Being able to accurately identify and assess the severity of AWS is therefore an important clinical skill.

AWS is best managed using a symptom driven approach, in which patients are assessed hourly using a standardized tool, and aggressively treated with benzodiazepines based on symptom severity [2,10,11]. The Clinical Institute Withdrawal Assessment for Alcohol, revised (CIWA-Ar) [12] is the most commonly used tool for AWS assessment. It covers 10 different domains (nausea/vomiting, tremor, diaphoresis, anxiety, agitation, tactile, auditory and visual hallucinations, headache and orientation). Though clinically validated, it is time consuming to administer (affecting ED usability), and subjective (many domains are impossible to measure reliably [13,14]). Tremor is the most commonly used domain in all scales measuring alcohol withdrawal severity [15]. Unfortunately,

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the assessment of tremor is also highly variable and dependent on experience, and the scale provides no description of the characteristic features of a typical AWS tremor to assist inexperienced clinicians with its application. A standardized method of assessing the tremor of AWS would greatly improve the accuracy and reliability of the CIWA-Ar, and may allow the development of a shorter, more useful ED tool for assessing AWS severity [13,16,20].

Although it is the current gold standard for AWS severity assessment, the CIWA-Ar has not gained widespread acceptance in the ED for two main reasons. Firstly, it is time consuming; proper completion of the 10-item score takes approximately 5 min to complete and patients require multiple assessments during their stay in the ED. Secondly, many of the elements it assesses are subjective, and proper interpretation of responses, including rating tremor, are experience dependent. The ability to objectively evaluate tremor severity, and determine the likelihood of a patient actually having alcohol withdrawal based on other characteristics of the tremor, open the possibility of developing shorter, faster, and more objective scoring systems for assessing withdrawal severity better suited to the ED setting.

The main purpose of this study is to quantify the severity of tremor in patients in AW on a 7-point scale to remove subjectivity in rating of tremor domain in CIWA-Ar protocol. This will help us improve the care of patients by standardizing the tremor rating and removing subjectivity. To address this purpose, we employed 3 steps: (1) to develop an app which uses the built in accelerometer of the iOS application to capture movement (frequency and amplitude) in three dimensions in order to standardize and quantify the severity of the AWS tremor, (2) to estimate the inter-rater reliability of clinicians with varying experience (junior and senior RNs and MDs) in assessing tremor during a training exercise where they were shown a series of videos demonstrating AWS tremors of varying severity, and (3) to compare the performance of the app to both "gold standard" expert clinician assessment and each of the above mentioned groups.

The creation of a tremor app is the first step in the eventual development of a shortened, more objective AWS assessment tool designed specifically for ED use. Furthermore, standardization of the tremor assessment is the key element of the CIWA-Ar app, as it is the clinical symptom most commonly used to quantify withdrawal severity, and subject to widely variable interpretation based on clinical experience. Two randomized controlled trials have shown that when AWS patients are treated using a CIWA-Ar based, symptom guided approach, their treatment is improved (faster symptom resolution, lower total administered doses of benzodiazepines) compared to other approaches [8,12]. In an environment in which demand for ED stretchers regularly exceeds availability, any strategy that both improves care and improves efficiency deserves further exploration.

AWS is commonly encountered in the ED, and potentially fatal if not treated appropriately. Preliminary data from our study indicates that when the CIWA-Ar is properly administered and interpreted, patients spend on average 3 h less in the ED, and receive lower total benzodiazepine doses. We anticipate that the use of our app will improve the care of patients in alcohol withdrawal by providing more reliable CIWA-Ar assessments.

2. Methods

2.1. Development of iOS application

We developed an iOS application to quantify tremor component of the CIWA-Ar protocol to assess patients in AW. The application uses the built-in accelerometer of a handheld iOS device to measure the magnitude of accelerations in three dimensions. Data was collected over a 20 second window with a sampling rate of 65 Hz. The base analysis was performed in Matlab and the final algorithm was implemented in an iOS platform.

2.2. Time-frequency analysis

Often with biologically derived periodic signals such as speech, heart signals, or body motion, a time-frequency view can provide unique insight [11]. We use spectrograms in this paper in order to better understand the nature and type of tremors. Short-time Fourier transforms (STFTs) with Hanning window of 4 s and 90% overlap were computed. The peak frequency (in the 0–15 Hz range) of each window was used for tremor detection analysis, as shown below [23,24]:

$$V(n) = \underset{k}{\operatorname{argmax}} |X_n(k)| \tag{1}$$

where $X_n(k)$ is the STFT of window n at frequency index k.

We define the mean peak frequency μ as:

$$\mu = \frac{1}{N}\sum_{n=1}^{N} V(n) \tag{2}$$

and, the RMSE (relative to the mean) as:

$$\sigma = \sqrt{\frac{1}{N}\sum_{n=1}^{N} (V(n) - \mu)^2} \tag{3}$$

with N being the total number of windows during 20 s.

We computed the energy of the tremor signal in the intervals $[f_s, 15]$ Hz. The energy of the tremor signal in the $[f_s, 15]$ Hz range is defined as the sum of the time frequency blocks in this range as shown bellow:

$$E(f_s) = \sum_{t}\sum_{m} |X_t(m)| \tag{4}$$

where $X_t(m)$ is the STFT of the time window at time index t at frequency of m-Hz. The time-frequency method introduced in this section is verified as a part of previous research study of the authors in [23,24].

2.3. Enrolment of study participants

This prospective, observational study was conducted in two large, urban, university teaching hospital emergency departments between July 2013 and October 2014, and was approved by the ethics review board at each hospital. Both sites have 60,000 visits/year and were staffed by clinicians with postgraduate certification in emergency medicine. Both sites have extensive experience managing patients with alcohol withdrawal, including the use of treatment algorithms incorporating the CIWA-Ar, for at least 5 years prior to the initiation of this project.

Data were collected from a convenience sample of patients presenting to EDs of either hospital when study staff were available to enrol patients. To be eligible, participants had to be identified as clinically having alcohol withdrawal by clinicians, have been placed on a CIWA Protocol in the ED for evaluation and treatment, and be competent to provide consent to participate in English. These patients were approached by a research assistant and provided informed consent for the study. The subjects included in this study were both women and men with ages between 23 and 71. We also visited 12 patients that were approached and not included (8 not in AW or severely in withdrawal and unable to take the assessment and 4 declined to participate). Some patients received treatment prior to participating in this research study. Enrolment of patients