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Time-frequency analysis of the ECG in the diagnosis of vasovagal syndrome in older people

M. J. Ebden[1*], L. Tarassenko[1], S. J. Payne[1], A. Darowski[2], J. D. Price[2]
[1]Department of Engineering Science, University of Oxford, Oxford, United Kingdom
[2]Division of Clinical Geratology, Nuffield Department of Medicine, John Radcliffe Hospital, Oxford, United Kingdom
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Abstract—**The Smoothed Pseudo Wigner-Ville Distribution (SPWVD) is used for the time-frequency analysis of variations in RR interval. A novel technique to determine the smoothing window lengths is implemented, and a new heart rate variability (HRV) metric is developed, instantaneous center frequency variability (ICFV), which uses the time-frequency map generated by the SPWVD. The technique is then applied to 50 patients with unexplained falls and age > 60, undergoing head-upright tilt table testing (HUT). Eighteen of the patients were diagnosed with vasovagal syndrome. Attempts at syncope prediction using the new metric is an improvement on traditional techniques: an ICFV less than 0.07 Hz from 90 s to 180 s after tilt is predictive of a negative test (negative predictive value: 0.77). The comorbidity and autonomic degeneration present in elderly patients are thought to be responsible for lowering the negative predictive value.**

Keywords—**ICF, instantaneous center frequency, SPWVD, smoothed pseudo Wigner-Ville distribution, vasovagal syncope**

I. Introduction

Vasovagal syndrome – the frequent occurrence of vasovagal syncope – is a problem affecting people of all ages. Often occurring from several minutes to an hour after assuming the upright position, episodes of vasovagal syncope are characterized by a loss of consciousness resulting from a temporary reduction of cerebral blood flow. Blood flow falls as a consequence of a sudden drop in blood pressure, with or without a decrease in heart rate, probably caused by a dysfunction of the nervous control of heart and blood vessels. Unfortunately, the disorder's pathophysiology is very poorly understood [2], but the associated loss of postural tone can lead to injury [1].

A common method to investigate vasovagal syndrome is head-upright tilt table testing (HUT). Patients lie flat on a specialized bed for several minutes, before being tilted to an angle of 60-80 degrees from horizontal. It is common for ECG and/or continuous blood pressure measurements to be made, to monitor the changes in the patient's cardiovascular system. If syncope occurs after characteristic symptoms are observed, the patient is diagnosed with vasovagal syndrome.

One significant disadvantage of HUT is its length: a negative test (failure to faint) can consume an hour for the patient and the physician, when setup time is included. A second disadvantage is its aggressive nature: the aim of the test is to provoke the loss of consciousness, and hence some patients report severe exhaustion, nausea or other adverse symptoms after syncope. Owing to these two disadvantages, during the past 20 years there have been many attempts to shorten the test. These attempts ordinarily involve examination of the minutes of cardiovascular data collected before and/or after tilt. The aim is to classify patients as vasovagal or normal early in the test, to save the physician's time and the patient's energy.

One of the most popular classes of metrics under exploration has been heart rate variability (HRV). As a typical example, Kochiadakis *et al.* [3] summed the spectral power in the LF (low frequency, 0.06-0.15 Hz) and HF (high frequency, 0.15-0.40 Hz) bands of the FFT of a patient's RR tachogram (sequence of beat-to-beat intervals). They found that the LF/HF ratio was significantly lower after tilt in syncopal patients as compared to control subjects. As another example, Kouakam *et al.* [4] found that a decreased LF component after tilt acted as a reasonably good predictor of vasovagal syncope. Besides LF and HF, an interesting HRV development in the late 1990s has focused on the investigation of ICF (instantaneous center frequency) [5], see below.

Unfortunately, results in the literature for HRV techniques have been conflicting [6], and so far no indicator has been widely accepted. A more significant problem is the effect of aging on the autonomic system, the system under study in HRV analysis. This effect is one of the reasons that traditional HRV metrics tend to fail in the elderly [7].

The present paper explores the use of a new HRV metric, known as ICFV (ICF variability), to predict vasovagal syncope in the elderly.

II. Methodology

A. Patient Selection

Seventy-four patients suffering from syncope of unknown origin were selected for HUT from January 2002 to November 2003. Patients were excluded for yielding poor ECG data (8), for an uncertain syncope diagnosis at the end of HUT (16). The total number of exclusions was 24, leaving 50 patients to be analyzed (mean age 79, range 61-90; 10 males).

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B. Tilt Test Protocol

Each HUT occurred during the morning hours. After a supine period of at least ten minutes to obtain baseline recordings, the patient was tilted upright to approximately 70 degrees. The test continued until either syncope occurred, or presyncope occurred, or (usually 30-60 minutes after tilt) the physician overseeing the test decided the patient was unlikely to faint. If symptoms consistent with syncope or pre-syncope occurred in conjunction with appropriate changes in pulse or blood pressure, then a diagnosis of vasovagal syndrome was made.

Patients were monitored using a multi-parameter patient monitor described elsewhere [8]. The signals analyzed in the current work were derived from an ECG based on three ordinary chest leads.

C. Generation of the Heart Rate Signal

The ECG signal was filtered using a 3-25 Hz bandpass filter. QRS complexes were detected using an algorithm based on that of Pan and Tompkins [9]. Further processing corrected errors in peak detection based on timing analysis, rather than amplitude analysis: missing beats were estimated and inserted, and extra beats were removed, based on timing information.

The resulting time series is an "RR tachogram", a sequence of unevenly sampled beat-to-beat intervals. To make the data evenly sampled, cubic spline interpolation was employed at a sampling rate of 3 Hz. In this evenly-sampled instantaneous heart rate signal (IHRS), regions of sudden heart rate change were marked as specious, to be excluded from analysis.

D. Generation of the time-frequency map

The Smoothed Pseudo Wigner-Ville Distribution (SPWVD) [10] was then applied to the IHRS to calculate a time-frequency map, *W(n,m)*, where *n* is the time coordinate and *m* is the frequency coordinate. The discrete version of the SPWVD is defined as

$$W(n,m) = \frac{N_h}{2} \sum_{k=-N_h+1}^{N_h-1} |h(k)|^2 \sum_{p=-N_g+1}^{N_g-1} g(p) f(n+p+k) f^*(n+p-k) e^{\frac{-2\pi i k m}{N_h}} \quad (1)$$

where N_h and N_g are parameters determining the length of the frequency-smoothing window *h(k)* and time-smoothing window *g(p)*, respectively. The asterisk denotes complex conjugation. *f(n)* is derived from the IHRS, *y(n)*, according to

$$f(n) = y(n) + i\,H[y(n)], \quad (2)$$

where *H[·]* is the Hilbert transform. The purpose of (2) is to remove the negative frequencies from the IHRS and hence create an analytic signal which is less susceptible to aliasing.

The smoothing functions *g(p)* and *h(k)* in (1) can take a number of forms. For the present SPWVD, a Hamming window function was selected:

$$w(n) = 0.54 - 0.46\cos\left(\frac{2\pi n}{M}\right), 0 \le n \le M, \quad w(n) = 0, \text{otherwise} \quad (3)$$

where *M* is the order of the filter, in this case either N_g or N_h in (1). Hamming windows provide a good trade-off between accuracy and versatility. In [11], it was recommended that the size *M* of these windows be chosen empirically, by visually comparing the results from various choices. This strategy was improved upon in the current work by calculating the rms error for various window sizes. The rms error *E* quantifies the degree of difference (error) between each of *D* data points, $x_o(t)$, and their expected values, $x_e(t)$:

$$E = \sqrt{\frac{1}{D}\sum_{t=1}^{D} [x_o(t) - x_e(t)]^2}. \quad (4)$$

The values $x_o(t)$ were chosen to be the LF/HF ratio of an artificial RR tachogram with varying sinusoidal spectral components at approximately 0.10 Hz and 0.25 Hz.

First, $x_o(t)$ was calculated using (1) for chosen values of N_g and N_h, applied to the artificial tachogram. Second, the rms error was calculated for the time series. These two steps were then repeated for new values of N_g and N_h, and the results plotted to compare the accuracy associated with various orders of filter (see Fig. 1). As can be seen in the figure, at low values of N_g or N_h, insufficient smoothing occurred, so the rms error was high. This was due to oscillations from spurious spectral cross-terms. At very high values of N_g or N_h, too much smoothing occurred, and the rms error rose again, due to insufficient time- or frequency resolution. The minimum rms error was found to occur with N_g = 45 and N_h = 57. These values were chosen to generate the ICFV.

E. Calculation of ICFV

The ICF of a signal is the "mean" frequency at any point in time; it is the time-dependent frequency average of *W(n,m)*. The variability of this signal across a given time duration was defined as the variance of the ICF (square of the standard deviation) and was named ICFV. ICFV was calculated for two segments of the IHRS, from 90-180 seconds after tilt (T1), and from 60-300 seconds after tilt (T2). These times were chosen as a balance between accuracy and efficiency of calculation. Also note that the first 60 seconds after tilt were discarded. This was done to allow the IHRS time to settle; during the first minute or so after tilt, it is typ-

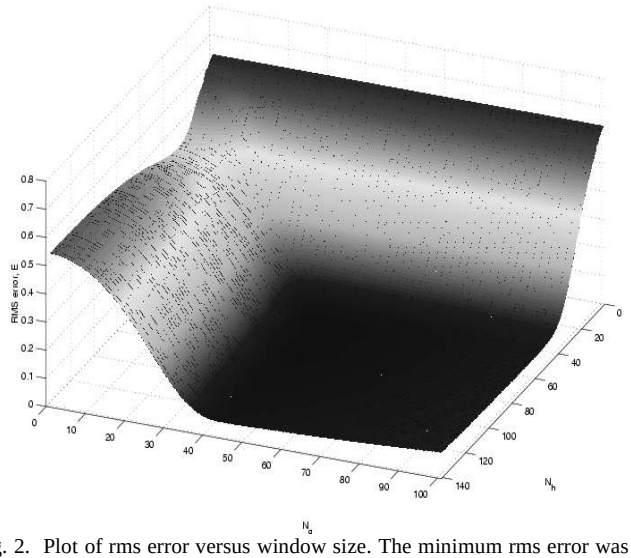

Fig. 2. Plot of rms error versus window size. The minimum rms error was found to occur with N_g = 45 and N_h = 57.

ical for the IHRS to increase sharply as part of the natural autonomic response to adopting an upright position.

F. Cross-Validation

The classification performance of the two ICFV metrics can be assessed using leave-one-out (LOO) cross-validation. For 49 patients at a time, the ICFV values for vasovagal syndrome patients were compared with those for normal patients, and a threshold was chosen that best differentiated the two groups on the basis of a receiver-operating characteristic (ROC) curve. This threshold was then compared with the ICFV of the one patient not included in the group of 49, and the classification success noted. The procedure was applied 50 times for both T1 and T2, since there were 50 patients.

III. Results

A. HUT Outcome

Of the 50 patients undergoing HUT, 18 were diagnosed with vasovagal syndrome ("abnormal") and 32 were classified as free from the disorder ("normal"). The mean time to the syncope or presyncope which terminated each positive test was 35 minutes (standard deviation 10 minutes).

B. Cross-Validation

The results of the application of the ICFV tests are given in Tables I and II. The optimal threshold to differentiate normal from abnormal was found to be 0.070 Hz. Included for comparison are the results of applying to the same dataset two traditional HRV algorithms, those of Kochiadakis *et al.* [3] and Kouakam *et al.* [4]. It should be noted that the other authors achieved success with their algorithms by applying them to patients of a broad range of ages, not just the elderly.

LF/HF 4: With the use of 0.06-0.15 Hz and 0.15-0.40 Hz as LF and HF ranges respectively, the first four minutes after tilt were observed. An LF/HF ratio below a certain threshold was deemed predictive of syncope. [3]

LF 5-5: With the LF spectral band defined as 0.04- 0.15 Hz, the last five minutes of baseline recording were compared with the first five minutes after tilt. A change below a certain percentage was deemed predictive of syncope. [4]

IV. Discussion

HRV analysis of elderly patients is often less fruitful than that of young patients [7], due in part to comorbidity (simultaneity of diseases) and in part to autonomic degeneration. The elderly suffer from comorbidity more than any other age group. Some of the patients studied in the current work were previously diagnosed with other disorders which might have affected their cardiovascular system. It is difficult to find elderly patients who suffer from vasovagal syndrome and no other disorder; one third of people over the age of 65 take three or more prescribed medications [12]. As to the issue of autonomic degeneration, it is known that aging decreases autonomic activity [12]. Hence, traditional autonomic indicators such as the LF/HF ratio are less effective in predicting syncope results in the elderly. Ruiz *et al.* described how devastating the effects of aging can be on traditional HRV analysis [7].

The present cross-validations show that within the traditional HRV analysis techniques, trends were identifiable in the data, but classification performance was poor. As shown in Table II, the new ICFV technique suffered from a degree of data-dependence, but on T1 it performed slightly better than the other classification algorithms, of Kochiadakis *et al.* and Kouakam *et al.*

The motivation for examining the variability of ICF was to identify autonomic instability, rather than assess the magnitude of particular spectral bands. The hypothesis is that patients with greater variability in their ICF (i.e., higher ICFV) might experience greater difficulty in controlling their autonomic response to tilt, and hence could be more prone to fainting. The lack of reliance on spectral bandwidth power magnitudes should have a normalizing effect to combat the results of aging on HRV analysis.

TABLE I
LEAVE-ONE-OUT RESULTS

Test	TP*	TN	FP	FN
ICFV T1	11	24	8	7
ICFV T2	9	16	16	9
LF/HF 4	6	13	19	12
LF 5-5	9	22	10	9

* TP = True Positive, TN = True Negative, FP = False Positive, FN = False Negative. See text for description of tests.

TABLE II
CROSS-VALIDATION PERFORMANCE SUMMARY

Test	Sensitivity	Specificity	PPV*	NPV
ICFV T1	0.61	0.75	0.58	0.77
ICFV T2	0.50	0.50	0.36	0.64
LF/HF 4	0.33	0.41	0.24	0.52
LF 5-5	0.50	0.69	0.47	0.71

* PPV = Positive Predictive Value, NPV = Negative Predictive Value.

V. CONCLUSION

The present work attempted to find thresholds for ICFV to differentiate positive from negative tilt test results, based on the first few minutes of data. The optimal threshold was found to be 0.07 Hz. Although the analysis suffered from data-dependence, as demonstrated by LOO cross-validation, the outcome was encouraging for the technique of ICFV T1 performed better than two methods published previously. Further work, using more sophisticated techniques such as correlational analysis, is required before the ICFV technique can be used clinically.

The importance of finding a predictor of vasovagal syncope cannot be over-emphasized. If HUT could be terminated early for some patients, the resulting time savings would enable a greater number of patients to undergo the procedure. At present, many patients who would benefit from HUT are not offered the test, due to healthcare resource limitations.

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