Clinical Assessment of Cardiovascular and Autonomic Function Using Virtual Instrumentation

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ABSTRACT

This paper presents a non-invasive virtual medical instrument for the clinical assessment of cardiovascular and autonomic function. The virtual instrument was developed with the aim of analysing and understanding the physiological changes that occurs in the heart and circulation during vasovagal blackout attacks. The automated virtual instrument allows impedance cardiography analysis, time and frequency heart rate and blood pressure variability analysis, invasive and non-invasive baroreflex sensitivity assessment and forearm blood flow measurements. Using this virtual instrument five control subjects (3 male, mean age 30.6 ± 5.4) and five vasovagal syncope suffers (2 male, mean age 38.6 ± 6.3) were used in a study to try to identify the differences between the two groups to tilt induced syncope. The results obtained suggest that there are fundamental differences in the physiological responses to orthostatic stress between vasovagal patients and controls, which are evident before the onset of major haemodynamic changes.

Keywords: Virtual Instrumentation, Vasovagal Blackout, Impedance Cardiography, Baroreflex Sensitivity, Heart Rate Variability, Blood Pressure Variability.

1. INTRODUCTION

Syncope, or loss of consciousness, is a common clinical problem. There are many different causes but the most common is vasovagal syncope, a severe form of fainting where loss of consciousness is caused by sudden vasodilatation due to withdrawal of sympathetic outflow to skeletal muscle arterioles resulting in profound falls in blood pressure, commonly accompanied by a variable degree of bradycardia/tachycardia, caused by increased parasympathetic activity. Several studies have used prolonged head-up tilt testing to reproduce vasovagal attacks in many susceptible patients; however the understanding of the pathophysiology of the vasovagal attack remains still incomplete. Nevertheless, the most popular theory is that passive head-up tilting causes blood to progressively pool in the legs, leading to a gradual fall in the amount of blood returning to the heart. This leads to a progressive fall in the volume of the right side of the heart, which ultimately triggers the vasovagal blackout [1]. An alternative theory is that the underlying problem is abnormal sensitivity of the pressure receptors that normally control the circulation [2]. It is clear, though, that the vasovagal reaction has two phases [3]. There is an initial phase lasting several minutes where the circulation fails to respond to the gravitational stress of tilt. This is followed by sudden collapse of the circulation with dramatic falls in the blood pressure and heart rate over the course of a few heartbeats. The key to treating vasovagal attacks is to characterize the changes, which occur in the circulation during the adaptive phase, to identify the point at which the progression to loss of consciousness becomes inevitable, and to identify the trigger factor for circulatory collapse. It is important to stress that treatment does not simply mean ending a particular attack; it also means preventing them from happening at all. In order to do this, an understanding of the physiological processes involved with vasovagal syncope is vital. These are not simple faints. The present work was motivated by this fact, with the aim of producing a medical instrument, which can help to increase the understanding of the physiological processes, which ultimately underlie vasovagal blackouts. Several widely used medical techniques were implemented in the virtual instrumentation solution developed, including impedance cardiography measurements, time and frequency heart rate and blood pressure variability analysis, baroreflex sensitivity assessment and forearm blood flow analysis. Several algorithms for identification of the important points in the physiological waveforms, which support the medical techniques mentioned above were also developed and implemented in the virtual instrument [4-7]. One of the aims in the design of the device was to replace human intervention for the most demanding task of identifying these key physiological waveform points.

2. THE VIRTUAL INSTRUMENT

Multiple non-invasive recorders were used to make continuous beat-to-beat recordings of the following physiological variables:

- Heart rate using a 3 lead ECG recorder.

- Phasic blood pressure (BP) using a "Finepres" (Ohmeda), a photoplethysmographic device using a finger-tip cuff.
- Impedance cardiography (BoMed NCCOM 3 cardiodynamic monitor) which allows beat-to-beat analysis of cardiac output, cardiac volumes and cardiac contractility. The device has analogue outputs for monitoring the beat-to-beat change in the thoracic impedance wave (delta Z) and the first differential of the thoracic impedance wave (dZ/dt).
- Forearm blood flow (FBF) measured by mercury-in-silastic strain gauge plethysmography (EC4 strain gauge and photoplethysmograph, DE Hokanson, Inc, Bellevue, WA) using the intermittent venous occlusion technique.

The analogue outputs available as peripheral interfaces in the above devices were collected through BNC connectors by a 16-bit DAQ board (National Instruments PCI-MIO-16XE-50) plugged into the PCI bus of a Pentium computer. The board is controlled by the relevant National Instrument software drivers, directly interfaced to a customized virtual instrument [4-5] designed using LabVIEW. Although each of these devices were designed for a specific function, having individual front panels and in most of cases microcomputer processed parameter display on screen, only the analogue outputs produced by each device was required for interfacing with the new virtual instrument. All parametric calculations required for the analysis were derived from these analogue signals in the virtual instrument. A schematic representation of the configuration used is shown in Figure 1.

The design concept and algorithms behind the virtual instrument developed are discussed in [5]. The design emphasized modularity, simplicity, compatibility and easy understanding. This kind of design was chosen in order to minimize the problems associated with development and maintenance. This is especially important when programs get larger as in this case. The system developed provides a powerful tool for increasing the understanding of the physiological processes, which underlie vasovagal blackouts. One of its main benefits is its ability to acquire and display multiple physiological signals from existing medical devices without any significant modification, at high sampling rates over prolonged duration (an important feature given that patients with vasovagal syncope may not black out for an hour or more on the tilt table). Complex off-line analysis may then be applied to the beat-to-beat changes in cardiovascular function during the vasovagal reaction and detailed information about changes in the autonomic nervous system, which are the key to understanding the mechanisms of vasovagal syncope. Although complex, the virtual instrument developed in this project works well and efficiently. The instrument is relatively inexpensive and simple to program, allowing rapid troubleshooting and easy modification if additional physiological measures need to be added. The internal organization of the virtual instrument was primarily designed to support further enhancements. The main difficulty with the mathematical analysis of the waveforms has been in the identification of the most important points in the waveforms. These points relate to key events in the mechanical cycle of the heart such as the opening and closure of heart valves, which are vital to the interpretation and analysis of cardiovascular waveforms. Complicated adaptive algorithms have been developed for this purpose; these algorithms are detailed in [5-7]. These calculations are transparent, so from a user's point of view the final interface is easy to understand and straightforward to use. Another advantage of the virtual instrumentation developed in this project is its modularity and flexibility; each algorithm was implemented as a single module, which can be easily re-used as a ready made component for other virtual instruments derived from the original virtual instrument. The system developed was extensively tested to determine its features and limitations [5]. Signal processing was an extremely important section of the complete system.

3. SUBJECTS AND METHODS

Five control subjects (3 male, mean age 30.6 ± 5.4) and five vasovagal syncope suffers (2 male, mean age 38.6 ± 6.3) were used in this study to try to identify the differences between the two groups to tilt induced syncope. Approval from the Central Manchester Local Research Ethics Committee was obtained prior to the study.

Data Recording and Protocol

All patients were tilted after an overnight fast. All cardioactive drugs were stopped for at least 5 half-lives before tilting. Tilting was performed in a darkened, quiet room with minimal stimulation. After the recorders were placed on the body, the patient lay in the horizontal position for 20 minutes, following which recording was commenced.

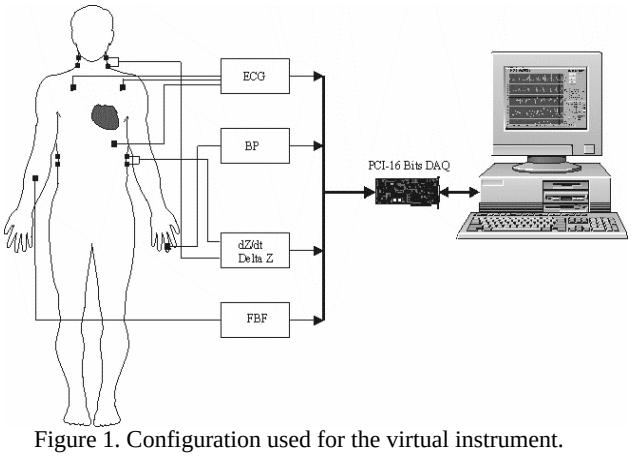

Figure 1. Configuration used for the virtual instrument.

After a further 15 minutes at the horizontal, the table was slowly tilted head-up to 60 degrees [8]. This was the maximum angle allowed in this test. Patients were supported on the tilt table so that there was as little activity as possible of the muscle pumps in the legs and pelvis to maximize reduction of venous return to the heart. Patients were left at 60 degrees for 45 minutes, or until loss of consciousness occurred, at which point the table was returned to the horizontal. Forearm blood flow was measured every 30 seconds during rest, with cuff occlusion for 15 seconds.

Data Analysis

The data was analysed in 2-minute segments. Rest data was taken from the last 2 minutes segment at rest prior to the onset

of tilt. Tilt data was analysed from the point at which patients reached 60 degrees head-up tilt to the point at which steady state was lost i.e. the start of the fall in blood pressure (hypotension) leading to loss of consciousness.

4. RESULTS AND DISCUSSION

The results obtained are shown in Tables 1 to 5. Results are expressed as mean ± standard deviation. Time domain measurements provide an overall analysis of the changes; frequency domain analysis instead provides information about the source of these variations, including changes in the sinus heart rate over time (heart rate variability HRV) and cyclical changes in arterial blood pressure over time (blood pressure variability BPV). Time domain analysis involves the statistical analysis of the sinus rate (sinus RR intervals). This includes the calculation of simple statistical variables in the time domain such as mean RR interval (RRm), the standard deviation of the normal-to-normal RR intervals (SDRR). Other commonly used time domain measurements are derived from interval differences such as the root-mean-square of differences in successive RR intervals (RMSSD), the number of interval differences of successive normal-to-normal (NN) RR intervals greater than 50 ms (NN50) and the proportion PNN50 obtained by dividing NN50 by the total number of NN intervals.
All these measurements of short-term variation are used to estimate the high frequency (fast) beat-to-beat variations in heart rate. The fluctuations present in the beat-to-beat heart rate and arterial blood pressure can be described in frequency domain using the Fourier Transform (FT) The power spectrum representation of these time variations decomposes the signal into its frequency components quantifying them in terms of their relative intensity. Two major bands can be identified from the power harmonic analysis of the variations in the heart rate: a high frequency band (PHF) between 0.15-0.40 Hz, reflecting parasympathetic activity, and the low frequency band (PLF) between 0.04-0.15 Hz, reflecting mixed sympathetic and parasympathetic activity. Similarly in the case of arterial pressure variation, three main bands can be identified: a low frequency band (PLF) between 20-60 mHz, a medium frequency (PMF) band between 70-140 mHz, and a high frequency band (PHF) between 200-300 mHz. PT represents the total power.

Figures 2 and 3 show typical waveform responses to tilting for both groups. As shown in Figure 2 in the case of the syncope patients, after tilting there is an initial phase lasting several minutes where the circulation fails to respond to the gravitational stress of tilt. This is followed by a sudden fall in the blood pressure commonly accompanied by a variable degree of bradycardia/tachycardia over the course of a few heartbeats. This behaviour in the circulation is not seen in the control group, as can be seen in Figure 3. From these results it is clear that there are very different reactions to tilt between the two groups. In the controls, there is initial vasoconstriction as expected in response to tilt, but then there appears to be minor vasodilatation with increasing tilt resulting in increased FBF. However, in the syncope patients, there is progressive vasoconstriction, perhaps in an attempt to maintain blood pressure at the time of increasing intravascular depletion.
Although the numbers are small, it suggests that there are fundamental differences in the physiological responses to orthostatic stress between vasovagal patients and controls, which are evident before the onset of major haemodynamic changes. For the 5 patients who developed syncope, 2-minute segments were also analyzed backwards for 12 minutes prior to the onset of hypotension to investigate changes in lower frequency (PLF) and high frequency (PHF) power components in HRV prior to syncope.

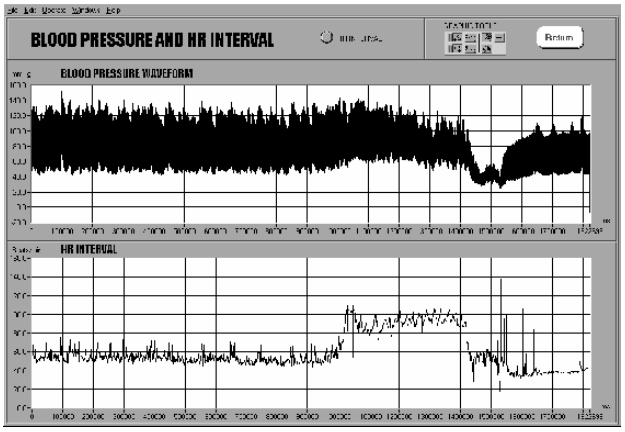

Figure 2. Changes in BP and HR for a patient who developed syncope after tilting.

The results obtained are shown in Table 6. An interesting result that can be observed from these data is that in the syncope group, there is a surge in the low frequency –high frequency ratio in the period leading up to the start of the fall in blood pressure, which is not seen in the control group. This happens several minutes before any visible change in the blood pressure, suggesting that abnormalities in autonomic innervation may play a key role in initiating the vasovagal process i.e. a relative overstimulation by the sympathetic system. Although the numbers are too small, the trends are highly suggestive and clearly further studies are needed for clarification.

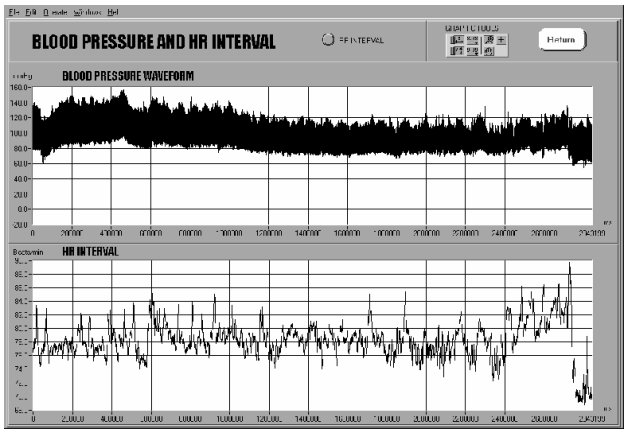

Figure 3. Changes in BP and HR for a control subjects after tilting.

5. CONCLUSION

A useful virtual instrument for clinical assessment of cardiovascular and autonomic function has been presented in this paper. It may enable a better understanding of the physiological processes that cause blackouts. The results

obtained from this study suggest that there are fundamental differences in the physiological responses to orthostatic stress between vasovagal patients and controls, which are evident before the onset of major haemodynamic changes.

	Rest	Immediate Tilt	10 mins Tilt	End Tilt
RRm	980.15 ± 225.6	791.87 ± 153.92	798.83 ± 176.71	754.18 ± 151.35
SDRR	52.36 ± 22.11	35.9 ± 21.6	33.65 ± 21.80	50.28 ± 35.58
PNN50	12.57 ± 13.48	2.15 ± 2.08	4.43 ± 8.99	3.14 ± 6.14
PT	37.13 ± 12.03	21.01 ± 5.20	25.98 ± 14.46	25.78 ± 10.78
PLF	27.31 ± 10.39	16.02 ± 4.64	20.62 ± 11.08	23.15 ± 10.86
PHF	9.82 ± 4.06	5.19 ± 1.58	5.36 ± 4.14	2.63 ± 0.94
PLF/PHF	3.16 ± 2.07	3.26 ± 1.27	5.09 ± 2.65	10.00 ± 6.18

Table 1. Changes in HRV parameters for patients with history of syncope.

	Rest	Immediate Tilt	10 mins Tilt	End Tilt
RRm	897.61 ± 173.57	731.90 ± 84.49	710.45 ± 84.01	708.03 ± 98.95
SDRR	42.18 ± 19.34	28.56 ± 13.95	38.32 ± 23.45	38.21 ± 33.54
PNN50	9.85 ± 9.99	0.33 ± 0.74	2.48 ± 3.09	2.15 ± 4.80
PT	41.64 ± 5.76	28.79 ± 8.64	34.29± 9.62	31.07 ± 5.08
PLF	28.08 ± 1.69	24.76 ± 9.15	28.07 ± 8.92	25.22 ± 3.79
PHF	13.56 ± 7.18	4.04 ± 1.39	6.22 ± 4.62	5.85 ± 1.91
PLF/PHF	2.65 ± 1.42	7.13 ± 4.18	6.38 ± 3.46	4.64 ± 1.32

Table 2. Changes in HRV parameters for control subjects.

	Rest	Immediate Tilt	10 mins Tilt	End Tilt
PLF	20.82 ± 5.67	17.66 ± 9.71	14.89 ± 5.12	20.12 ± 10.37
PMF	7.49 ± 3.01	12.69 ± 7.55	8.83 ± 3.51	5.31± 0.88
PHF	2.12 ± 1.68	1.28 ± 1.14	2.53 ± 1.45	2.59 ± 1.41

Table 3. Changes in systolic BPV for patients with history of syncope.

	Rest	Immediate Tilt	10 mins Tilt	End Tilt
PLF	18.52± 7.36	18.09 ± 6.74	17.24 ± 5.12	19.32 ± 10.26
PMF	14.03 ± 6.04	18.28 ± 11.29	13.58± 3.51	8.38 ± 2.49
PHF	3.20 ± 2.04	3.17 ± 3.97	2.39 ± 2.38	2.10 ± 2.28

Table 4. Changes in systolic BPV parameters for control subjects.

	Rest	Immediate Tilt	10 mins Tilt	End Tilt
Control n=5	1.729 ± 0.950	1.421 ± 0.715	1.689 ± 0.988	1.948 ± 0.910
Syncope n=5	2.885 ± 1.319	2.454 ± 1.248	2.118 ± 0.967	1.917 ± 0.779

Table 5. Forearm blood flow changes during head-up tilt.

	0-2	2-4	4-6	6-8	8-10	10-12
PLF	23.15 ± 10.86	20.86 ± 5.98	29.82 ± 14.51	27.48 ± 14.02	23.08 ± 11.59	22.46 ± 8.39
PHF	2.63 ± 0.94	4.39 ± 4.15	5.43 ± 4.08	4.78 ± 2.87	5.79 ± 2.36	8.19 ± 5.52
PLF/PHF	10.00 ± 6.18	10.15 ± 11.03	8.66 ± 9.03	7.88 ± 8.01	4.07 ± 1.12	3.70 ± 2.71

Table 6. Change in low & high frequency components of heart rate variability in 12 minutes prior to *onset* of hypotension for patients with syncope.

The trends are highly suggestive and clearly further research is required in this area. Despite the limited extent of the medical tests performed, interesting and very encouraging results have been obtained, showing the potential use of the device as a tool for medical research. Although the device has been primarily intended and developed for studying patients suffering vasovagal attacks, it can be used in any study involving the autonomic nervous system. With further refinements a useful commercial medical instrument could be produced.

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