Multi-biosignals Analysis
The Effect of Peripheral Nerve Stimulation on Skin Conductance and Heart Rate Variability

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Abstract. Objectives: This study aims to evaluate the influence of standard electrical stimulation on human electrophysiology. Methods: A total of 10 healthy subjects were submitted to the same protocol. The electrical stimuli were applied on the median nerve of the left wrist. Blood Volume Pulse (BVP) and Electrodermal Activity (EDA) signals were acquired from the index finger through an oximeter and from both the abductor pollicis muscle and the 3rd palmar interosseous muscle of the right hand, respectively. Nerve stimulation was performed using increasing intensities current: range from 5 to 30 mA, with 1mA step and applying 20 stimuli per step. Heart Rate (HR) and Heart Rate Variability (HRV) were computed, from the analysis of the latency between BVP pulses, in basal state and during stimulation. EDA parameters response latency, response rise time and readaptation slope were computed for each burst.
Discussion: Electrical stimulation reveals to influence several parameters of the Autonomic Nervous System (ANS). It was easily detected an EDA rise response for each of the applied bursts and also an increase of the HRV during stimulation.

1 INTRODUCTION

Recently, the importance of studying biosignals has been increasing due to its role finding physical and mental stress. It has already been determined that the Autonomic Nervous System (ANS) exerts a constant influence over heart rate (HR) and skin conductance. Despite all the studies, there has always been a gap in the understanding of the effects of electrical stimulation in human physiology (Shetter, A., 1997; Dimitrijevic, M., 2008).

Skin Conductance (Electrodermal Activity) has been reported as a potential non-invasive marker for sympathetic activity, and has been used recently in psychophysiological research. The Electrodermal activity (EDA) measurement is based on content of water and electrolytes in individual parts of the organism and the spreading of low electrical current through two electrodes localized on skin surface.

The conductance depends on the amount of sweat produced by eccrine glands, which are regulated by the sympathetic nervous system (Visnovcova, 2013). It's the sweat level changes that modify the resistance, and alterations in the EDA signal are noticed.

The total EDA is composed of a baseline and a phase level. The baseline is the EDA on a daily basis. Providing the EDA is not a constant value it was noted that its oscillations are very small over a small time interval. Therefore we considered the EDA baseline to be linear. The phase level is a variation of a subject's EDA due to external stimuli applied on the wrist and reflects the arousal of the sympathetic nervous system (Dominik, B., 2010). The EDA parameters usually analysed are the response latency, response rise time and readaptation slope.

EDA latency is the time interval between the application of the first stimulus and the detection of a response from the subject's EDA. EDA rise time is the time taken by an EDA response to rise and peak. Finally, EDA readaptation slope is defined as the slope of the line obtain from a linear regression with all data points past the last stimulus.

The heart rate is very sensitive and readapts quickly to different stimuli. The sympathetic and parasympathetic neurons, which are linked to the sinoatrial node in the heart, have a major contribution to changes in its beating rate (although there are more contributions, like the physical and

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mental state). Heart rate variability (HRV) is the physiological phenomenon in which the heart rate oscillates around its mean value due to external influences from the autonomic nervous system (ANS), or other mental and physical factors (Malik, M., 1990; Malik, M., 2006). It's a marker to study the activity of the regulatory mechanisms and to analyse the effects (excitatory and inhibitory) they have upon the heart rate.

HRV can be analysed on time or frequency domains. Through the analysis of the root mean square of the successive RR intervals we can obtain a measure of the sympathetic and parasympathetic vagal activity (Clifford, G., 2002). One way to measure the HR is through the Blood Volume Pulse (BVP) sensor. With the cardiac pulse, erythrocytes will change the spatial alignment and this will affect the blood's opacity. The BVP sensor makes use of opacity variations from the tip of the finger to gather the cardiac pulse on a certain instant.This study aims to analyse the effects of electrical stimulation on human physiology, based on skin's galvanic response and on Blood Volume Pulse (BVP) signals.

2 METHODS

2.1 Subjects and Room Conditions

In this study a total of 10 healthy subjects, composed of 5 males and 5 females, with a mean age of 24.10 years (standard deviation of 2.38 years), were submitted to a previously developed heart rate and skin conductance acquisition protocol. All of the subjects were healthy, with no physical or neurophysiological disorders registered.

The subjects were seated on a comfortable chair with both their arms relaxed. It was required of them to feel comfortable for the acquisition to begin. Earmuffs were placed on the subjects' ears to prevent any noise distraction. Moreover the room was kept silent during the acquisition and the subjects were asked to remain motionless and relaxed.

The stimuli were applied through two disposable electrodes on the median nerve of the left wrist and two electrodermal activity acquisition electrodes were placed on the abductor pollicis muscle and on the 3rd palmar interosseous muscle of the right hand. An oximeter was also placed on the index finger of the right hand to measure the heart rate of the subjects. The sensor makes use of colour variations from the tip of the index finger (due to blood's opacity) to gather the blood volume on a certain instance in time.

Although the majority of the subjects didn't know about the acquisition protocol, the acquisition had to be repeated on two of the subjects (1 and 2) due to low quality signal reading.

2.2 Acquisition Protocol

The first part of the acquisition took 4 minutes and no stimuli were applied to the subjects. This segment of the acquisition protocol had the purpose of acquiring the basal BVP and EDA.

The second segment featured the application of the electrical stimuli on the medial nerve of the left wrist. Square current modulated waveform was used. The electrical stimuli consisted of 6 bursts of 20 repetitive stimuli each and with increasing intensities (ranging from 5 to 30 mA). In each burst the interval between stimuli was 0.9 seconds and the time interval between bursts was of 10 seconds.

The final segment of the acquisition was similar to the first one, a 4-minute acquisition to record the subjects' recovery after the application of stimuli.

Through all of the phases, these segments were recorded at a 2000Hz acquisition rate. A combined wireless, miniaturized and synchronized unit was specifically developed for multi-biosignal acquisition (Plux, 2014) and nerve stimulation (Araújo, T., 2012).

2.3 Processing

After the acquisition from all subjects the data was processed using a script in Python. The data was stored in a .txt file (for each subject) and organized in columns, each column belonging to a certain parameter and each line to a recorded frame.

The data recorded was processed according to steps bellow:

1. Conversion of frames to seconds, since 1000 frames corresponded to a single second.
2. Search for all HR peaks. HR data was plotted in a time/HR graph to ensure all peaks found by the script matched the plotted peaks.
3. Determination of mean heart rate for all 3 segments.
4. Determination of HR amplitude and HRV for all 3 segments.
5. Analysis of EDA time latency, response rise time and readaption slope via plotting and linear regression.

These steps were repeated for all 10 subjects.

3 RESULTS

Although it might be a difficult task to study the influence of electrical stimulation due to external factors, which are hard to control, the parameters chosen provide a subjective analysis of the subjects' reactions to stimulation. Parameters chosen for EDA include EDA latency time, EDA rise time and EDA readaptation slope.

Table 1 shows the HR and HRV for each subject by determining standard deviation of the successive hearth pulses intervals.

Table 1: Mean values and respective standard deviation error for the heart rate (in beats per minute) obtained during segments 1, 2 and 3.

	Heart Rate (bpm)					
	Segment 1		Segment 2		Segment 3	
	Mean	(SD)	Mean	(SD)	Mean	(SD)
Subject 1	80.32	(8.79)	81.57	(8.24)	79.00	(8.26)
Subject 2	66.57	(7.99)	64.87	(5.91)	66.99	(8.24)
Subject 3	69.52	(2.89)	71.96	(3.81)	69.32	(3.25)
Subject 4	64.28	(5.57)	61.05	(4.15)	64.49	(5.44)
Subject 5	70.09	(5.62)	64.40	(4.88)	69.84	(5.38)
Subject 6	72.43	(5.68)	69.80	(3.72)	72.07	(4.66)
Subject 7	67.14	(4.40)	71.01	(6.43)	65.47	(4.85)
Subject 8	83.23	(5.53)	83.85	(5.86)	83.19	(5.97)
Subject 9	61.94	(6.32)	61.74	(5.01)	60.63	(6.36)
Subject 10	63.17	(4.22)	62.37	(3.22)	63.18	(3.68)

Figure 1 shows the subjects' EDA during segment 1 and segment 2. Regarding the subject's EDA from segment 1 (Figure 1A), analysis of the results showed that prior to the application of the stimuli small oscillations were detected but deemed of low importance. For segment 3, the behaviour was the same as presented in Figure 1A. The EDA signals from all subjects during segment 2 of the acquisition protocol are presented in Figure 1B.

Table 2 presents EDA latency for all subjects and for each burst of 20 stimuli. Negative values are result of a response that was detected before the burst was applied. There was no measurable response from subjects 8 and 10 and subject 5 presented a signal with very low activity, which was particularly hard to analyse.

Table 3 presents the EDA rise time for each of the detected subjects' EDA pulses to rise and peak.

4 DISCUSSION

The EDA signal in its absolute value has high inter-subject variability, which makes it difficult to establish a measurement range capable of comprising significant population. To overcome this effect, it is mandatory to establish amplitude / gain independent objective parameters. In this study, only 7/10 subjects revealed significant responses of sympathetic nervous system to the electrical stimulation. For segment 1, EDA results showed, in general, a continuous smooth descent tendency for all subjects (Fig. 1A). For segment 2, EDA results showed, for most of the subjects, that the EDA signal has some events in response to the electric stimulus (Fig. 1B). This allows the analysis of the time latency between the reception of the stimulus by the median nerve and the ANS reaction to it.

The stimulus/response latency is a parameter inherent to the personal physiology and consequently has high inter-subject variability. In half of the subjects analysed, a slight tendency to decrease the latency with the increase of the stimulation intensity is noticed. This was expected given the ANS constant re-adaptations.

One subject reveals a notorious response arousal even before the stimulus application. Curiously, due to poor quality of the acquisition for this subject, the protocol needed to be repeated and the results here exposed are from the second acquisition. This was the only subject who had been exposed to the protocol before.

When analysing the EDA rise time, a lower standard deviation both intra and inter subject is observed, when compared with Segment 1. The response rise time seems to be a parameter which does not correlate with the increase of stimulus intensity, presenting very stable results within the same subject.

Another pointer for the ANS management used in this work was the analysis of BVP signal.

The BVP signal constitutes *per se* a direct signal from the vascularization physiology. With the cardiac pulse, erythrocytes will change the spatial alignment and this will affect the blood's opacity.

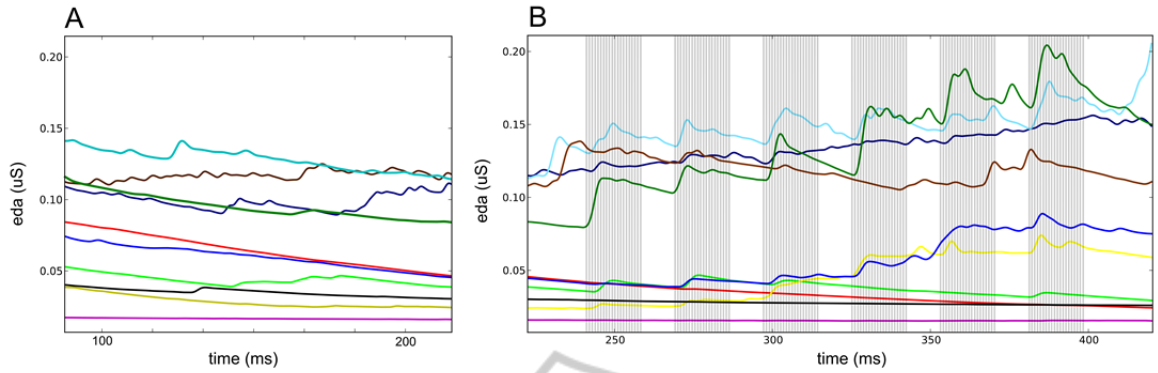

Figure 1: EDA signals obtained for all subjects. A) Example window obtained from segment 1 of the acquisition protocol (basal activity); B) Signal obtained from segment 2 of the acquisition protocol (six bursts of electrical stimulation).

Table 2: Stimulus response latency of EDA signal for each stimulation burst.

	Latency (s)						
	Burst 1 5mA	Burst 2 10mA	Burst 3 15mA	Burst 4 20mA	Burst 5 25mA	Burst 6 30mA	**Mean (SD)**
Subject 1	2,05	1,60	1,30	0,92	2,34	1,19	1,57 (0,49)
Subject 2	0,00	0,00	0,95	1,00	0,88	0,89	0,63 (0,43)
Subject 3	--	--	--	--	--	--	--
Subject 4	0,92	0,83	0,80	1,14	1,16	0,73	0,93 (0,17)
Subject 5	--	--	--	--	--	--	--
Subject 6	2,42	2,16	1,55	0,59	1,02	0,97	1,45 (0,66)
Subject 7	-- *	1,20	4,40	--	1,92	-- *	2,51 (1,37)
Subject 8	2,94	2,00	2,00	1,66	1,70	1,13	1,91 (0,55)
Subject 9	2,81	2,80	3,00	--	--	0,99	2,40 (0,82)
Subject 10	--	--	--	--	--	--	--

*subject with event previous to stimulation

Table 3: Stimulus response rise time of EDA signal for each stimulation burst.

	Rise Time (s)						
	Burst 1 5mA	Burst 2 10mA	Burst 3 15mA	Burst 4 20mA	Burst 5 25mA	Burst 6 30mA	**Mean (SD)**
Subject 1	2,74	4,00	3,70	3,00	2,36	3,94	3,29 (0,63)
Subject 2	4,74	4,19	4,55	4,92	3,47	4,54	4,40 (0,47)
Subject 3	--	--	--	--	--	--	--
Subject 4	7,63	3,13	6,40	3,28	2,93	5,60	4,83 (1,82)
Subject 5	--	--	--	--	--	--	--
Subject 6	3,14	3,15	3,93	5,03	2,50	2,83	3,43 (0,84)
Subject 7	-- *	3,10	2,59	--	3,00	-- *	2,89 (0,22)
Subject 8	3,84	4,00	4,09	3,75	4,20	2,90	3,79 (0,43)
Subject 9	5,68	4,56	4,30	--	--	3,93	4,62 (0,65)
Subject 10	--	--	--	--	--	--	--

*subject with event previous to stimulation

The BVP signal of 5/10 subjects showed an amplitude decreasing with the beginning of the electrical stimulation. An example of this pattern can be seen on the subject of Fig. 4. This is justified by a vasoconstriction effect caused by adaptations of the ANS to the electrical stimulation. Vasoconstriction of the blood vessels increases the spatial density and consequent alignment of erythrocytes. This fact will increase the opacity of the finger, leading to lower signal detection by the sensor used for the detection of the BVP signal.

The BVP peaks also enable the analysis of the HR and HRV through the computation of the standard deviation (SD) of subsequent peaks latency. Regarding the HR analysis it was observed that the majority of the subjects (5/10) showed a decrease in the HR and HRV during stimulation. In 2/10 subjects the opposite effect is verified: the HR and HRV increase during the stimulation period. The remainder subjects do not show a direct influence of the stimulation stage.

For the majority of the subjects, it is understandable that the electrical stimulation has an influence on the ANS, which affects the vagus nerve and thus the sinus node. For all subjects, on Segment 3, HR and HRV return to the Segment 1 basal values. We can assume that after the stimulation the subject's ANS recovered easily. Therefore, peripheral nerve stimulation did not have any short-term consequences on the subjects' HRV.

Electrical stimulation revealed to influence several parameters of ANS. This influence can now be taken into account on standard uses of peripheral nerve stimulation.

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