

Noninvasive detection of the hemodynamic stress of exercise using the photoplethysmogram

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Exercise induced hemodynamic stress has been studied extensively using a wide range of physiological sensors. While athletes can modulate their training intensity using EKG-based heart rate monitors, there are currently no noninvasive monitors that can be used to ascertain with a high degree of certainty the hemodynamic stress an individual is experiencing because of fatigue or an underlying pathology. We hypothesize that the low frequency spindle waves observed in the photoplethysmographs (PPG) of individuals exercising to volitional fatigue provide a mechanism for noninvasively detecting hemodynamic stress to the human vascular system. In a clinical trial with eleven healthy subjects performing the Bruce Protocol treadmill test these low frequency spindle waves were observed in both the forehead and ear PPG in all subjects before the onset of volitional fatigue. As volitional fatigue approached, the spindle waves became more pronounced; then, within several seconds of the cessation of the protocol, they disappeared. Using a software-based detector, these distinct spindle waves are reliably detected with a low incidence of false positives. This technique holds promise for the automatic detection and characterization of exercise induced hemodynamic stress.

running; thermoregulation; baroreflex; morphological signal processing; skin blood flow; respiratory rate

Moderate hemodynamic stress can be detected by monitoring increases in heart rate, blood pressure and respiration; however, it is more difficult to ascertain noninvasively the degree of physical and hemodynamic stress an individual is experiencing because of fatigue or an underlying pathology [2]. In many professions, such as fire fighting and military operations, excessive hemodynamic stress can lead to task failure[15]. If reliable algorithms for detecting stress and fatigue, both in healthy and compromised individuals, can be developed, it will aid in the management of human resources in critical activities and potentially prevent unnecessary injury or death.

Exercise has been used a model for increasing hemodynamic stress. Exercise induces stress by decreasing by peripheral vascular resistance, increasing blood flow to muscles and skin [14]. While increased blood flow to the skin helps the body meet thermoregulation requirements, it also reduces mean arterial blood pressure. In part to increase blood flow to the muscles and to maintain blood pressure,

when individuals exercise at very high intensities, the blood flow to skin has been shown to attenuate, despite higher thermoregulation requirements[8].

Low frequency oscillations in skin blood flow have been observed using laser Doppler infrared flowmetry when the carotid arterial baroreflex is stimulated using a negative pressure cuff on the neck [3]. These oscillations were associated with sympathetic neural activity in the muscles under the skin and were close to the resonance frequency of the skin vasculature. These low-frequency oscillations, with a period between five and fifteen seconds, have been used as a metric for physical fitness [7, 11], and relaxation [26].

These studies all used frequency domain techniques to ascertain low and high frequency characteristics of the blood flow, but this approach may overlook morphologically distinct responses to stress, some of which cannot be discerned by frequency analysis.

Our study monitored blood flow using morphological techniques to discern patterns in the photoplethysmogram (PPG) from a pulse oximeter situated on the finger, ear and forehead. Using a modified Bruce treadmill protocol, subjects were exercised until volitional fatigue. In each subject we detected low frequency oscillations in the height of the cardiac peaks, seen in Figure 1 and Figure 2, distinct from respiration. We refer to these waveforms, characterized by periodic decrease or “pinching” in the PPG waveform, as *spindle waves*. These waveforms, with oscillating cardiac peak height have a morphology that is distinct from the Mayer waves described [19, 29] where the peak heights stay the same and the baseline oscillates.

PPG WAVEFORM

A pulse oximeter illuminates the skin with light from a Light Emitting Diode (LED), and measures the amount of light either transmitted or reflected to determine changes in volume, the PPG. Though the cardiac pressure pulse is damped by the time it reaches the skin, it is sufficient to distend the arteries and arterioles in the subcutaneous tissue and produce a distinct pulse in the PPG. A reduction of pulsatile amplitude can be directly attributable either to a loss of central blood pressure or to constriction of the arterioles perfusing the skin [27].

One way respiration affects the cardiac cycle is by varying the intrapleural pressure. When the frequency and depth of respiration increase, the venous return increases, leading

to increased cardiac output [20]. When respiration is not shallow it can be seen as a modulation to the cardiac cycle in the PPG, which is often referred to as the Respiratory Induced Variation (RIV) [9, 23].

Vasoconstrictive and vasodilative systems of the skin used to mediate temperature and arterial pressure also contribute to the morphology of the PPG waveform. Exercise increases the core temperature which results in vasodilation and an increase in skin blood flow. At the onset of exercise, vasoconstriction typically increases until about 38° C, when vasodilation begins [16].

Low frequency oscillations in arterial pressure and peripheral blood flow, called Traube-Hering-Meyer (THM) waves [12, 22] also contribute to oscillations in the PPG. THM waves appear as a rhythmic rise and fall in the baseline of blood pressure and vascular blood flow (as measured by laser Doppler) with superimposed cardiac and respiratory cycles. THM waves are thought to result from multiple physiological phenomena, including thermoregulation, respiration, and baroreflex [26].

METHODOLOGY

A group of twelve active healthy subjects, including six un-

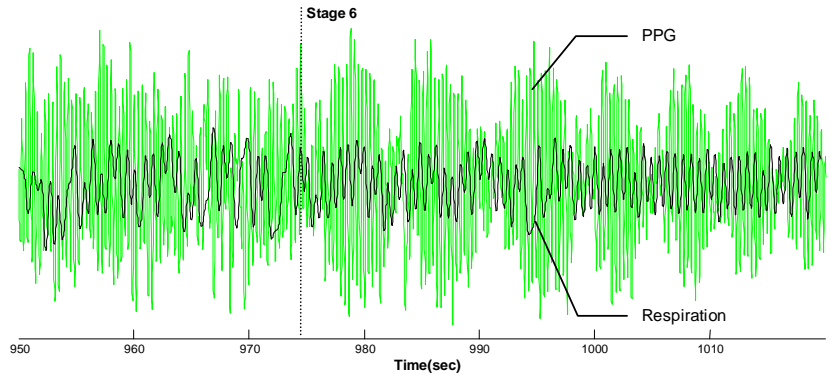


Figure 1. PPG from a Nonin ear pulse oximeter. The PPG becomes organized at the start of Stage 6 (8.85 km/h, 20% incline) and remains consistent until the treadmill slow down. Respiration (black), from EKG-based impedance pneumography, shows a maximum of 80 respirations per minute while there are between 11 and 12 spindle waves per minute. This high breathing rate is consistent with results for trained runners running at maximal effort.

dergraduate, and three graduate students, participated in the study with informed verbal consent. Subjects were screened for known cardiovascular conditions, and medications that would influence the results of the study. All subjects were nonsmokers, physically active and normotensive, including four women (average age 25, range 21-27), and seven men (average age 25, range 19-47) The experimental protocol were approved by the IRB of Dartmouth-Hitchcock Medical Center.

FDA-approved Nonin PureLight® pulse oximeters were placed on the subject’s finger and ear using the standard clip, and the forehead using a standard Nonin-supplied holder. Each sensor was connected to a Nonin OEM III Module interface (Nonin Medical Inc., Plymouth, MN, USA) which performs proprietary notch filtering to the 12-bit data. With a serial RS-232 interface a personal computer recorded data at 75 Hz using a Java-based program. The annotated data was saved in text files for later analysis using Matlab® (Mathworks, Natick, MA, USA).

A Datex S5 Collect® monitor (Datex-Ohmeda, Inc. Madison, WI, USA) was used to collect an EKG, a second finger PPG and an impedance pneumograph. Data was recorded to a text file at a rate of 300 Hz. The respiratory rate was calculated from the impedance pneumography using a Matlab®-based algorithm. Blood pressure was taken manually with a standard cuff during each stage.

Experimental Protocol

The treadmill-based Bruce Protocol

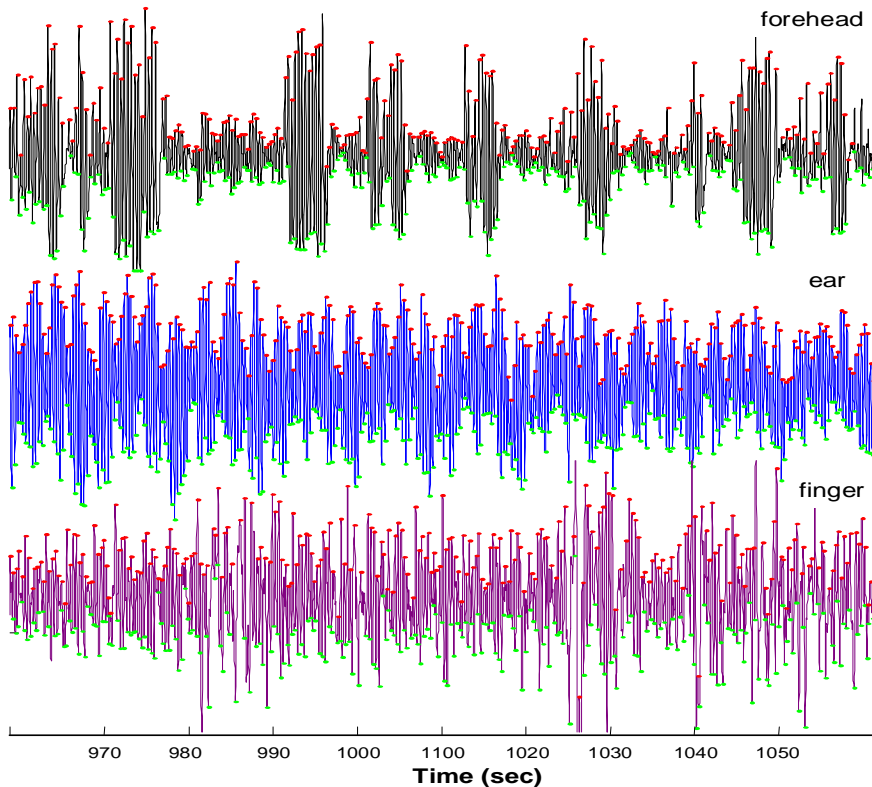


Figure 2. PPG data during, Stage 5. Spindle waves are seen in the forehead and ear but not clearly in the finger PPG. This section of data shows a difference in period and structure of spindle waves between the forehead and the ear that is not seen as distinctly in other subjects.

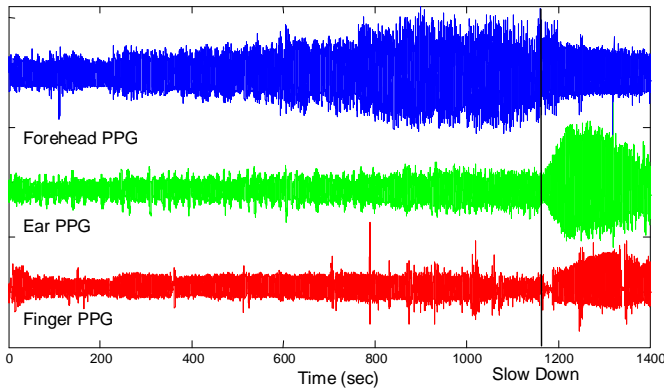


Figure 3. PPG data from Subject 2 shows amplitude of the PPG increases more for the forehead than for the finger or ear during the trial. After the treadmill slows, the forehead PPG amplitude decreases while the finger and ear increases. Periodic pinching in the finger PPG is from blood pressure measurements.

Stress Test was used to elicit cardiac stress [25]. The test protocol was run automatically by the treadmill (a Case 8000 testing system controlling a Series 2000 treadmill from GE Healthcare, Waukesha, WI, USA), and consisted of successive three minute stages, described in Table 1, with each stage made more challenging by increased pace and incline. Subjects were asked to keep their hands on the treadmill railing at all times. All subjects exercised to volitional fatigue. Blood pressure was recorded before the end of each stage.

Spindle Wave Detector

Using Matlab®, a spindle wave classifier was developed that detected the morphological characteristics of the spindle waves. This technique was based on a related method developed for detecting morphological features of the PPG indicative of hypovolemia [17]. The detector was constructed with the following stages.

Stage 1 – Cardiac Peak Detection

The peaks and valleys of each cardiac cycle in the PPG were detected using a timed automata. The temporal characteristics of a cardiac cycle are parameters of the algorithm: the minimum and maximum cardiac period, and the maximum change in period between cycles. Detection is accomplished without prior knowledge about peak height or shape. The algorithm therefore does not detect and reject motion artifact with the same temporal characteristics as a cardiac peak.

Stage 2 – Envelope Peak Detection

Using the peak detection algorithm from Stage 1 with the temporal characteristics of the spindle waves as parameters, the top envelope of the PPG was analyzed and the peaks and valleys in the envelope were detected.

Stage 3 – Motion Artifact Detection

Cardiac cycles corrupted by motion artifact were auto-

matically detected in software. Cardiac cycles with aberrant morphology, such as a severely skewed shape, were marked as motion artifact and not used in subsequent calculations

Stage 4 - Spindle Wave Detection

A classifier was tuned to detect spindle waves using the following metrics to minimize false positives caused by motion artifact and respiratory induced variation:

- no cardiac cycles with large motion artifact detected in Stage 3;
- significant pinching at both beginning and end;
- relatively smooth envelope;
- symmetrical envelope; and
- at least five cardiac cycles.

RESULTS

All twelve subjects completed the Bruce protocol, with the twelfth subject being excluded from the study because of apparent sensor failure. The distribution of Bruce Protocol Stages reached by each subject is shown in Table 1.

None of the subjects exhibited detectable cardiac abnormalities: all showed nominal EKG and blood pressure. Dehydration was not considered to be a factor since these trials were of short duration, averaging less than 20 minutes [10]. As subjects approached their maximum heart rate, the variability in heart rate disappeared. Oxygen saturation levels for the forehead at maximum heart rate were in the range of 95 to 100% while the ear was consistently 5 - 9% lower. The finger PPG gave inconsistent and noisy heart rate and oxygen saturation readings.

Examination of the finger PPG showed that the signal was generally of poor quality because of motion artifact that often obscured any trend in the overall amplitude of the PPG. Visual inspection showed short trains of over 10 spindle waves for just two subjects: Subject 2, Stage 4 and Subject 5, at the transition to Stage 6.

The forehead PPG amplitude increased in 10 of 11 subjects as the trial progressed and then decreased after the treadmill slowed down. The exception, Subject 8, had a PPG amplitude that undulated over a small range. The ear PPG amplitude gradually decreased in 8 of 11 subjects, and only increased in Subject 1. After the treadmill slowed down, the ear PPG increased in all subjects. Figure 3 shows the typical response shown by Subject 2.

As shown in Figure 4 we detected spindle waves in the forehead and ear PPG of all eleven subjects during the final stage before volitional fatigue. All subjects had more pronounced spindle waves as they approached volitional fatigue and the spindle waves disappeared immediately when the treadmill was slowed to a walking pace. Visual examination of the EKG showed no low frequency phenomena that could be correlated with the spindle waves in the PPG.

Table 1. Bruce Protocol Stage Descriptions and Distribution of Maximum Stage Reached.

Stage	Time (min)	km/hr	Slope	Number of Subjects
1	0	2.74	10%	
2	3	4.02	12%	
3	6	5.47	14%	
4	9	6.76	16%	2
5	12	8.05	18%	2
6	15	8.85	20%	5
7	18	9.65	22%	2

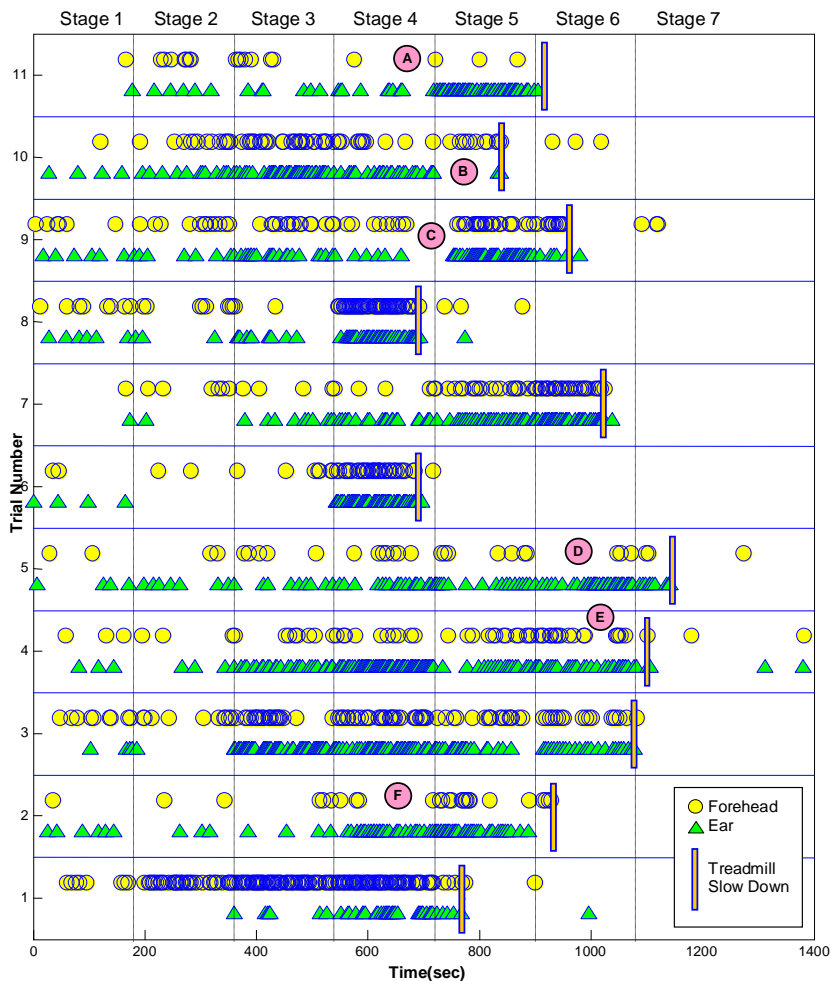


Figure 4. Spindle wave detections in the PPG from forehead and ear pulse oximeters during the stages of the Bruce Protocol stress test. Spindle waves appearance often correlates with the start of stage, and become more frequent in the PPG as the subject become more fatigue, and disappear after cessation of protocol. Annotated gaps in detections are explained in the text.

Gaps in spindle wave detection are marked by letters in Figure 4. In all but one gap, (E), visual inspection shows regular, periodic pinching in the PPG, but the spindle shape is obscured because of motion artifact or other “noise”. Details are as follows:

(A) The entire recording is extremely noisy, possibly due to a weak sensor battery;

(B) (D) (F) The spindle shapes are obscured by motion artifact;

(C) In this subject the ear PPG has oscillations in the baseline of 10 seconds and longer, superimposed on the spindle shapes before and after the start of Stage 5. The finger PPG has no spindle waves before the start of Stage 5, and then noisy spindle waves begin immediately;

(E) In this subject, at the end of Stage 6, the periodic pinching is not significant, and is some what obscured by motion artifact.

Spindle waves did not appear to be an exaggerated *respiratory induced variation*, as the spindle showed no correlation to respiration waveforms collected by impedance pneu-

mography. In all subjects the spindle waves were of a longer period than breathing. For example, the minimum breathing rate for Stage 5, the first stage that requires running, is 28 breaths per minute (brpm) and the maximum is 81 brpm which is consistent with studies done with long-distance runners [13]. As shown in Figure 1, Subject 6, during Stage 6, shows a respiration of 80 breaths per minute while there are only 11 and 12 spindle waves per minute.

All subjects showed correlation between the spindle waves of the ear and forehead PPG. However, at times the two PPGs had distinctly different patterns of spindle waves, as seen in Figure 2. In this example, Subject 11 during Stage 5 shows low amplitude spindle waves in the forehead PPG with the same phase and period as the spindle waves in the ear PPG, but the forehead PPG has a superimposed train of large amplitude spindles not present in the ear.

As seen in Figure 5, the number of spindle waves per minute increased with fatigue except for Subjects 3 and 10. Subject 3 during Stages 5 and 6 had well formed spindle waves, but since their periods lengthened, fewer occurred. Subject 10 had fewer spindle waves during Stage 4 and 5 because of motion artifact in the ear PPG, while the forehead spindle waves become longer, with a period of up to 8 seconds. Additionally, the number of spindle waves detected per minute correlated with the number of cardiac cycles per spindle wave.

The amount of pinching in the PPG waveform caused by the spindle waves increased with fatigue. As shown in Figure 6, as volitional fatigue approached, the ratio of the smallest to the largest cardiac peaks in a spindle wave decreased and then returned to near unity after the treadmill slowed. When the ear PPG pinches during the final stages of the protocol, it pinches to an amplitude less than the minimum amplitude at the onset of the protocol for ten of eleven subjects

DISCUSSION

Exercise induced stress produces a wide range of systemic and localized physiological responses, including hemodynamic responses similar to circulatory shock and myocardial ischemia [6]. Additionally, exercise has been shown to induce an inflammatory response similar to that caused by septic and cardiogenic shock, i.e. Systemic Inflammatory Response Syndrome (SIRS).

A diagnosis of SIRS is indicated if two of the following signs occur: (1) temperature exceeds 38°C; (2) heart rate exceeds 90 beats/min; (3) respirations exceed 20 breaths/min; (4) inflammation is present. All these signs occur to some

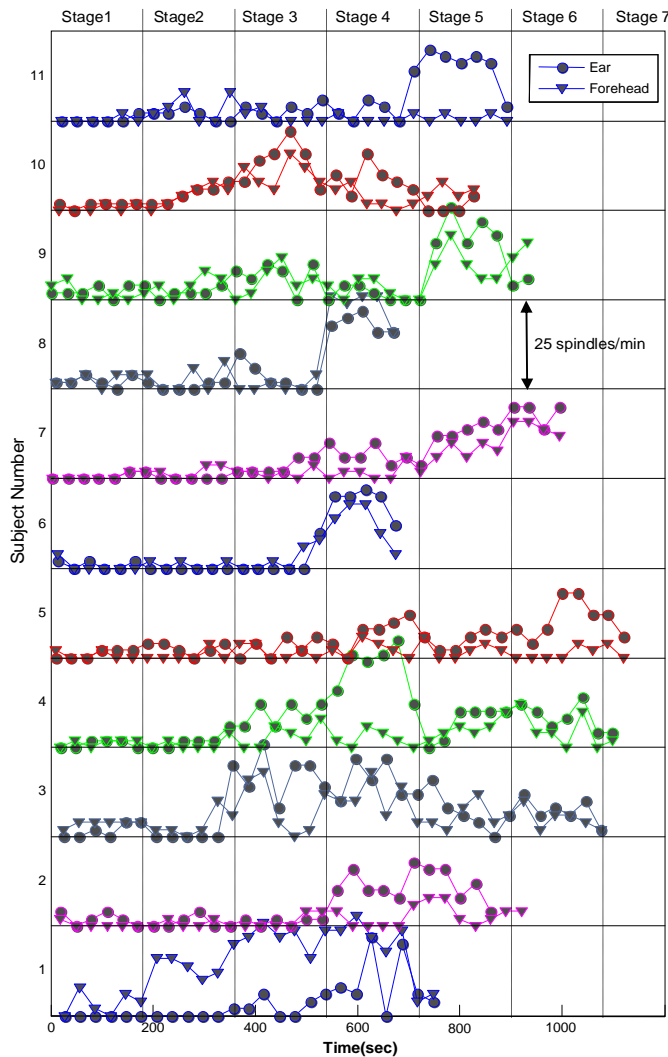


Figure 5. Frequency of well formed spindle waves for the ear and forehead PPG for all 11 subjects.

extent in athletes exercising to volitional fatigue, allowing exercised induced stress to serve as a model for studying SIRS.

A cardiologist examining EKG, blood pressure and cardiac output of a healthy subject approaching volitional fatigue would find markers for SIRS, but no markers for hemodynamic stress [2]. However, our study shows that the forehead and ear PPG had distinct changes in morphology. As with low frequency arterial pressure waves described in other studies, the origin of these spindle waves is debated, but it appears to be related to changing vascular resistance in the arterioles perfusing the dermis of the skin [3]. One hypothesis for the genesis of these spindle waves is that the periodic decrease in the blood flow to the skin, causing a pinching in the PPG, is a mechanism to increase blood flow to other organs.

Studies of exercise at different ambient temperatures show that at warmer temperatures an individual's cardiac output increases to compensate for the increased blood flow to the skin. The up to seven fold increase in skin blood flow can consume as much as 60% of the cardiac output [5, 21].

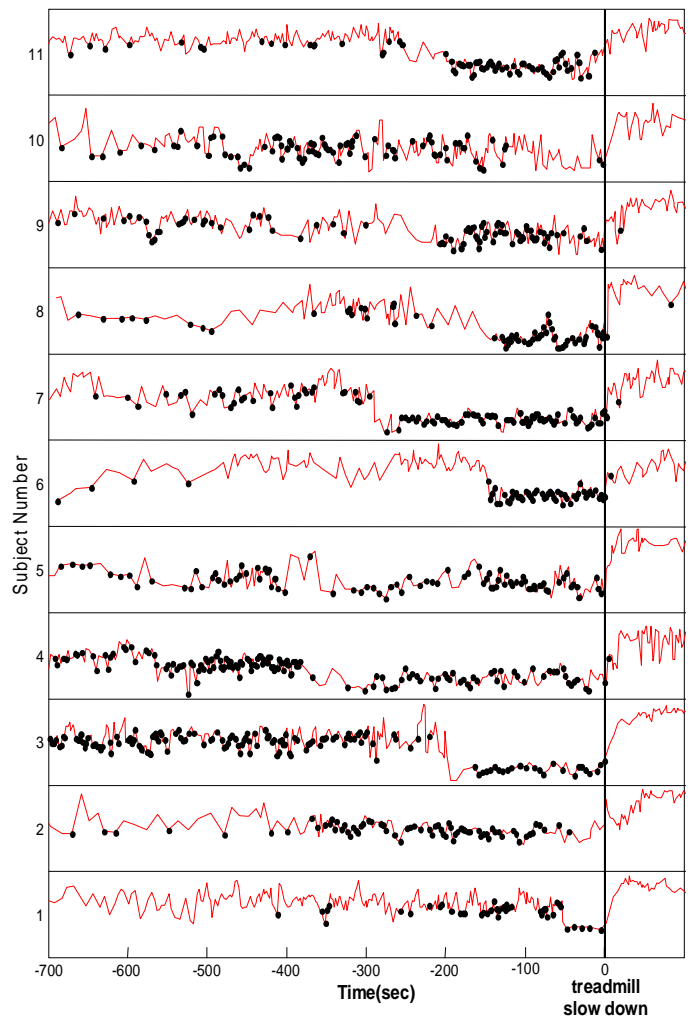


Figure 6. The ratio of the minimum to maximum cardiac peak amplitude for each candidate spindle wave in the ear PPG envelope for each subjects. All subjects shows spindle waves which suppressed amplitude before volitional fatigue, and un-suppressed amplitude after treadmill slow down. Black dots show the location of the well formed spindle waves: smooth and symmetrical envelope, with no significant motion artifacts. Data is aligned so the treadmill slow down occurs at 0 sec.

With the cessation of exercise, a greater portion of the cardiac output is available for thermo regulation, increasing the perfusion of the forehead, as seen in Figure 3 [21].

Normally the baroreflex maintains cerebral perfusion by increasing the heart rate and constricting the periphery. Because exercise increases vascular conductance in the muscles, and because the blood supply to the viscera has already been suppressed [28], shunting blood from the skin may be the only way to increase the cranial and muscular blood supply. When individuals are subjected to baroreceptors unloading via blood sequestration using lower-body negative-pressure, skin blood flow is suppressed during exercise. Suppression occurs because of a reduction in vasodilator drive, most likely originating in the central nervous system [18].

This hypothesis is supported by the observation in [8]

that cutaneous blood flow is attenuated at higher exercise intensities and our observation that spindles becomes more pronounced as the skin blood flow to the forehead increases during exercise. Increased PPG amplitude appears not to be the only precursor for spindle waves since they do not appear after treadmill slow-down, when the finger and ear PPG amplitude increases, as see Figure 3.

While changes in the local physiological requirements of the skin might be hypothesized to induce spindle waves it is thought unlikely because the structure of the ear and forehead microvasculature are different. The microvasculature of the forehead contains venous plexuses that are used to radiate heat, while the ear contains arteriovenous anastomoses (as in the hands, feet and lips) that are used to keep the ear warm in the cold [1]. Arteriovenous anastomoses act as low resistant shunts for the capillary bed of the skin. When these shunts are open large volumes of blood can pass through the skin and provide warming to the periphery, but this blood flow provides no nutrients of the skin. This is shown in our results: during the protocol the forehead shows an increase in average blood flow while the ear does not. The forehead microvasculature is part of cooling system that can keep the brain cooler than the core while the human ear is not [1, 4].

Peripheral origins of low frequency oscillations in the blood flow to the forehead have been shown in a study of anesthetized patients during nonpulsatile cardiopulmonary bypass [24]. It is hypothesized that under sympathetic stimulation the oscillations (with periods close to 7 seconds) in the diameter and blood flow of the cutaneous vascular are synchronized. While the capillaries in the forehead normally oscillate without coherence, under low perfusion they oscillate coherently, but not synchronized with mean arterial pressure or blood flow in the finger [24]. These oscillations are perhaps the genesis of the PPG spindle waves, but require further study because they have not been documented in the arteriovenous anastomoses present in the ear.

In summary, automatic spindle wave analysis of forehead and ear PPGs may provide a noninvasive technique for detection of the suppressed peripheral circulation induced by the stress of exercise or circulatory shock.

Limitations

The subjects in this trial were physically active individuals. Because endurance trained individuals have higher cutaneous blood flow than untrained individuals, further experiments need to be done with an untrained population [8]. A more diverse population of subjects will be need to be studied to determine if the presence of spindle waves can be used reliably to trigger an intervention before the onset of fatigue or shock.

Additional study would lead to a better understanding of the physiological genesis of spindle waves. Studying pharmacologically-induced stress would eliminate the complicating factors of physical and respiratory motion and help determine if spindles occur without exercise. Also study is required to ascertain the significance of the changing period of the spindle waves. While in most subjects the period decreased with fatigue, in some subjects the period increased,

especially after the start of a new stage, with periods of up to 15 seconds observed.

The Nonin pulse oximeters used in this study came with auto-zeroing software that made it impossible to monitor changes in the baseline of the PPG. While the forehead PPG appears to have few baseline shifts, the ear PPG often contains artifacts indicative of a slowly varying baseline. While this filtering has minimal impact on the cardiac peak height, further study needs to be done with a sensor that does not auto-zero. Additionally, future studies should use a better sensor for respiration to conclusively characterize the effect of breathing on the PPG.

The respiratory rate calculated from the impedance pneumograph seems higher than some clinicians would expect and should be verified by other methods. Future studies will employ a more robust method, such as the detection of exhaled CO₂.

Our spindle wave detector was developed to detect individual spindle waves. A more sophisticated version of the detector would detect trains of waves, providing greater sensitivity with a lower false alarm rate.

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