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Power Spectral Density Analysis of Electrodermal Activity for Sympathetic Function Assessment

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Abstract—Time-domain features of electrodermal activity (EDA), the measurable changes in conductance at the skin surface, are typically used to assess overall activation of the sympathetic system. These time domain features, the skin conductance level (SCL) and the nonspecific skin conductance responses (NS.SCRs), are consistently elevated with sympathetic nervous arousal, but highly variable between subjects. A novel frequency-domain approach to quantify sympathetic function using the power spectral density (PSD) of EDA is proposed. This analysis was used to examine if some of the induced stimuli invoke the sympathetic nervous system's dynamics which can be discernible as a large spectral peak, conjectured to be present in the low frequency band. The resulting indices were compared to the power of low-frequency components of heart rate variability (HRVLF) time series, as well as to time-domain features of EDA. Twelve healthy subjects were subjected to orthostatic, physical and cognitive stress, to test these techniques. We found that the increase in the spectral powers of the EDA was largely confined to 0.045–0.15 Hz, which is in the prescribed band for HRVLF. These low frequency components are known to be, in part, influenced by the sympathetic nervous dynamics. However, we found an additional 5–10% of the spectral power in the frequency range of 0.15–0.25 Hz with all three stimuli. Thus, dynamics of the normalized sympathetic component of the EDA, termed $EDASymp_n$, are represented in the frequency band 0.045–0.25 Hz; only a small amount of spectral power is present in frequencies higher than 0.25 Hz. Our results showed that the time-domain indices (the SCL and NS.SCRs), and $EDASymp_n$, exhibited significant increases under orthostatic, physical, and cognitive stress. However, $EDASymp_n$ was more responsive than the SCL and NS.SCRs to the cold pressor stimulus, while the latter two were more sensitive to the postural and Stroop tests. Additionally, $EDASymp_n$ exhibited an acceptable degree of consistency and a lower coefficient of variation compared to the time-domain features. Therefore, PSD analysis of EDA is a promising technique for sympathetic function assessment.

Keywords—Electrodermal activity, Sympathetic function, Autonomic nervous system, Power spectral density, Postural stimulation, Cold pressor, Stroop test.

ABBREVIATIONS

$EDASymp_n$	Normalized electrodermal activity index of sympathetic nervous system
HRVLF	Low frequency component of heart rate variability
NS. SCR	Non-specific skin conductance response
PSD	Power spectral density
SCL	Skin conductance level

INTRODUCTION

Assessment of the changes in the dynamics of sympathetic tone with certain diseases and pathophysiological conditions is one of the major fields in cardiovascular research, as it has been demonstrated to have important prognostic and diagnostic value.[9,22] In many cardiovascular diseases, sympathetic control impairment participates either in the development or in the progression of the pathological process.[2,3,17,38] In cardiovascular autonomic neuropathy, for instance, sympathetic denervation is a marker of the progress of the disease from early to severe stages.[18,29]

A noninvasive and quantitative way to assess the dynamics of the autonomic nervous system (ANS) is to

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compute the power spectral density (PSD) of heart rate variability (HRV).[25] Postural changes have been used to elicit sympathetic and parasympathetic nervous system dynamics and their frequencies were determined *via* the PSD. The high-frequency (HF) components of HRV are known to be solely influenced by the parasympathetic system. In contrast, the low-frequency components (LF, 0.045–0.15 Hz), termed HRVLF, are influenced by both the sympathetic and parasympathetic nervous systems. Hence, the LF/HF ratio, which has been used to assess the sympathetic and parasympathetic balance, has not been fully accepted as an accurate measure of the ANS balance since the LF band also contains parasympathetic dynamics.

Given the current need to fully elucidate and delineate sympathetic nervous system dynamics using noninvasive means, new instrumentation for and signal processing of electrodermal activity (EDA) have gained some popularity in recent years.[6,10,20] This recent impetus is because EDA is a measure of the changes in electrical conductance of the skin, with strong correlation to sweat production. EDA reflects only activity within the sympathetic branch of the autonomic nervous system because there is no parasympathetic innervation of eccrine sweat glands. EDA measures, as a reflection of autonomic innervation of sweat glands, have been used recently to assess the sympathetic nervous system arousal.[12]

Signal analysis of EDA in response to specific tasks has decomposed the signal into two time-domain measures: skin conductance level (SCL) and skin conductance responses (SCRs).[6] SCL (usually expressed in microsiemens, μS) is a measure related to the slow shifts of EDA, and specifically refers to the level of skin conductance. SCL is typically computed as a mean of several measurements taken during a specific non-stimulation rest period. The skin conductance responses (SCRs) are the rapid transient events contained in the EDA signals. The non-specific SCRs (NS.SCRs) are the number of SCRs in a period of time, and are considered a tonic measure because they occur post-stimuli. The event-related SCRs (ER-SCRs) are those that occur right after the stimulus which can be due to posture change, cold pressor or Stroop test. These ER-SCRs, which last very short periods of time,[15] are not the dynamics of interest to our study since we are mainly interested in tonic stress responses. The post-transient SCRs or the NS.SCRs due to posture, cold pressor or Stroop test, which occur after the ER-SCRs, are the information we are most interested in for this study. NS.SCRs are regularly expressed as the number of responses per minute.[6] A key concern for the SCL and NS.SCRs is that these indices are highly variable between subjects.[11] This is due to the frequent occurrence of a second response before the completion of a given SCR, which can be detected by visual inspection, but its detection is not easy to automate.[6] In addition, periodic shifts in the background SCL (like a DC shift) could be important if they appear to occur in conjunction with specific components of the experiment, and only a visual analysis would reveal the difference between a SCR and unimportant drift factors (artifacts).[7] Furthermore, obtaining NS.SCRs requires an observer to count SCRs but this could be problematic if there are motion artifacts during EDA measurements. These circumstances necessitate a trained observer to compute NS.SCRs, thereby limiting the full potential of the usefulness of EDA. Moreover, it has not yet been established whether or not dynamics of the sympathetic tone measured from EDA can be used as a surrogate for HRV's derived LF response. This would require EDA analysis similar to HRV analysis using the PSD. The response to stress of the spectral components of EDA signals has rarely been examined. To the best of our knowledge, only one study has explored the matter. This study found elevation of power within the 0.03–0.5 Hz band in response to increased mental workload.[43]

Thus, the aim of this work is to examine if a similar association of LF components of HRV to sympathetic function also exists with the sudomotor function as measured by EDA. Specifically, we are interested in examining if EDA analysis yields similar frequency dynamics at the HRV's prescribed LF range of 0.045–0.15 Hz. If such relation occurs, we can overcome the main disadvantage of LF domain analysis of HRV because EDA is not influenced by the parasympathetic branch of the autonomic nervous system, and we could provide a better quantitative evaluation of sympathetic tone. To test our aim, we determined the EDA differences between baseline conditions and three maneuvers to elicit sympathetic activation: postural stimulation, cold pressor test, and Stroop test. These tests were selected because they are among the stimuli that most efficiently release sympathetic neurotransmitters,[37] and they cover three relevant types of stressors (i.e., orthostatic, physical and cognitive).

MATERIALS AND METHODS

Protocol

Twelve healthy volunteers (ten males, two female) of ages ranging from 19 to 36 years old (26.2 ± 6.14; mean ± SD), weight 64.63 ± 7.01 kg, and height 171.45 ± 9.64 cm, were enrolled in this study. No gender-related differences have been reported for EDA or sympathetic function. To induce a wide variety of sympathetic arousal types, subjects underwent three

tests: postural stimulation (orthostatic stress), cold pressor (physical stress) and Stroop task (cognitive stress).

Before any test, subjects were asked to stay in the supine position for at least 5 min to ensure hemodynamic stabilization, before the start of data recording. Postural stimulation tests consisted of 5 min in the supine position (baseline) followed by 5 min standing. Similarly, the cold-pressor test included 5 min of baseline with the subjects supine; then the subjects were asked to immerse their left hand to the wrist level into a 0–1 °C water bath for a period of 3 min. For Stroop tests, 5 min of baseline were also recorded with subjects relaxing in the supine position. Then, subjects were asked to speak a word which named a color. They were shown a congruent visualization (the word was written in the color it expressed) and an incongruent visualization (the word and the color it was printed in were different) to induce cognitive stress.[44] The words and colors were "blue," "yellow," "green," "red," "purple," and "black." The background also changed to be randomly congruently or incongruently colored with the word. A computerized version of the original Stroop task was developed in our lab using customized software. The Stroop task was 5 min total, and the first minute was used for training.

Participants were asked to avoid caffeine and alcohol for 24 h preceding the test, and instructed to fast for at least 3 h before testing. The experiments were carried out in a quiet, dimly lit room (ambient temperature 26–27 °C), in order to avoid other stimuli. The study protocol was approved by the Institutional Review Board of The University of Connecticut and all volunteers consented to be subjects for the experiment. ECG and EDA signals were simultaneously recorded throughout all tests. An HP 78354A (Hewlett-Packard, FDA approved) and a GSR amplifier FE116 (fully isolated AC excitation and automatic zeroing low voltage amplifier, 22 mV_{rms} @75 Hz, ADINSTRUMENTS) were used to collect ECG and EDA, respectively. No on-line filtering was applied during the signal recording. ECG electrodes were placed following the recommendation to acquire Lead I, and EDA electrodes were placed on the index and middle fingers for all subjects. Skin was prepared with alcohol before placing the electrodes. Signals were digitized using a PowerLab system at 400 Hz, 12 bits resolution.

Signal Processing

Figure 1 shows heart rate and EDA signals for 2 min of baseline and the corresponding three tests (postural, cold pressor and Stroop) for a given subject. Negative values in EDA signals refer to a reduction of the skin conductance with respect to the level at the beginning of the test, when the calibration was performed (zeroing of the signal). Note that HR and EDA differences between the baseline and each of the test cases are pronounced. Figure 2 delineates the signal processing procedures used to compute the set of HRV and EDA indices used in this study. The HRVLF power (and normalized power, HRVLFn), SCL, NS.SCRs, and the PSD of high-pass filtered data of EDA were computed in order to quantify the elicited changes of the sympathetic nervous system due to postural stimulation and the cold pressor and Stroop tests.

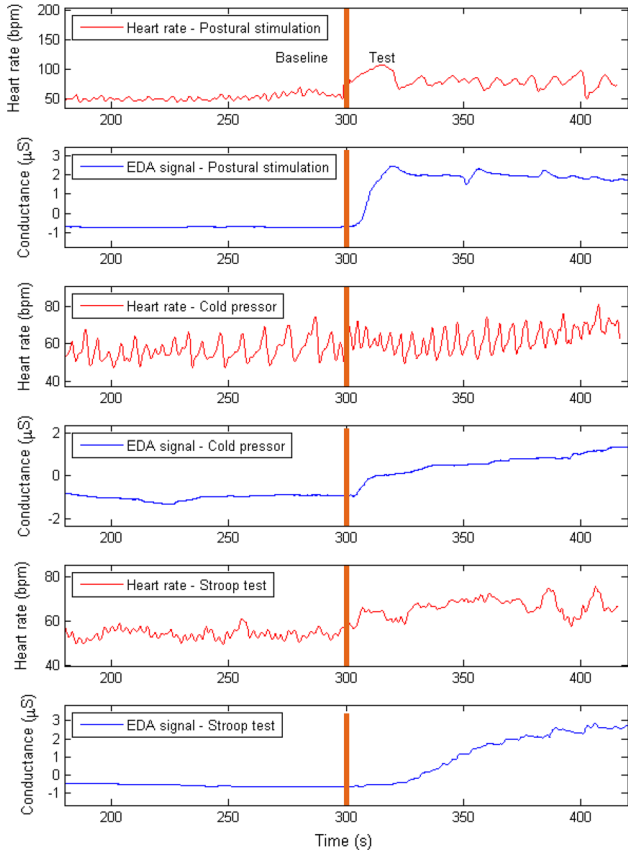

FIGURE 1. ECG and EDA signals for a given subject, undergoing postural stimulation (top), cold pressor test (middle) and Stroop test (bottom).

Heart Rate Variability Indices

For HRV analysis, ECG signals were band-pass filtered (0.05–40 Hz) to reduce noise and motion artifacts. The R-waveform peaks were detected using the detection algorithm that defines a delineation function based on the envelope of the ECG signal.[33,45] All the segments were visually inspected to ensure that no beat was missed. After accounting for the missed R-wave beats, the HR time series were computed. The power

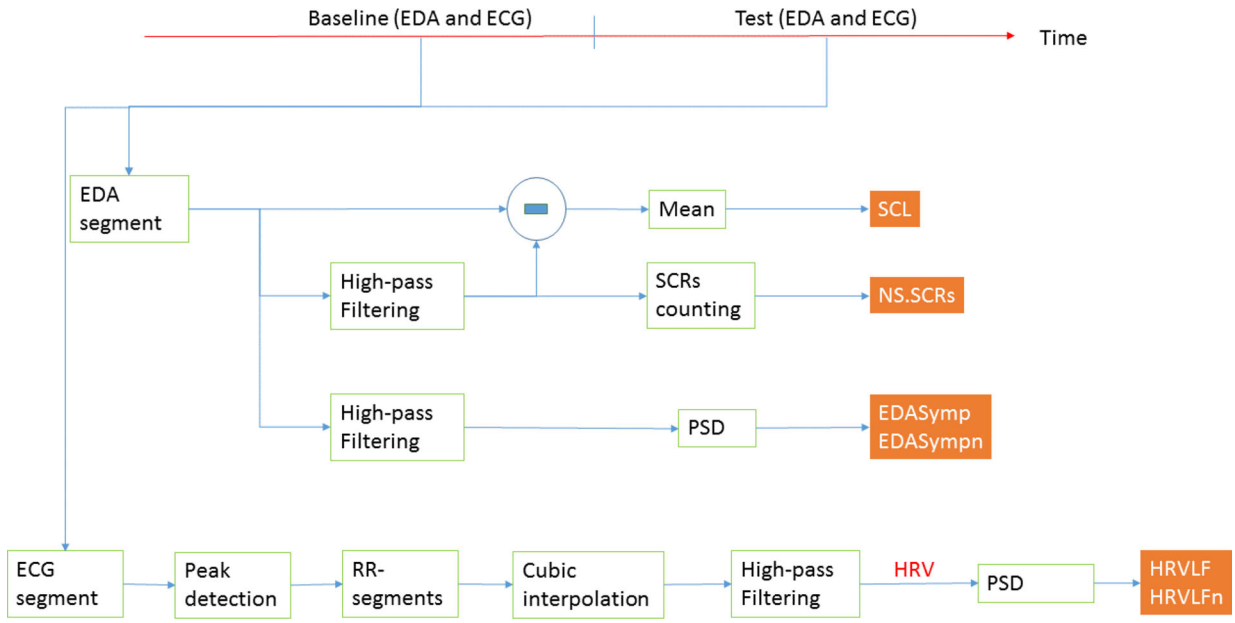

FIGURE 2. Signal processing procedures to compute HRV and EDA indices.

spectra of HRV were then calculated using Welch's periodogram method with 50% data overlap. The RR interval series were converted to an evenly time-sampled signal (4 Hz) by cubic spline interpolation. A Blackman window (length of 256 points) was applied to each segment and the Fast Fourier Transform was calculated for each windowed segment. Finally, the power spectra of the segments were averaged. The low-frequency index [HRVLF (ms^2), 0.045–0.15 Hz][25] and normalized LF [HRVLFn = (HRVLF)/Total power, normalized units (n.u.)] were computed. Four minutes of clean ECG signals were used to compute HRV for postural stimulation and the Stroop test, and 3 min for the cold pressor test as most subjects could not withstand the cold temperature for 4 min. For each test, the same data length was used consistently for baseline and test segments.

Time-Domain Indices of Electrodermal Activity

Two minutes of baseline EDA and 2 min of test EDA were selected for each test. Figures 2 and 3 illustrates the process of computing SCL and NS.SCRs. Baseline signals were always the 2 min prior to the subject performing a test. For the postural stimulation test, the 2-min EDA test signal was extracted starting from 30 s after the subject stood up, to avoid the motion artifacts during the movement process. For the cold pressor test, the first minute was avoided because the maximal discomfort occurs during this time. The subsequent 2 min were used as the test EDA signals. For the Stroop test, the 2-min segments were extracted after discarding the first minute of data after the training period.

To extract the tonic component of the EDA signals (SCL), a 10th-order low-pass finite impulse response filter with a cut-off frequency of 0.0004 Hz was applied. The remaining signal (raw signal minus tonic component, see Fig. 2) was used to compute the NS.SCRs. The SCL index was computed using the mean of the tonic EDA over the 2-min period. NS.SCRs were obtained manually for each minute and then averaged over the 2-min period. It is important to note that for defining a non-negligible occurrence of NS.SCRs, a minimum change in conductance needs to be considered. A recommended threshold value of 0.05 μS was used.[6] In addition, when a second response occurred before completion of the prior response, the two responses were counted as two positive NS.SCRs even though they overlapped.

Power Spectral Density Analysis of Electrodermal Activity

For frequency-domain analysis, EDA signals were down-sampled to 2 Hz. Before down-sampling, the data was filtered with an 8th-order Chebyshev Type I low-pass filter (0.8 Hz). Down-sampling from 400 to 2 Hz was performed in two steps (using consecutive down-sampling factors of 1/20 and 1/10, respectively). Finally, signals were high-pass filtered (0.01 Hz, Butterworth, 8th order) to remove any trend. The power

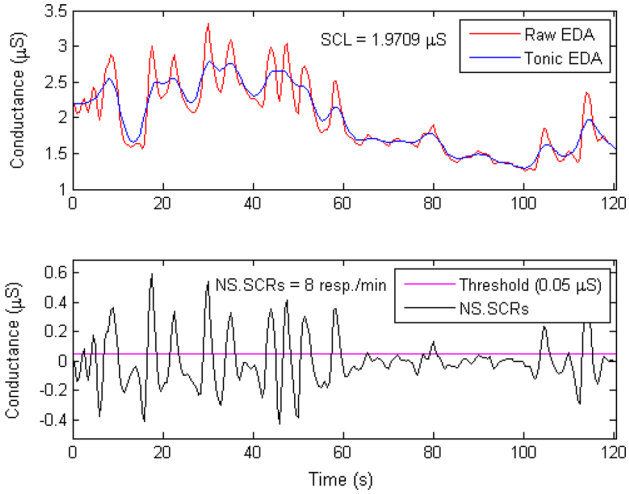

FIGURE 3. Measures of tonic EDA. SCL (μS) is measured as the mean of tonic EDA (top). The NS.SCRs (responses per minute) are extracted by removing the tonic EDA components from the EDA; a threshold is fixed in order to determine which NS.SCRs will be considered as a positive response (bottom).

spectra of EDA signals were calculated using Welch's periodogram method with 50% data overlap. A Blackman window (length of 128 points) was applied to each segment, the Fast Fourier Transform was calculated for each windowed segment, and the power spectra of the segments were averaged. Note that the down-sampling frequency for EDA was half of the sampling frequency for HRV. This down-sampling frequency (2 Hz) is sufficient given that the dynamics of the EDA spectrum are largely confined to frequencies less than 0.4 Hz as observed in this work and as reported.[43] Total power [μS^2] and the power within the frequency bands of interest (VLF = 0–0.045 Hz, LF = 0.045–0.15 Hz, HF1 = 0.15–0.25 Hz, HF2 = 0.25–0.4 Hz and VHF = 0.4–0.5 Hz) were computed. After determining the frequency range for sympathetic assessment, EDASymp and EDASymp_n (n.u.) = EDASymp/(total power) were computed.

Statistics

The full set of indices is HRVLF, HRVLFn, SCL, NS.SCRs, EDA-Total power, EDASymp and EDASymp_n. First, the paired t test was applied to test the null hypothesis that elicited responses as measured by each of the above-defined indices are equal to the baseline values. These results are useful to evaluate the suitability of the indices to quantitatively assess the sympathetic function on healthy subjects, for the types of stress induced in the present study.

Time- and frequency-domain indices of EDA (SCL, NS.SCRs and EDASymp_n) were further compared using a detection theory for which summary statistics are provided, including the maximum Youden's index (J = Sensitivity + Specificity − 1, a measure of the performance of the detector), the area under the ROC curve (AUC, the probability that the index will assign to a positive instance a higher value than to a negative one), and the maximum accuracy of the given index used as detector. This analysis allows us to test the ability of these indices to correctly identify the presence of the stressors.

In order to assess inter-subject variability and degree of consistency of each index, the coefficient of variation (CV) (i.e., the standard deviation between all the measurements divided by the mean) and the intra-class correlation (ICC) were computed for the SCL, NS.SCRs and EDASymp_n indices, respectively. ICC has been computed as defined in the literature,[30] for the $N = 12$ independent subjects, using the six available measures (three tests, baseline and test measure).

RESULTS

Figure 4 shows the NS.SCRs throughout the experiment (during postural stimulation, cold pressor and Stroop tests), for a given subject. Note that during baseline periods, there were no positive NS.SCRs for this subject, for any test. Some subjects exhibited a few NS.SCRs in the supine position but this was a rare occurrence. All subjects consistently produced more NS.SCRs when performing the tests than during the baseline for all three tests.

The power spectra of the HRV series and the EDA signal for a given subject are included in Figs. 5 and 6. Note that for both, this subject exhibits marked differences between baselines and each of the three induced tests. As expected, HRV power spectra show frequency components above 0.15 Hz. These components are known to be related to parasympathetic function. For EDA spectra, spectral power beyond 0.25 Hz is minimal at best for all three induced stimuli.

To quantitatively assess the dynamic frequency ranges of the EDA, we computed the percentage of energy within the five frequency bands as shown in Table 1. For HRV, the HF was computed from the standard frequency band of 0.15–0.4 Hz. As shown in Table 1, the VLF power is consistently high for EDA for all three baseline and test stimuli conditions. The largest increase in EDA spectral power was found in the LF, post-stimuli, for all three test conditions. With stimuli, the EDA's HF1 (0.15–0.25 Hz) and HF2 (0.25–0.4 Hz) contain 5–10 and 1–4%, respectively, of the total spectral power, and the VHF of EDA contains less than at most 2% of the total spectral power. Given that HF1 comprises 5–10% of the power associated with the sympathetic dynamics, and as 95% of

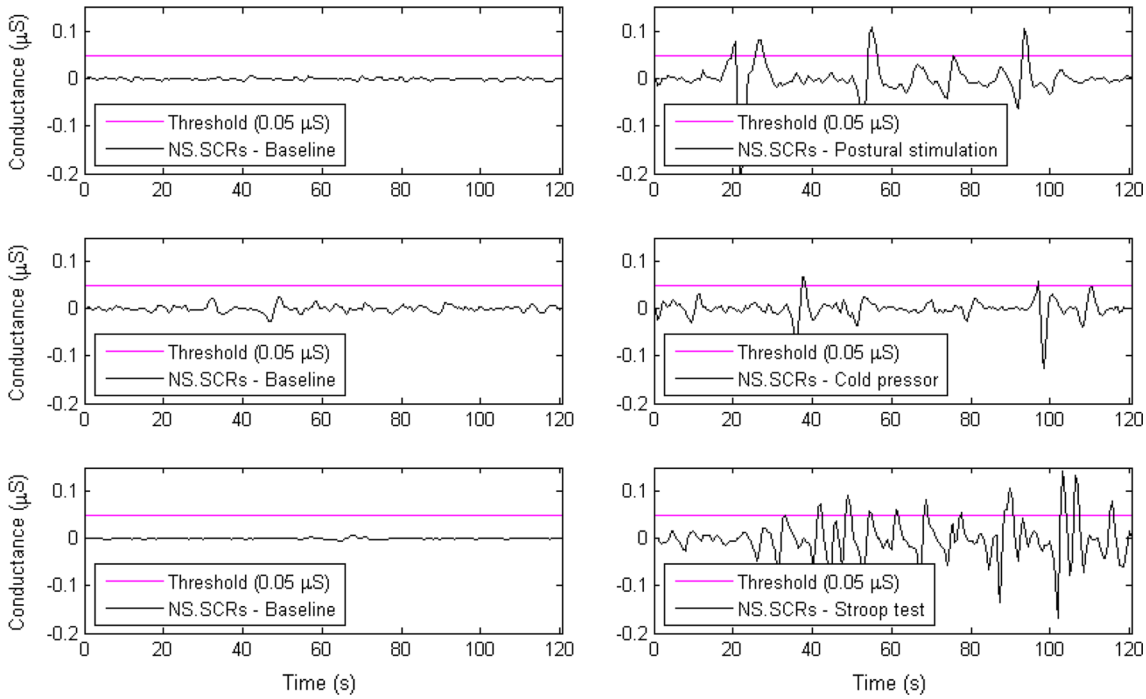

FIGURE 4. NS.SCRS for a given subject during baseline (left) and test (right), for postural stimulation, cold pressor and Stroop test.

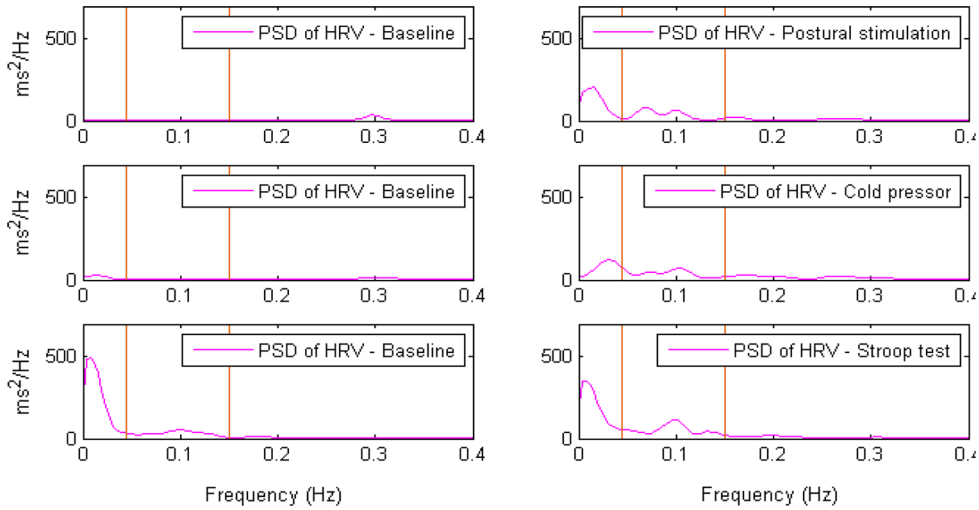

FIGURE 5. Power spectra of HRV for a given subject during baseline (left) and test (right), for postural stimulation, cold pressor and Stroop test. Lines denote 0.045 and 0.15 Hz.

the total spectral power of EDA is accounted for by including VLF, LF and HF1, the frequency range relevant to the sympathetic component of the EDA (EDASymp) can be defined to be in the range of 0.045–0.25 Hz. This excludes VLF because, as shown in Table 1, its power decreases with stress induction. Henceforth, "EDASymp" refers to spectral dynamics in the frequency range of 0.045–.25 Hz.

Table 2 incorporates the mean time- and frequency-domain results for all subjects. The postural stimulation test (orthostatic stress) produced significant increases in HRVLF, HRVLFn, SCL, NS.SCRs and $EDASymp_n$ indices. Total EDA and EDASymp were not found to be statistically different under this test. The cold pressor test (physical stress) elicited differences in the SCL, NS.SCRs and $EDASymp_n$. Note that these three indices were found to be statistically different than under postural stimulation. However, HRV indices were not significantly different during this test. Total EDA and EDASymp were not found to

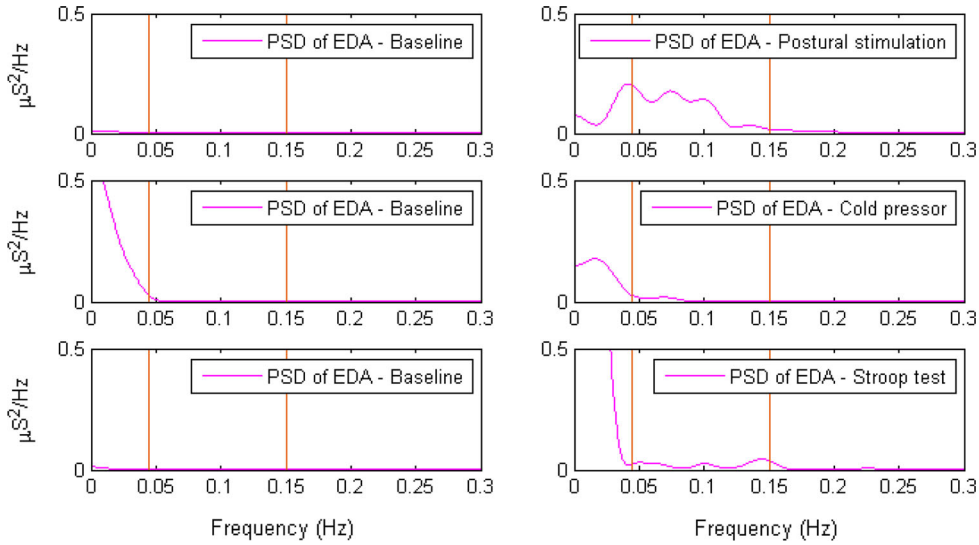

FIGURE 6. Power spectra of EDA for a given subject during baseline (left) and test (right), for postural stimulation, cold pressor and Stroop test. Lines denote 0.045 and 0.15 Hz.

TABLE 1. Percentage of energy within the frequency bands for EDA and HRV.

	Postural stimulation		Cold pressor		Stroop test	
	Baseline (%)	Test (%)	Baseline (%)	Test (%)	Baseline (%)	Test (%)
EDA						
VLF (0–0.045 Hz)	86.2	65	79.2	51.2	87.3	51.6
LF (0.045–0.15 Hz)	11.6	28.5	14.6	31.7	8.07	32.9
HF1 (0.15–0.25 Hz)	1.24	4.67	3.7	10.9	2.07	10.7
HF2 (0.25–0.4 Hz)	0.36	1.3	1.35	4.44	1.44	3.77
VHF (0.4–0.5 Hz)	0.19	0.25	0.86	1.72	0.7	0.96
HRV						
VLF (0–0.045 Hz)	36.8	36	29.2	34.8	27.8	29.6
LF (0.045–0.15 Hz)	23.5	51.4	32.1	27	36.6	39.2
HF (0.15–0.4 Hz)	36.5	10.9	35.6	34.4	32.8	25.9
VHF (0.4–1 Hz)	2.17	0.93	2.53	2.91	2.33	4.63

Values represent percentage of power considering all the subjects together.
HRV heart rate variability, *EDA* electrodermal activity, *VLF* power of very low-frequency components, *LF* power of low-frequency components, *HF* is power of high-frequency components, *VHF* power of very high-frequency components.

be statistically different either. The stroop task test (cognitive stress) induced differences in HRVLF, SCL, NS.SCRs, total EDA, EDASymp and EDASymp$_n$. In other words, while low-frequency components of HRV (HRVLF) were sensitive to orthostatic and cognitive stress, normalized HRVLF (HRVLFn) was different only under orthostatic stress. The SCL and NS.SCRs always exhibited statistically-significant differences under any kind of stress tested in this study. EDASymp and total power of EDA were significantly increased by only cognitive stress, and normalized low-frequency components of EDA were sensitive to all three types of stress. This suggests that the normalized low-frequency components of EDA and the time domain SCL and NS.SCRs are the most sensitive markers for differentiating changes induced by stressors.

We used a detection theory and receiver operating characteristic (ROC) curves to test the ability of the different indices to correctly identify the presence of the stressors (orthostatic, physical or cognitive) when compared to their baseline conditions. Table 3 shows the maximum Youden's index, the area under the ROC curve, and the highest possible accuracy for each index used as a detector. EDASymp$_n$ had better results than SCL and NS.SCRs for these three measures for the cold pressor test. However, for both orthostatic and Stroop stimuli, the NS.SCRs provided the best results for the Youden's index, AUC, and the accuracy values.

The high variability of EDA measurements has been a concern among researchers, impeding the widespread use of these indices for assessing the general state of activation of the sympathetic system. Table 3 shows

TABLE 2. Sympathetic function indices.

	Postural stimulation		Cold pressor		Stroop task	
	Baseline	Test	Baseline	Test	Baseline	Test
HRV indices						
HRVLF (ms^2)	4.8 ± 5.98	27.67 ± 31.45*	7.14 ± 6.396	4.77 ± 3.27	4.18 ± 3.36	6.11 ± 4.44*
HRVLFn (n.u.)	0.24 ± 0.06	0.54 ± 0.17*	0.33 ± 0.13	0.27 ± 0.14	0.35 ± 0.13	0.39 ± 0.08
Time-domain indices of EDA						
SCL (μS)	4.14 ± 8.11	10.79 ± 7.47*	0.77 ± 4.68	4.47 ± 7.50*	−1.28 ± 3.92	6.31 ± 4.01*
NS.SCRs (#/min)	1.83 ± 2.03	6.00 ± 2.86*	2.67 ± 2.9	4.958 ± 4.53*	0.96 ± 1.5	9.75 ± 3.89*
Frequency-domain indices of EDA						
Total EDA (μS^2)	1.71 ± 4.49	0.50 ± 0.46	0.11 ± 0.19	0.24 ± 0.42	0.019 ± 0.036	0.46 ± 0.45*
EDASymp (μS^2)	0.82 ± 2.48	0.28 ± 0.31	0.028 ± 0.056	0.15 ± 0.28	0.008 ± 0.016	0.198 ± 0.25*
$EDASymp_n$ (n.u.)	0.29 ± 0.17	0.47 ± 0.22*	0.23 ± 0.158	0.42 ± 0.20*	0.28 ± 0.20	0.48 ± 0.18*

Values are expressed as mean ± standard deviation.
HRV heart rate variability, *LF* power of low-frequency components, LFn is normalized power of low-frequency components, *SCL* skin conductance level, *NS.SCRs* non-specific skin conductance responses, *EDASymp*, $EDASymp_n$ non-normalized and normalized power spectra, respectively, in the frequency band between 0.045 and 0.25 Hz.
* Statistically significantly higher with respect to baseline ($p < 0.05$).

TABLE 3. Statistics of EDA indices.

	Postural stimulation			Cold pressor			Stroop task				
	J	AUC	Acc	*J*	AUC	Acc	*J*	AUC	Acc	Average CV	ICC (LB UB)
SCL	0.58	0.69	0.79	0.50	0.66	0.75	0.83	0.85	0.92	1.32	0.88 (0.68 0.98)
NS.SCRs	0.83	0.87	0.92	0.33	0.61	0.67	0.92	0.92	0.96	0.93	0.93 (0.79 0.99)
$EDASymp_n$	0.5	0.6	0.75	0.7	0.78	0.85	0.5	0.71	0.75	0.55	0.82 (0.48 0.97)

EDA electrodermal activity, *SCL* skin conductance level, *NS.SCRs* non-specific skin conductance responses, $EDASymp_n$ indicates the normalized spectral power in the frequency band between 0.045 and 0.25 Hz, *J* Youden's index, *AUC* area under the ROC curve, *Acc* is accuracy, *CV* is coefficient of variation, *ICC* iIntra-class correlation, and *LB*, *UB* upper and lower bounds of the ICC with a level of significance of 0.05.

the coefficient of variation (CV) and intra-class correlation (ICC) for SCL, NS.SCRs and $EDASymp_n$. The total average of CV for the given index is also shown. Although the NS.SCRs showed lower variability than did SCL, both SCL and NS.SCRs exhibited higher variability compared to $EDASymp_n$ for all stimuli. Finally, ICC was higher for the SCL and NS.SCRs, which suggests that these indices are more consistent than $EDASymp_n$.

DISCUSSION

The main goal of this work was to determine the dynamic frequency response characteristics of EDA through the use of power spectral density. Specifically, the intent was to systematically determine the frequency band limits of the sympathetic nervous activities derived from the EDA signal. Moreover, we were interested in examining the hypothesis that if EDA does represent the dynamics of the cardiac and peripheral sympathetic nervous systems, the spectral power should be largely present in the low frequency band (0.04–0.15 Hz). Indeed, this was the case, as we found that most of the significant increase in the spectral power is confined in the low frequency band for all three test stimuli and this observation is in agreement with the LF band derived from HRV which contains the dynamics of the cardiac sympathetic nervous system. To account for the additional 5–10% of spectral power largely seen in the HF band with induction of stimuli, we determined that the frequency response of the sympathetic activities represented in the EDA signal can be defined to be within 0.045–0.25 Hz (EDASymp).

EDA data analysis in either the time or frequency domain consistently provided significantly elevated responses for all test stimuli in this study. However, for HRV, the cold pressor stimulus did not provide significant changes whereas the other two stimuli (posture and Stroop tests) did. The increase of the sympathetic tone with postural stimulation is a consistent finding

when compared to previous studies.[18,47,48] However, the reliability of low-frequency components of HRV for sympathetic assessment is a sustained scientific concern. For example, in the supine position, it has been shown that HRVLF and HRVLFn exhibit poor relative reliability (i.e., high inter-subject variability), and all HRV indices have poor absolute reliability (i.e., high intra-subject variability).[34,39] Another study reported poor reproducibility of HRV measured after an orthostatic challenge in healthy subjects, also suggesting an even poorer reproducibility in a clinical population.[41] EDA has been used to provide a quantitative functional measure of sudomotor activity,[4,16] which is controlled by the sympathetic nervous system.[24,26,42] More recently, EDA has been used as a surrogate measure of the sympathetic activities.[20] However, due to the high variability of the time-domain measures of EDA, which largely consist of the SCL and NS.SCRs, its use has not yet been popularized. Surprisingly, the PSD of EDA, similar to the PSD of HRV, is not yet a widely-adopted measure. With $EDASymp_n$, we found evidence that postural stimulation invokes the central and cardiac sympathetic nervous dynamics.[20] The added benefit of analyzing EDA in the frequency domain is that it can lead to less variability in the features estimated due to the inherent filtering properties of the frequency domain. More importantly, the EDA represents only the sympathetic nervous activities whereas the LF of the HRV exhibits both the parasympathetic in addition to the sympathetic tone. The other main objective of this work was to determine if non-cardiac related sympathetic-inducing stressors such as the cold pressor test could also be assessed *via* EDA analysis, and if their frequency responses are also in the prescribed LF range.

Scant results have been reported about the influence of postural changes on EDA, because EDA measurement has been mainly used in psychophysiological research.[6] However, the SCL and NS.SCRs have shown good correlation with sympathetic arousal.[5,49,50] Note that the SCL and NS.SCRs can also be interpreted as the response of EDA in two different frequency bands, as the SCL comprises the slow changes (low frequency) and NS.SCRs represent rapid shifts (higher frequencies). We also tested the variability of EDA, from which we concluded that frequency-domain components are more reproducible than time-domain measures (number of SCRs and changes in SCL). In this study we found significant differences in SCL and NS.SCRs after postural stimulation when compared to the baseline. We found that the main drawbacks of these indices are their high variability (in the case of SCL) and the need for manual computing (to count NS.SCRs) (Tables 2, 3). It is worth mentioning that there are many studies that have examined automatic ways to count spontaneous SCRs, extract amplitude or other measures of a single causal SCR, and deal with motion artifacts and superposition on the SCRs.[1,4,8,23] There are also publically-available toolboxes for these tasks (pspm.sourceforge.net and www.ledalab.de). While these time-domain methods are reliable, the proposed $EDASymp_n$ does not rely on either manual or automatic SCR detection, which is usually more complex and time consuming. Using PSD analysis on EDA signals, we were able to determine that $EDASymp_n$ was significantly increased in healthy subjects, when they changed their posture from supine to standing. $EDASymp_n$ exhibited lower variability, and can easily be implemented in an automated fashion for sympathetic function assessment under orthostatic stress.

The cold pressor stimulus has been increasingly used in clinical practice to evaluate autonomic function in cardiovascular regulation, because stressful cooling evokes an increase in sympathetic neurotransmissions.[37] The responses of HRV dynamics and EDA to cold stress are also poorly understood. In this study, no significant differences were found in HRVLF and HRVLFn between cold pressor and baseline. The reported results on HRVLF and HRVLFn in response to cold pressor are not congruent. Although some studies reported increases,[35,40] decreases or insignificant changes are reported more often.[13,19,28,32] In this study we found non-significant decreases in HRVLF and HRVLFn.

Previous studies have tested EDA dynamics in response to the cold pressor test.[31,36] Those works found increases in SCL and NS.SCRs in healthy subjects when cold stressor was applied. Consistently with those reports, we found significant differences in NS.SCRs and SCL indices when comparing cold pressor to baseline. Nonetheless, these indices showed higher variability on this test when compared to postural stimulation. Using PSD analysis of EDA signals, we found significant increases in $EDASymp_n$ between cold pressor and baseline, with much less variability when compared to NS.SCRs and SCL.

Significant increases in the low-frequency components of HRV during Stroop tests have been previously reported.[14,21,46] We also found significant differences in HRVLF between Stroop tasks and baseline, but not in HRVLFn. The SCL and NS.SCRs indices were significantly higher during the Stroop test when compared to baseline. Besides the sensitivity of these indices, their variability was also high for this test. In frequency-domain analysis, not only the normalized index ($EDASymp_n$) was significantly increased, but the integral of sympathetic components (EDASymp) also exhibited a significant increase. The effect of the Stroop test on the power

spectrum of EDA was a combined increase in the LF + HF1 (EDASymp) and VLF range, which influence the total power (Table 2).

While the number of subjects enrolled for this study was relatively low, significant differences between baseline and stimuli-induced conditions enabled the opportunity to examine if time- and frequency-domain indices can discriminate between the absence and presence of the specific stressor. We were also interested in further investigating the ability of SCL, NS.SCRs and $EDASymp_n$ indices to discriminate whether the stressors (orthostatic, physical or cognitive) were present when the data were collected. To compare the indices' performance on these task stimuli, the Youden's index (J), the area under the ROC curve (AUC) and the maximum accuracy of the detector (Acc) were computed (Table 3). The $EDASymp_n$ exhibited the best performance in detecting the induced cold pressor stimuli as measured by the Youden's index. However, both SCL and NS.SCRs performed better than $EDASymp_n$ for orthostatic and cognitive stress. It should be noted, however, that the $EDASymp_n$ provided the lowest coefficient of variation values for all three stimuli conditions.

Even though SCL and NS.SCRs have been shown in the literature to be elevated by administration of dextroamphetamine, caffeine, and threatening instructions[5,49,50] (consistent with sympathetic arousal), they are only moderately positively correlated with each other and have relatively low within-subject variability (correlation of test–retest ranges from 0.50 to 0.70) and high variability between subjects.[11] We also found evidence of such high variability in this study, as SCL exhibited a coefficient of variability more than four times larger than the $EDASymp_n$ index. The NS.SCRs also had a higher coefficient of variability. As for the consistency of the indices, although the SCL and NS.SCRs demonstrated a higher degree of consistency (ICC) than $EDASymp_n$ (Table 3), all three indices presented a consistency beyond chance (>0.75).[27]

Because of the high sensitivity to three different types of stimuli and relatively low variability, $EDASymp_n$ can be recognized as a suitable index of sympathetic function during such stressors in healthy individuals. While there are many and varied approaches to directly measure the sympathetic response, due to high cost, or the invasiveness of the technique, or the inability to provide continuous monitoring, or the inaccurate assessment of the sympathetic dynamics, the widespread use of these techniques in practice is not practical.

In summary, the $EDASymp_n$ index is a suitable discriminator of orthostatic, physical and cognitive stress, and has the potential to be used as a reliable marker of quantitative assessment of the sympathetic function. It was found to be more reliable and sensitive than the LF index of HRV, was consistent between the subjects, and exhibited a lower variability compared to the time-domain measures of EDA. Finally, the frequency bands of the sympathetic nervous activities can be defined to be within 0.045-0.25 Hz based on spectral analysis of EDA.

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