Skin Conductance and RR Interval for Regulated Discrete Physiological Stimuli: A Two Prong Strategy to Detect Sympathetic Activation

Nepal O,[1] Manandhar L,[2] Jha RK[1]

[1]Department of Physiology

[2]Human Biology

Kathmandu University School of Medical Sciences

Dhulikhel, Kavre, Nepal.

Corresponding Author

Ojashwi Nepal

Department of Physiology

Kathmandu University School of Medical Sciences

Dhulikhel, Kavre, Nepal.

E-mail: ojan2nep@gmail.com

Citation

Nepal O, Manandhar L, Jha RK. Skin Conductance and RR Interval for Regulated Discrete Physiological Stimuli: A Two Prong Strategy to Detect Sympathetic Activation. *Kathmandu Univ Med J.* 2019;68(4):267-72.

ABSTRACT

Background

Several studies have found skin conductance a good indicator for detection of sympathetic response. But, valid and reliable tool for detection of sympathetic outflow in health and disease is still a quest. Thereby, comparison of superficial and, at core sympathetic effluence induced by deliberately supplied discrete external stimuli has been attempted in this study.

Objective

To assess the degree of sympathetic outflow for discrete cognitive and physical stimuli through perturbations in skin conductance and variations in heart rate in healthy adults.

Method

Quantitative and cross-sectional study was performed in 104 healthy subjects following random sampling method. Induction of sympathetic activity was realized by providing separate time bound cognitive exercises intervened with change in posture. Recordings to detect sympathetic responses at rest and, for supplied stimuli were made by electrocardiogram and galvanic skin response.

Result

Cognitive performance and postural change shifts baseline effluence and increases the sympathetic outflow significantly (p=0.000). There occurs no detectable rise in sympathetic effluence at the core (p=0.362) but, eventuate significantly appreciable sympathetic outflow to sweat glands in skin (p=0.000), when compared cognitive versus physical stimuli.

Conclusion

Sympathetic outflow induced by cognitive challenge and physical change in posture is readily assessable through sympathetic skin response yet core sympathetic effluence for latter stimuli is steady and unwavering. Differential effluence for sympathetic response called upon by discrete stimuli is operational for maintenance of steady state in healthy subjects.

KEY WORDS

Galvanic skin response, Psychogalvanic reflex, Sympathetic outflow

INTRODUCTION

Galvanic skin response (GSR) is easy to measure and has been used as an index for providing measurable parameter to understand a person's autonomic function state. Skin conductance reflects changes in the sympathetic system through sweat glands which are not involved in thermoregulatory activity. Applications of Sympathetic skin response have been tried and tested in clinical neurophysiology. However, the central organization of skin conductance response (SCR) is not completely understood.[1] Nevertheless, GSR has been utilized widespread as non-invasive tool to study stress through sympatho-cholinergic stimulation.[2-4] The waveforms analyzed vary considerably in population thus is complicated to quantify the physiological response yet, has been widely utilized either for diagnosis of diseases along with other lab tests or related pain analysis.[5,6] In our previous study, GSR has been proved to be useful for detection of sympathetic arousal for cognitive load. Now, we wanted to couple the test to one of the vitals i.e. heart rate, to detect the sympathetic arousal, during cognitive and physical tasks. Thus, we provided discrete cognitive and physical stimuli separated in time-intervals, to record sympathetic activation in vivo.

METHODS

It is a quantitative and cross-sectional study. Participants were healthy medical undergraduates, aged between 18-25 years from Kathmandu University, School of Medical Sciences (KUSMS). Subjects with dysautonomia and anhydrosis were excluded based on history. The study site was Department of Physiology at KUSMS where the device is available in the exercise physiology laboratory. Selection was made by allocating the serial numbers after blinding the names of students to their registered roll numbers. First and second year students of medicine and allied health sciences were subjected to the study. Registered roll numbers of students pooled from different streams were shuffled and, the serial number was allocated to the shuffled roll numbers. Students were contacted in the order of the serial number and were explained the procedure before the consent was obtained. Students those who consented were included after matching the inclusion criteria. Study was performed in 104 subjects (44 male and 60 female) from May-Oct, 2017.

Subjects were made to sit on chair by the side of the instrument after 10 minutes of rest. Transducers for measuring GSR and ECG were connected to the instrument. GSR electrodes were wiped with a clean tissue paper and were wrapped around forefinger and middle finger of the non-dominant hand. The electrodes of electrocardiogram (ECG) were then placed in the right wrist, left wrist and right leg to evaluate RR interval. The subject was then instructed to remain calm and silent. The software labchart 7.0 was turned on. For the recording of GSR, zeroing was done by making open circuit zero and subject zero. For the ECG recording, main filter was put on and one minute baseline recording was made. Subjects visualized three or four digits number in colored chart paper for only five seconds and were asked to memorize it. Thereafter, subjects were visualized with a word in colored chart paper for five seconds and were requested to memorize it. The words were selected online at 'http://mentalfloss.com' for words with difficult to remember meanings, which stated these words to be, the most difficult to remember. In the third step of the task, subjects had to subtract list of numbers shown to them in a colored chart paper in 30 seconds. They only had to subtract the number mentally, as fast and correct as they could, within the time limit. They were not to verbally answer the calculated number or to memorize it.

Immediately after the mental subtraction task, the subjects were asked to stand up with minimal disturbance to the attached electrodes. They were to remain stood for thirty seconds without any movement and this step is said to be as 30 seconds physical task.

In the last step of the task, subjects were to answer the number and the word while in sitting posture which was shown to them at the beginning of stimulation procedures, after the baseline recording. Subjects had only ten seconds to recall and answer. This procedure was to test the memory performance and termed as 10 seconds memory task in this study.

Finally, subject was asked to rest for 20 seconds and the recording was termed 20 seconds post task recording. From the baseline to post task recoding, the electrodes as well as the software were closely monitored.

The recordings of GSR have various parameters that can be obtained from waveforms in the software. We analyzed the GSR parameters including the metrics from x-axis and y-axis i.e. amplitude- "Apeak", rise time- "Time to peak", peak wave height- "Height" and "Tmax slope" to confirm the change detection in skin conductance. However, the major parameter utilized across the task is the "peak amplitude" i.e. Apeak in our study. These values were obtained and entered in the excel file, underwent various analysis as per need. The values have been analyzed using SPSS software version 21.0 for windows 10.

The differences between groups have been compared using different t-tests and ANOVA as required. P value ≤ 0.05 has been deemed significant.

RESULTS

Skin conductance for peripheral detection and, RR interval (ECG) for core detection has been utilized. Tasks performed by subjects were distinctively cognitive and physical. Out of 6 steps performed i.e. 5 seconds number, 5 seconds word, 30 seconds mental subtraction, 30 secs physical task, 10

Table 1. Mean of GSR variables and RR interval for tasks performed by 104 respondents.

Tasks		Apeak	Tmax slope	Height	Time to peak	RR interval
1 min baseline	Mean	2.00	1324.80	0.75	2422.64	0.72
	Std. Deviation	3.83	1367.93	0.80	1475.55	0.12
5 sec number	Mean	1.42	89.29	0.51	472.82	0.66
	Std. Deviation	3.47	276.01	1.44	1032.00	0.12
5 sec word	Mean	2.99	226.15	0.84	741.05	0.64
	Std. Deviation	4.90	574.28	1.83	1256.26	0.12
30 sec subtraction	Mean	6.23	1040.80	0.96	2229.13	0.64
	Std. Deviation	5.25	1299.14	1.01	1690.78	0.11
30 sec physical task	Mean	6.21	1956.10	16.01	3122.42	0.66
	Std. Deviation	5.14	2643.82	153.47	3078.84	0.09
10 sec memory	Mean	7.37	891.00	2.10	2419.06	0.69
	Std. Deviation	5.98	1228.42	2.21	1931.96	0.17
20 sec posttask record	Mean	5.97	2070.59	12.64	3672.10	0.75
	Std. Deviation	5.99	3051.40	124.79	3202.15	0.11

secs memory and 20 secs post task recording, initial three steps are categorized as cognitive in origin. Mean values of the GSR parameters i.e. Apeak, Tmax slope, Height, Time to peak and RR interval in ECG recording from all the provided tasks, including baseline was subjected to one-way ANOVA (Analysis of variance). Mean and standard deviation for all tasks performed is depicted in table 1.

Table 2. Significance for mean of parameters obtained during sympathetic activation in all respondents.

Parameters	p value	Mean
Apeak	0.000*	4.21*
Tmax slope	0.000*	828.09*
Height	0.566	4.58
Time to peak	0.000*	1641.36*
RR interval	0.000*	0.65*

The GSR variables and RR interval recorded was analyzed during sympathetic activation tasks. ANOVA for GSR parameter "Height" is seen insignificant (p=0.566) whereas other parameters are seen to rise significantly and RR interval is observed to be decreased significantly as shown in table 2. To compare "Apeak" and "RR interval" among all subjects during sympathetic stimulation tasks, mean of Apeak from both male and female was obtained during each task. Thereafter, these values were compared task-wise for both the genders. Similarly, mean of values from RR interval of both male and female during different tasks was obtained and compared with other tasks. The values were separated according to the different tasks along with the baseline and, ANOVA test was performed. In the result obtained, P value for Apeak was found to be 0.000 and RR interval was 0.000 depicted in table 2.

Hence, it was evident that significant rise in the values takes place in GSR parameter during sympathetic activation tasks, when the subjects are given physical and cognitive stimuli. Analysis of core sympathetic activation by RR interval (heart rate) showed significant decrease in values i.e. rise in heart rate.

For inter-gender analysis of sympathetic activation by comparing 7 different tasks, the mean for Apeak and RR interval in a specific task for both gender, was calculated. The mean obtained for 44 male subjects and mean obtained for 60 female subjects in the same particular task was compared using ANOVA. The significance obtained are shown in table 3.

Table 3. Significance compared for Apeak and RR interval between genders during different stimulating tasks.

Tasks	Significance for Apeak $p<0.05$	Significance for RR interval $p<0.05$
Baseline	0.314	0.009
5 sec number	0.434	0.000
5 sec word	0.684	0.005
30 sec subtraction	0.170	0.000
30 sec physical	0.045	0.002
10 sec memory	0.210	0.000
20 sec Post-task recording	0.054	0.000

GSR amplitude is significantly different (p=0.045) between male and female subjects during 30 seconds of physical task whereas the RR interval is significantly different in all the procedures they performed.

To compare cognitively obtained values and physically performed task for GSR amplitude among all the individuals, the mean values of all cognitive tasks (5 sec number, 5 sec word and 30 sec subtraction) were added and, their mean was obtained. The obtained value was compared with the 30 sec physical task performed by paired't' test as depicted in table 4.

Table 4. Comparison of cognitively obtained values and physically performed task for Apeak.

Apeak at different tasks	Mean	N	Std. Deviation	p value
Mean value of Apeak of 3 cognitive tasks	3.55	104	3.38	
Apeak at 30sec physical task	6.21	104	5.14	0.000

It is observed that the physically performed task have significantly higher value than the cognitively obtained value for the GSR amplitude.

To compare cognitively obtained values and physically performed task for core sympathetic activation among all subjects, mean of RR interval for the cognitive tasks ie. 5 sec number, 5 sec word and 30 sec subtraction was obtained. It was then compared with the mean value of RR interval obtained during the 30 sec physical task using paired t test, is in table 5.

Table 5. Comparison of cognitively obtained values and physically performed task for RR interval.

RR interval at different task	Mean	N	Std. Deviation	P value
Mean value of RR interval of 3 cognitive tasks	0.65	104	0.10	0.362
RR interval at 30sec physical task	0.66	104	0.09	

It is observed that RR interval during the cognitive tasks and physical task do not show significant differences in the values.

DISCUSSION

To our knowledge, after going through available studies searchable online, there is a scarce of autonomic work as expressed through this article. This study is pertinent for emerging in vivo concept of autonomic function and its regulation by central nervous system. For which, skin conductance to observe peripheral nerve activation of sweat glands and changes in heart rate through RR interval has been compared. Since the psychogalvanic reflex operates through multi-synaptic system, the latency, amplitude, waveform and tendency to habituation are variable in population for measured skin conductance response (SCR).[7] Though clinically reticent, study of skin conductance is useful to determine sympathetic arousal in healthy individuals. Addition to this, abolition of ipsilateral SCR has been reported after sympathectomy and, the absence of galvanic response by pharmacological intervention of atropine is also documented.[8]

But, valid and reliable tool for detection of sympathetic outflow in health and disease is still a quest due to complexity in function of central autonomic network. Thereby, comparison of superficial and, at core sympathetic effluence induced by deliberately supplied discrete external stimuli has been attempted in this study. In our findings, significant rise in the values of GSR parameters along with decrement in RR interval, mark the remarkable surge in peripheral and core sympathetic system during, allocated physical and cognitive activities. In addition, skin conductance was significantly different between genders only for physical task with higher amplitude in men but, heart rate was significantly different between genders throughout, across all allocated activities with greater heart rates in female respondents. Further, GSR amplitude is significantly higher for physically performed task than cognitively delivered activities when compared in all respondents whereas, change in heart rate was interestingly insignificant between two modalities of task applied for all subjects.

As we see the significance level tested for different variables recorded for the tests applied, except the 'Height' of the wave, rest of all variables are significantly sensitive enough for detection of sympathetic activation applied in this study as shown in table 2. Amplitude i.e. Apeak was found to be different only for physical task performed between genders. Peripheral sympathetic activation was not different between genders except during physical activity. In the result, for task "5 second number" the GSR variables dropped than baseline whereas, RR interval shortened. Peak amplitude was not detected during this step of the test in 30 men and 42 women thus, mean obtained was decreased. Since the 'Apeak' could not be delineated during the cognitive activity in this step, we surmise, the peripheral sympathetic activity was silent.

In table 3, it is quite obvious that the heart rate between male and female was significantly different and remained different through all tests performed. Sinus cycle length has been found to be longer in men in regard to the exercise capacity i.e. heart rate is lowered in men during exercise than women but there exists no gender related intrinsic properties of sinus node to such difference.[9] As stated in the earlier work for different parameters of conductance response, amplitude and related variables are found to be reliable indicators to detect sympathetic responses for supplied stimuli.[10] Interestingly, it is noticed that physical stimuli brings stronger superficial sympathetic response through activation of eccrine sweat glands to that of cognitively challenging exercises in healthy subjects. Meanwhile, no significant change in heart rate when compared for supplied cognitive and physical exercises is sui generis to our findings. Rising from sitting posture leads to racing of heart beats through baroreceptor responsiveness to avoid sudden drop of blood pressure.[11] Though heart rate gradually was risen from baseline to cognitive exercises, the difference in rate did not occur between mental exercises and postural change brought about by standing task within 30 seconds. But, there was superficial sympathetic discharge detection through sympatho-cholinergic pathway i.e. rise in skin conductance without rise in heart rate during, 30 second physical task as depicted in table 4 and 5.

Since the rise in heart rate was not obvious during sudden posture change i.e. from sitting to standing, the physiological functioning of baroreceptor reflex, could not be detected thus, postural orthostatic tachycardia syndrome (PoTS) was not obvious. Part of stretch receptor function could have been well documented had the blood pressure changes been recorded in the study but, the muscle heart reflex is not found to be accelerating the heart too.[12] Here, sitting to standing instead of lying (supine) to standing was performed without any support. Norepinephrine secreted in venous blood, which increases the force and rate, of heart though is documented to be higher during quiet standing than in resting supine, the rate of contraction is not found to be greater during quiet standing i.e., physical task, in our study.[13] Nevertheless, 'Apeak' the amplitude for conductance was significantly higher during physical task due to sympatho-cholinergic activation to sweat glands and to the blood vessels of muscles also, which originate at higher centers above the medulla and innervate the muscle vessels.[14-16] Discrete activities of different nuclei at higher centers above the vasomotor center (VMC) supplying downstream organs for sympathetic activation is possible.[17] The rise in peripheral nerve activity uncoupled to core sympathetic activity to heart reflects the differential outflow of sympathetic nerves to heart and sweat glands in skin. Though our findings suggest, the rise in sympathetic effluence occurs during mental and physical tasks, further analysis distinctively differentiates sympathetic outflow into independent diversion to the skin but the heart. Tasks provided do not show significant change in heart rate yet the skin conductance does. And, has been warned in the previous study, skin conductance should be coupled with vitals such as heart rate to detect sympathetic response, and is cautioned, not to use galvanic response as solitary parameter exclusively, to detect sympathetic activities.[1,10] Though hypothalamus regulates the sympathetic outflow to skin, the regulatory action from VMC in medulla to heart and, the feedback loop therein, operates independently. Here, simultaneous sympathetic response for rise in beats and in conductance during provided cognitive exercise is through different sets of centers in central nervous system regulating sympathetic output and, is discrete from centers responding to stimuli for change in posture, supplied as physical task. Neural sympathetic functions should be appraised to be originating in layers of higher centers from cortex, hypothalamus, medulla and the feedback existing thereof, for the needful homeostatic regulations. Sympathetic effluence eventuating to sweat glands in skin and to heart, is not due to solitary isolated site in nervous system responding to the afferent sensory stimuli rather, is a multifaceted response to diverse sensory inputs.

CONCLUSION

Cognitive performance and physical task shifts baseline effluence and increases the sympathetic outflow. There occurs no detectable rise in sympathetic effluence at the core but eventuate significantly appreciable sympathetic outflow to sweat glands in skin, for discrete physiological stimuli. Differential effluence for sympathetic response called upon by discrete stimuli is operational for maintenance of steady state in healthy subjects. This suggests peripheral autonomic sympathetic outflow operates under strict regulation by multilayered central autonomic network through multidisciplinary feedback loops and is not isolated from central nervous system.

ACKNOWLEDGEMENT

The authors are thankful to staff and students at KUSMS for their support in this work.

REFERENCES

1. Vetrugno R, Liguori R, Cortelli P, Montagna P. Sympathetic skin response. Basic mechanisms and clinical applications. *Clin Auton Res.* 2003 Aug; 13(4): 256-70.
2. Nourbakhsh N, Chen F, Wang Y, Calvo RA. Detecting users' cognitive load by galvanic skin response with affective interference. *ACM Transactions on Interactive Intelligent Systems (TiiS)*. 2017 Sep 19;7(3):1-20.
3. Conway D, Dick I, Li Z, Wang Y, Chen F. The Effect of Stress on Cognitive Load Measurement. *Lecture Notes in Computer Science*. 2013;659-66.
4. Wen W, Tomoi D, Yamakawa H, Hamasaki S, Takakusaki K, An Q, et al. Continuous Estimation of Stress Using Physiological Signals during a Car Race. *Psychology*. 2017; 8: 978-86.
5. Selçuk B, Ersoz M, Inanir M, Kurtaran A, Akyuz M. Sympathetic skin responses in hemiplegic patients with and without complex regional pain syndrome. *Neurology India.* 2006 Sept; 54(3):279-82.
6. Haapaniemi TH, Korpelainen JT, Tolonen U. Suominen K, Sotaniemi KA, Myllyla VV. Suppressed sympathetic skin response in Parkinson disease. *Clinical Autonomic Research.* 2000; 10: 337-42.
7. Kucera P, Goldenberg Z, Kurca E. Sympathetic skin response: review of the method and its clinical use. *Bratisl Lek Listy.* 2004 Feb; 105(3): 108-16.
8. Claus D, Schondorf R. Sympathetic skin response. Recommendations for the practice of clinical neurophysiology. Guidelines of the International Federation of Clinical Physiology (EEG Suppl. 52). 2nd ed. Edited by; Deuschl G, Eisen A. Elsevier Science BV 1999; 277-82.
9. Burke JH, Goldberger JJ, Ehlert FA, Kruse JT, Parker MA, Kadish AH. Gender differences in heart rate before and after autonomic blockade: evidence against an intrinsic gender effect. *The American journal of medicine.* 1996 May 1;100(5):537-43.

10. Nepal O, Jha RK, Bhattarai A, Khadka P, Kapoor BK. Galvanic Skin Response as a Simple Physiology Lab Teaching Tool- An Alternative Indicator of Sympathetic Arousal. *Kathmandu Univ Med J.* 2018 Apr-Jun;16(62):156-160.

11. Charkoudian N, Rabitts JA. Sympathetic neural mechanisms in human cardiovascular health and disease. *Mayo clinic proceedings*. 2009 Sep; 84 (9):822-30.

12. Hollander AP, Bouman LN. Cardiac acceleration in man elicited by a muscle-heart reflex. *Journal of applied physiology.* 1975;38(2):272-8.

13. Bleich HL, Moore MJ, Cryer PE. Physiology and Pathophysiology of the Human Sympathoadrenal Neuroendocrine System. *New England Journal of Medicine.* 1980 Aug 21; 303(8), 436-44.

14. Matsukawa K, Shirai M, Murata J, Tsuchimochi H, Komine H, Ninomiya I, et al. Sympathetic cholinergic vasodilation of skeletal muscle small arteries. *Jpn J Pharmacol.* 2002 Jan;88(1):14-8.

15. Wong BJ, Hollowed CG. Current concepts of active vasodilation in human skin. *Temperature.* 2017;4(1):41-59.

16. Dampney RAL. Central neural control of the cardiovascular system: current perspectives. *Advances in Physiology Education.* 2016;40(3): 283-96.

17. Coote JH. Landmarks in understanding the central nervous control of the cardiovascular system. *Experimental Physiology.* 2007; 92(1): 3-18.