Effect of Cannabis Consumption on ANS and Conduction Pathway of Heart of Indian Paddy Field Workers

Suraj K Nayak[1], Srikant Suman[1], Bichitra M Nayak[1], Indranil Banerjee[1], Kunal Pal[1]*
[1]Dept. of Biotech& Medical Engg.
NIT-Rourkela, Odisha,
India-769008
[*]kpal.nitrkl@gmail.com

Biswajeet Champaty[1#]
Dept. of Biomedical Engg.
A D Y Patil University,
Pune, Maharashtra,
India-412105
[#]biswajeet.champaty@adypu.edu.in

Biswajit Mohapatra
Vesaj Patel Hospital
Rourkela, Odisha,
India- 769004

D N Tibarewala
School of Bioscience & Engg.
Jadavpur University, Kolkata
West Bengal, India-700032

***Abstract*—The current study reports the effect of regular *Cannabis sativa* (bhang) consumption on the autonomic nervous system (ANS) and the conduction pathway of the heart of the Indian paddy field workers. Twenty-four paddy field workers were selected for the study and electrocardiogram (ECG) signal was recorded. The physiological modulation in the ANS was analyzed in a non-invasive manner using heart rate variability (HRV) parameters. The results suggested a sympathetic dominance in the bhang users. ECG signal divulges information about the cardiac physiology and the conduction pathway of the heart. Time-domain and joint time-frequency domain analyses of ECG signal suggested alterations in the cardiac conduction pathway of bhang users. Artificial neural network based classification using the important predictors as categorical inputs resulted in an efficiency of ≥ 80%.**

Keywords*—*heart rate variability; ECG; autonomic nervous system; heart; artificial neural network

I. Introduction

The abuse of *Cannabis sativa* based products has been considered just next to the abuse of alcohol. Such products are used due to their euphoric effects [1]. The use of such products in India is quite common. This is because the cost of production of the cannabis products is very low. The weed grows very easily in the Indian climate. Apart from this, the toxicity associated with the consumption of cannabis products is very low [1]. The use of such products is quite common amongst the common people, even though there are restrictions by the Indian government. But, the restrictions are not so strong for the use of Bhang, a product made from cannabis. Bhang is used mostly by the people following Hindu religion due to their religious belief. It is used as a drink during specific festivals. Even though the toxicity associated with cannabis consumption is very low, many reports were found which suggested that coronary and cerebral ischemia, tachyarrhythmia and even sudden death are precipitated in the persons consuming cannabis products [2-3]. The consumption of cannabis products has been reported to modulate the cardiac activity by exerting an agonistic effect on the effect on the cannabinoid receptor type 1, which is present in the cardiac tissue. This can result in the increase in the heart rate, which is independent of the sympathetic activity [4]. A comprehensive literature review suggested that though many case reports have been published on the effect of cannabis products on the direct activity of the heart, no attempts were made to understand the physiology of the ANS in the persons who regularly consume bhang. In this study, we have conducted the HRV analysis along with time domain and joint time-frequency domain analyses on ECG of the bhang consuming paddy field workers. Paddy field workers who restrained themselves from the consumption of bhang were used as the control group. The parameters obtained from the afore-mentioned analyses were subjected to linear and non-linear classification methods to understand, whether the consumption of bhang has any effect on the ANS and electrical conduction pathway of the heart.

II. Methods

A. Volunteers

Twenty-four paddy field workers of either sex in the age group of 40.44 ± 14.68 years were selected to take part in this study. Amongst the paddy field workers, thirteen workers were regular consumers of bhang (Category-WB). The rest eleven workers never consumed bhang and were regarded as the control group (Category-NB). They were verbally informed regarding the study in detail and an informed consent form was obtained from them after they agreed to take part in the study. The approval for the acquisition of ECG signal was received for the Institute ethical clearance committee vide office order No. NITRKL/IEC/ FORM/2/25/4/11/001, dated 13/12/2013. The workers were requested to sit on a chair and the ECG signal was recorded for 8 min.

B. ECG signal acquisition

The ECG signal was sensed using reusable ECG clamp electrodes placed in lead I configuration and Vernier EKG sensor (Vernier Software and Technology, USA). The ECG signal was acquired into a laptop with the help of NI USB 6009 data acquisition device (National Instruments, USA).

978-1-5090-3646-2/16/$31.00 ©2016 IEEE

C. HRV analysis

Five min recording of the acquired ECG signal was used for the HRV analysis, which was performed using biomedical toolkit available in LabVIEW 2013. After loading of the 5 min ECG recording into the biomedical workbench toolkit, the QRS complex was extracted using a band-pass filter (BPF) having lower and higher cut-off frequencies of 10 and 25 Hz, respectively. The extracted QRS complex was analyzed to obtain 29 HRV parameters. These HRV parameters were tabulated in a Statistica (trial version 13.0, Dell Inc., USA) spreadsheet. The statistically significant features (important predictors) were obtained using statistical methods, namely, t-test, classification and regression tree (CART), boosted tree (BT) and random forest (RF). These features, in various combinations, were used as categorical inputs for classification using ANN.

D. Time Domain Analysis

The time domain analysis was carried out using five sec recording of the ECG signal. The statistical features were obtained using an in-house developed LabVIEW program. The afore-mentioned statistical methods were used to obtain the important predictors, which were used in different combinations as categorical input for ANN based classification.

E. Joint Time-frequency Analysis

Afive sec extracted recording of ECG signal was subjected to processing using discrete wavelet transform-based joint time-frequency analysis. The ECG signal was decomposed using Daubechies wavelet (db06) upto the level 8 and reconstruction was performed using D7 and D8 sub-bands. TheDaubechies waveletwas chosen as the mother wavelet in this study due to its good correlation with the ECG signal [5]. Similar to the time domain analysis, statistical features of the reconstructed signal were obtained. Finally, the important predictors were selected using the statistical methods mentioned earlier and used for classification using ANN.

III. Result and Discussion

A. HRV analysis

HRV refers to the measurement of the variation in the time interval between consecutive heart beats. Various researchers have reported that HRV can be used as a marker to analyze the effect of ANS on the heart activity[6-8]. This canbe attributed to the fact that the ANS controls the working of the sino-atrial (SA) node (regarded as the pacemaker of the heart) with its two branches, namely, sympathetic nervous system (SNS) and parasympathetic nervous system (PNS). This, in turn, is responsible for the rhythmic contraction of the heart muscles. t-test was performed to identify the statistically significant parameters out of the 29 HRV parameters. It is a linear statistical method, usually preferred to compare the mean values of parameters belonging to two different groups when the sample size is less. The t-test results (with p-value ≤ 0.05) suggested that the HRV parameters, namely, NN50, HRV triangular index, triangular interpolation of NN interval histogram (TINN), SD2, very low frequency (VLF) power, low-frequency power (LF power) and VLF (%) were the statistically significant parameters (Table 1). However, the mean heart rate was found to be statistically insignificant. Interestingly, the values of all these parameters were lower in the bhang consuming population than that of the control group. NN50 is a statistical time-domain measure and refers to the number of NN intervals with the difference of successive intervals being greater than 50 msec. NN50 has been reported to be useful for estimating the high-frequency variations in heart rate [6]. A lower value of NN50 suggested a reduction in the parasympathetic activity. HRV triangular index is a time domain geometric measure and is obtained by dividing the total number of the NN intervals in the NN interval histogram with the height of the histogram, measured on a discrete scale with bins of 7.8125 sec [6]. TINN is another time domain geometric measure and is defined as the baseline width of the NN interval histogram [9]. A lower value of HRV triangular index and TINN again suggested a reduction in the parasympathetic activity in the bhang consuming population. SD2 is one of the two standard deviations obtained from the Poincaré plot, which is regarded as an important non-linear method for quantifying the RR interval fluctuations. Poincaré plot presents the graphical illustration of the correlation between the consecutive RR intervals [10]. SD2 is reported to be an inverse function of sympathetic activity [11]. A lower value of SD2 in the bhang consuming population than that of the control group suggested that the consumption of bhang is associated with sympathetic dominance. The power spectral density (PSD) analysis of ECG signal divulges information about the distribution of power (variance) as a function of frequency. For short-term ECG signal (2-5 min), the power spectrum comprises of three distinct components, namely, very low frequency (VLF), low frequency (LF) and high frequency (HF) components with frequency ranges of 0.003-0.04 Hz, 0.04-0.15 Hz and 0.15-0.4 Hz, respectively [6, 9]. These power components are also expressed as the percentage of total power. For example, VLF% refers to the ratio VLF power to total power expressed in percentage. Although the exact physiological phenomena responsible for VLF power is yet to be established, some researchers have reported VLF power to be a marker of parasympathetic activity. This is because the VLF power is abolished by atropine [12]. Hence, a lower value of VLF power and VLF% suggested the reduced parasympathetic activity in the bhang consuming people. The LF power is regarded as a marker of sympathovagal activity. Apart from t-test, the nonlinear decision tree-based methods, namely, CART, BT and RF were also used to recognize the statistically significant parameters. The CART analysis suggested that the standard deviation of heart rate (HR SD) is the only important predictor. On the other hand, VLF (%) was obtained as the only important predictor from BT and RF analysis.

TABLE I. STATISTICALLY SIGNIFICANT HRV FEATURES

Statistical Methods	HRV Features	Mean ± SD		Predictor Importance	p-wave
		Category-NB	*Category-WB*		
t-test	NN50	107.273±107.866	33.846±51.017	-----------	0.039
	HRV triangular index	11.673±6.753	7.069±3.069	-----------	0.037
	TINN	168.900±88.361	104.753±47.454	-----------	0.033
	SD2	144.909±167.044	46.923±26.631	-----------	0.048
	VLF power	1108.364±1623.504	111.538±138.156	-----------	0.037
	LF power	909.273±1206.981	188.230±194.200	-----------	0.044
	VLF(%)	33.273±11.172	23.5923±11.0721	-----------	0.045
CART	HR SD	43.764±70.130	4.8846±4.6191	1.000	-----------
BT	VLF(%) FFT	33.273±11.172	23.5923±11.0721	1.000	-----------
RF	VLF(%)	33.273±11.172	23.5923±11.0721	1.000	-----------

In gist, the statistically important predictors suggested a sympathetic dominance (associated with a reduction in the parasympathetic activity) in the bhang consuming people. These predictors were used in different combinations as categorical inputs for ANN based classification. Multilayer perceptron (MLP) and radial basis function (RBF) ANN networks were implemented using the automated neural networks provided by Statistica software. The MLP (4-10-2) network provided the best classification efficiency of 100.00% when NN50, HRV triangular index, TINN, SD2, HR SD, VLF power, LF power and VLF(%) were used as inputs. The classification summary of the MLP (4-10-2) network is given below in Table 2. On the other hand, a classification efficiency of 86.50% was obtained from RBF (4-7-2) network using the same parameters as inputs, whose classification summary is provided below as Table 3. The details of MLP (4-10-2) and RBF (4-7-2) networks are tabulated in Table 4.

TABLE II. CLASSIFICATION SUMMARY OF MLP 4-10-2NETWORK

	Category-NB	Category-WB	Final
Total	11.00	13.00	24.00
Correct	11.00	13.00	24.00
Incorrect	0.00	0.00	0.00
Correct (%)	100.00	100.00	100.00
Incorrect (%)	0.00	0.00	0.00

TABLE III. CLASSIFICATION SUMMARY OF RBF 4-7-2NETWORK

	Category-NB	Category-WB	Final
Total	11.00	13.00	24.00
Correct	9.00	12.00	21.00
Incorrect	2.00	1.00	3.00
Correct (%)	81.82	92.31	87.06
Incorrect (%)	18.18	7.69	12.94

TABLE IV. DETAILS OF MLP AND RBFNETWORKS

Network	Inputs	Classification Efficiency	Training Algorithm	Error Function	Hidden Act.	Output Act.
MLP 4-10-2	NN50, HRV triangular index, TINN, SD2, VLF power, LF power VLF(%)and HRSD	100.00%	BFGS 18	CE	Entropy	Softmax
RBF 4-7-2	NN50, HRV triangular index, TINN, SD2, VLF power, LF power VLF(%)and HRSD	86.50%	RBFT	Entropy	Gaussian	Softmax

TABLE V. STATISTICALLY SIGNIFICANT FEATURES OF TIME-DOMAIN PROCESSED ECG

Statistical Methods	Timedomain features	Mean ± SD		Predictor Importance	p-value
		Category-NB	Category-WB		
t-test	AM	0.00005 ± 0.00048	0.00097 ± 0.00133	-	0.04109
CART	Mode	-0.00335 ± 0.01279	-0.00058 ± 0.02319	1.00000	-
BT	SUM	3.15984 ± 0.71237	2.98608 ± 0.84895	1.00000	-
RF	AM	0.00005 ± 0.00048	0.00097 ± 0.00133	1.00000	-

B. Time domain analysis

The statistical features obtained from time domain processing of the five sec ECG signals were arithmetic mean (AM), standard deviation (SD), root mean square value (RMS), variance, kurtosis, skewness, summation (SUM), mode and median. Analysis of these features using t-test (with ap-value ≤ 0.05) suggested that AM was the only important predictor (Table 5). AM was obtained as the important predictor, also from RF analysis. The CART analysis suggested mode as the important predictor, whereas, SUM was found to be the important predictor from BT analysis. Various combinations of these important predictors were used as inputs for ANN based classification. The MLP (3-6-2) network provided the best classification efficiency of 100.00% (Table 6) when AM, mode and SUM were used as the inputs. On the other hand, the highest classification efficiency obtained from RBF (3-8-2) network was 87.76% (Table 7) using the same parameters as inputs. The details of MLP (3-6-2) and RBF (3-8-2) networks are tabulated in Table 8. The classification results suggested the alteration in the conduction pathway of the heart of the bhang users.

TABLE VI. CLASSIFICATION SUMMARY OF MLP 3-6-2 NETWORK

	Category-NB	Category-WB	Final
Total	11.00	13.00	24.00
Correct	11.00	13.00	24.00
Incorrect	0.00	0.00	0.00
Correct (%)	100.00	100.00	100.00
Incorrect (%)	0.00	0.00	0.00

TABLE VII. CLASSIFICATION SUMMARY OF RBF (3-8-2) NETWORK

	Category-NB	Category-WB	Final
Total	11.00	13.00	24.00
Correct	10.00	11.00	21.00
Incorrect	1.00	2.00	3.00
Correct (%)	90.90	84.62	87.76
Incorrect (%)	9.10	15.38	12.24

TABLE VIII. DETAILS OF MLP AND RBFNETWORKS

Networks	Inputs	Classification Efficiency	Training Algorithm	Error Function	Hidden Act.	Output Act.
MLP 3-6-2	AM, Mode and SUM	100.00%	BFGS 43	Entropy	Logistic	Softmax
RBF 3-8-2	AM, Mode and SUM	87.76%	RBFT	Entropy	Gaussian	Softmax

C. *Joint Time-frequency Analysis*

Similar to the time domain analysis, nine statistical features of the wavelet processed ECG signals were also calculated. None of the features were found to be statistically significant from t-test (with p-value $\leq$ 0.05). The CART analysis suggested AM and skewness as the important predictors (Table 9). SUM was found to be the important predictor from BT analysis. Medianwas obtained as the important predictor from RF analysis. These important predictors were used as the inputs for ANN based classification. When AM, mode and SUM were used as the inputs, the MLP (3-7-2) network provided the maximum classification efficiency of 83.22% (Table 10). However, the highest classification efficiency obtained from RBF (4-11-2) network was 96.16% (Table 11) using the same parameters as inputs. The details of MLP (3-7-2) and RBF (4-11-2) networks are tabulated in Table 12. The alteration in the conduction pathway of the heart with regular usage of bhang was again evident from these classification results.

TABLE IX. STATISTICALLY SIGNIFICANT FEATURES OF WAVELET PROCESSED ECG

Classifiers	Wavelet Features	Mean+SD		Predictor Importance
		Category-NB	Category-WB	
CART	AM	-0.00006±0.00065	0.00030±0.00099	1.00000
	Skewness	-0.28799±3.26502	1.51814±4.96048	1.00000
BT	SUM	0.31186±0.26794	0.34202±0.23805	1.00000
RF	Median	-0.00076±0.00418	-0.00123±0.00426	1.00000

TABLE X. CLASSIFICATION SUMMARY OF MLP 3-7-2 NETWORK

	Category-NB	Category-WB	Final
Total	11.00	13.00	24.00
Correct	9.00	11.00	20.00
Incorrect	2.00	2.00	4.00
Correct (%)	81.82	84.62	83.22
Incorrect (%)	18.18	15.38	16.78

TABLE XI. CLASSIFICATION SUMMARY OF RBF (4-11-2) NETWORK

	Category-NB	Category-WB	Final
Total	11.00	13.00	24.00
Correct	11.00	12.00	23.00
Incorrect	0.00	1.00	1.00
Correct (%)	100.00	92.31	96.16
Incorrect (%)	0.00	7.69	3.84

TABLE XII. TABLE 12. DETAILS OF MLP AND RBFNETWORKS

Network	Inputs	Classification Efficiency	Training Algorithm	Error Function	Hidden Act.	Output Act.
MLP 3-7-2	AM, Median and SUM	83.22%	BFGS 9	Entropy	Tanh	Softmax
RBF 4-11-2	AM, Median and SUM	96.16%	RBFT	Entropy	Gaussian	Softmax

IV. CONCLUSION

The current study was designed to understand the effect of bhang consumption on the ANS and the electrical conduction pathway of heart. The effect of bhang on the ANS was analyzed using the non-invasive HRV parameters. The results of HRV analysis suggested a sympathetic dominance over the parasympathetic activity in the people regularly consuming bhang. The mean heart rate values were observed to be statistically insignificant. The effect on the cardiac electrophysiology of the heart was explored using the time domain and the joint time-frequency analysis of ECG signal. The results suggested that someof the ECG features weresignificantly different. The important predictors ascertained from HRV, time domain and joint time-frequency analyses were employed as categorical inputs for ANN classification using MLP and RBF networks. In all the cases, both MLP and RBF networks resulted in a classification efficiency of $\geq 80\%$. This canbe accountedto the fact that there might be any physiological alteration in the electrical conduction pathway of the heart. An in-depth analysis is required to explore the exact changes.

References

[1] L. Bachs and H. Mørland, "Acute cardiovascular fatalities following cannabis use," *Forensic Science International,* vol. 124, pp. 200-203, 2001.

[2] V. Wolff*, et al.*, "Cannabis-related stroke myth or reality?," *Stroke,* vol. 44, pp. 558-563, 2013.

[3] S. Menahem, "Cardiac asystole following cannabis (marijuana) usage–Additional mechanism for sudden death?," *Forensic Science International,* vol. 233, pp. e3-e5, 2013.

[4] G. Dumont*, et al.*, "Cannabis coadministration potentiates the effects of" ecstasy" on heart rate and temperature in humans," *Clinical pharmacology and therapeutics,* vol. 86, p. 160, 2009.

[5] S. K. Nayak*, et al.*, "Effect of Slow and Fast Music on the Autonomic Nervous System and Cardiac Health: A Preliminary Investigation," *Classification and Clustering in Biomedical Signal Processing,* p. 198, 2016.

[6] T. F. o. t. E. S. o. Cardiology, "Heart rate variability standards of measurement, physiological interpretation, and clinical use," *Eur Heart J,* vol. 17, pp. 354-381, 1996.

[7] S. K. Nayak*, et al.*, "Automated Neural Network Based Classification of HRV and ECG Signals of Smokers: A Preliminary Study," in *Advancements of Medical Electronics*, ed: Springer, 2015, pp. 271-279.

[8] S. Nayak*, et al.*, "Development of a simultaneous acquisition system for ECG, PCG and body temperature signals," in *2015 Annual IEEE India Conference (INDICON)*, 2015, pp. 1-6.

[9] M. P. Tarvainen*, et al.*, "Kubios HRV–heart rate variability analysis software," *Computer methods and programs in biomedicine,* vol. 113, pp. 210-220, 2014.

[10] M. Brennan*, et al.*, "Do existing measures of Poincare plot geometry reflect nonlinear features of heart rate variability?," *IEEE transactions on biomedical engineering,* vol. 48, pp. 1342-1347, 2001.

[11] C. Marina Medina*, et al.*, "Normal values of heart rate variability at rest in a young, healthy and active Mexican population," *Health,* vol. 2012, 2012.

[12] R. E. Kleiger*, et al.*, "Heart rate variability: measurement and clinical utility," *Annals of Noninvasive Electrocardiology,* vol. 10, pp. 88-101, 2005.