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Research Paper

Comparison of Electrocardiogram and Heart Rate Variability in Anaesthetised Versus Non Anaesthetised Wistar Rats

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ABSTRACT
Aims*: The present study was conducted to compare; (a) ECG parameters anaesthetised versus non-anaesthetised wistar rats and (b) Heart rate variability in anaesthetised versus non-anaesthetised wistar rats*
Material and methods*: The present study was conducted in the Department of Physiology, King George Medical University, Lucknow. The study comprised of 10 anaesthetised and 10 non-anaesthetised wistar rats. Ketamine – xylazine cocktail was used as anaesthetic agent .A customised table with velcro was designed and developed for the conscious rat to fix it for ECG and HRV recording. ECG leads i.e. red, white and black were placed on left forearm, right forearm and left leg respectively. ECG leads were fixed using micropore tape. High-quality ECG signals were obtained, being feasible for HRV analysis. The data was collected and analysed using SPSS version 24.*
Results*: HR was significantly less in anaesthetised (277.9)as compared to non-anaesthetised wistar rats (378.7).RR interval (s) and QTc interval (s) was significantly more in anaesthetised as compared to non-anaesthetised wistar rats as $p<0.05$. VLF, LF, HF and LF/HF was 12.46, 31.01, 53.45, 0.58 and 71.32, 10.55, 16.6, 0.64 among anaesthetised and non-anaesthetised wistar rats respectively. When VLF, LF and HF was compared statistically among anaesthetised and non-anaesthetised wistar rats, it was found to be statistically significant as $p<0.05$.*
Conclusion*: Significant relation is observed between Heart rate, RR interval and QT_c in the electrocardiogram. Significant relation is observed between VLF, LF, HF in HRV assessment.*
Keywords*: Electrocardiogram; Heart Rate, Anaesthesia, Wistar Rats*

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I. INTRODUCTION:

Electrocardiography (ECG) in rats is a widely used experimental method in basic cardiovascular research. Heart rate variability (HRV) analysis is a well-established tool for the assessment of cardiac autonomic control, both in humans and in animal models. Conventionally, ECG and HRV recording was performed using invasive surgical procedures which required electrode/transmitter implants[1]. Presently, non invasive method for ECG recording (HRV assessment) is being carried out in animal research.

Electrocardiography (ECG) in humans was introduced in 1903 by Willem Einthoven. Since then, it has become one of the most widespread diagnostic tools in clinical medicine. ECG recording reflects the electrical activity of the heart and may provide important insights into functional and structural characteristics of the myocardium. The physiological and pathological criteria of ECG recordings have been thoroughly described in multiple handbooks and research papers (Hall et al[2]. 2011, Wagner et al[3]. 2009).

Despite some differences, such as the lack of Q wave in most leads (Farraj et al[4]. 2011), there are essential similarities between rat and human ECG (Sambhi and White 1960)[5]. Therefore, ECG in rats has been exploited in basic cardiovascular research dealing with the heart's performance under physiological conditions and in animal models of cardiovascular diseases. Electrocardiographic parameters in rats, their range, as well as the effect of experimental settings on the parameters variation varies according to rat's consciousness. Hence the present study was conducted to compare ECG parameters and heart rate variability in anaesthetised versus non-anaesthetised wistar rats.

II. MATERIAL AND METHODS

The proposed study has been conducted in the department of Physiology of KGMU, Lucknow after taking ethical clearance. The animals were procured from Indian Institute of toxicological research (IITR) Lucknow. The study was approved by the animal ethics committee of King George's Medical University, Lucknow. The study comprised of 10 anaesthetised and 10 non-anaesthetised wistar rats. Ketamine – xylazine cocktail (KX anesthesia) was used as anaesthetic agent. Ketamine, the general anesthetic component of KX anesthesia, has a rapid onset of action and high lipid solubility. Initially, ketamine is distributed to highly perfused tissues, such as the brain. Ketamine has a high hepatic clearance (1 L/min) and a large volume of distribution (3 L/kg), resulting in an elimination half-life of 2 h. This characteristic means that the limiting factor in ketamine metabolism is the hepatic blood supply's ability to deliver drug to hepatocytes and not the enzymatic ability of the hepatocytes to metabolize the drug. Xylazine has a large volume of distribution after administration and a rapid metabolic clearance that is not primarily dependant on hepatic blood flow.

Rats (250-300g) were kept in cages floored with hay, in a room with constant temperature (23◦C) and 12h dark-light cycle. All animals had access to food and water ad libitum. Prior to ECG recordings, animals were conditioned for 7 consecutive days, 20 minutes each day on a custom made board with velcro. All recordings were conducted on a constant environment, during the morning (10-12h). A day before ECG was firstly recorded, the limb region of each animal was carefully shaved. A customised table with velcro was designed and developed for the conscious rat to fix it for ECG and HRV recording. ECG leads i.e. red, white and black were placed on left forearm, right forearm and left leg respectively. ECG leads were fixed using micropore tape (Figure1). High-quality ECG signals were obtained, being feasible for HRV analysis.

ECG parameters, i.e., RR interval, QRS duration, and QT interval were measured from the lead II using calipers. ECG parameters were measured from the lead II and analyzed by one of the authors herself. ECG was recorded for 5 min in each group. The mean value of six consecutive waves was calculated.

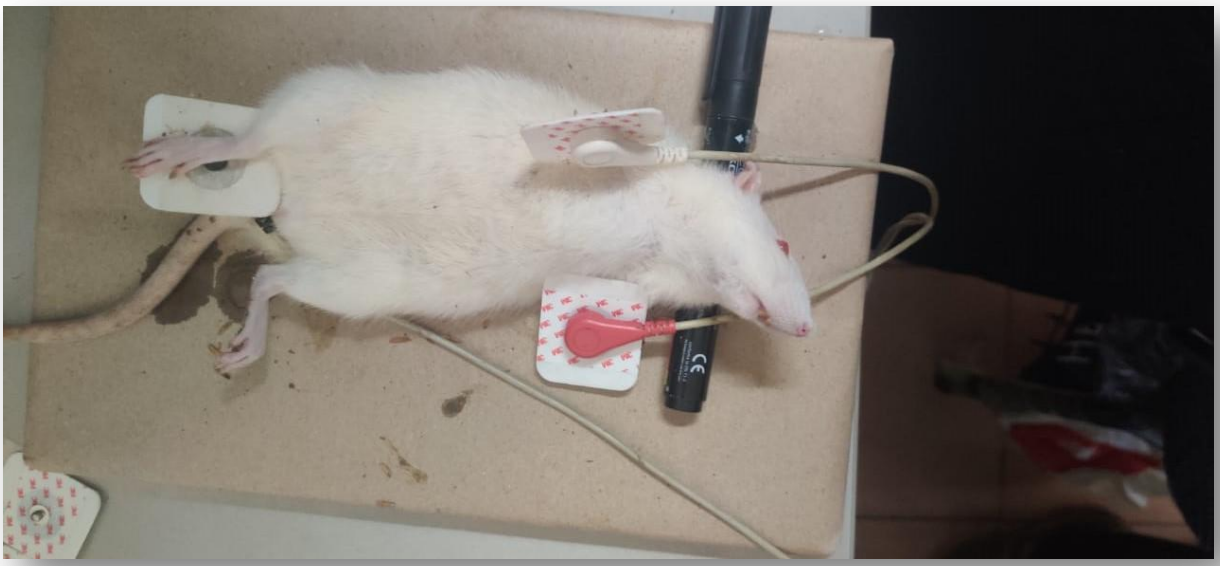

Figure 1: ECG acquisition method

Statistical Analysis: The data was collected and analysed using SPSS version 24. Difference between two groups was determined using student t-test and the level of significance was set at $p < 0.05$.

III. RESULTS

Mean HR was significantly less in anaesthetised (277.9) as compared to non-anaesthetised wistar rats (378.7). Mean RR interval (s) and QTc interval (s) was significantly more in anaesthetised as compared to non-anaesthetised wistar rats as $p<0.05$ (Table 1).

Mean VLF, LF, HF and LF/HF% was 12.46, 31.01, 53.45, 0.58 and 71.32, 10.55, 16.6, 0.64 among anaesthetised and non-anaesthetised wistar rats respectively. When mean VLF, LF and HF% was compared statistically among anaesthetised and non-anaesthetised wistar rats, it was found to be statistically significant as $p<0.05$ (Table 2).

Table 1: Comparison of ECG parameters among anaesthetised and non-anaesthetised wistar rats

Parameters	Anaesthetised		Non-anaesthetised		t test	p value
	Mean	SD	Mean	SD		
HR	277.9	4.18	378.7	7.43	37.39	<0.01*
RR int (s)	0.22	0.04	0.16	0.03	3.79	0.001*
PR int (s)	0.05	0.02	0.04	0.02	1.12	0.28
QRS int (s)	0.02	0.01	0.02	0.01	0	1
QT int (s)	0.07	0.02	0.05	0.02	0.97	0.43
QTc int (s)	0.16	0.03	0.12	0.04	2.53	0.02*

*: statistically significant

Table 2: HRV comparison among anaesthetised and non-anaesthetised wistar rats

Parameters	Anaesthetised		Non-anaesthetised		t test	p value
	Mean (%)	SD	Mean (%)	SD		
VLF	12.46	2.91	71.32	6.48	54.19	<0.01*
LF	31.01	3.16	10.55	2.14	68.13	<0.01*
HF	53.45	5.12	16.6	1.89	46.17	<0.01*
LF/HF	0.58	0.09	0.64	0.13	1.2	0.25

IV. DISCUSSION

Reduced heart rate variability (HRV) constitutes an independent prognostic factor for cardiac events. To date, evidence exists suggesting also a possible prognostic value of HRV in rodents[7,8]. The rat has been shown to constitute an important model for the study of HRV, being suitable for investigations involving diseases, toxicological, and environmental approaches. Conventional methods for conscious state ECG recording in rats rely on surgical procedures for electrodes/transmitter implants, which are generally conducted one or a few more days before records take place. With the present noninvasive method, we have shown the possibility of acquiring a high-quality ECG signal in non-anesthetized as well as anesthetized rats in the present study.

Long-term ECG recording has already been described with telemetric systems (Howarth et al. 2008)[8]. Nevertheless, to our knowledge, no previous report describes long-term ECG recordings using setups based on custom-made implanted electrodes and direct cable connection. Thus, the present method may represent an interesting and inexpensive alternative to telemetry, allowing ECG repeated measures to be taken across a given time period, which may benefit study designs such as the ones used to assess the time course of complications in cardiovascular disease models, drug therapies, or cardiovascular adaptations to exercise training. Besides that, if adequate safety precautions are taken in animal handling, using a noninvasive method may possibly represent a way of reducing the risk of accidental infection, compared to surgical methods, in cases where conscious state ECG recording is necessary in rat models of infectious diseases[2].

In the present study, mean HR was significantly less in anaesthetised (277.9) as compared to non-anaesthetised wistar rats (378.7). Mean RR interval (s) and QTc interval (s) was significantly more in anaesthetised as compared to non-anaesthetised wistar rats. HRV variables i.e. VLF, LF and HF%, when compared statistically among anaesthetised and non-anaesthetised wistar rats, it was found to be statistically significant as $p<0.05$ in the present study. These results indicates that variability in these parameters (mentioned above) must be taken care, when ECG and HRV analysis need to be done in humans, i.e. whether they are conscious or unconscious. Therefore it can be said that anesthesia may influence the ECG parameters. Pradeep Kumar et al[8] in their study revealed that there was no statistically significant difference among anaesthetised and non-anaesthetised wistar rats in relation to ECG and HRV parameters.

The method described, in this study, has many advantages over existing methods for recording ECG in conscious laboratory animals. Only a time of a week is needed to be spent on training/acclimatization of animals for this recording procedure.

The present study had some limitations such as small sample size. Animal restraining may represent a potential limitation of our method, as no free activity or grooming was possible in case of unconscious rats. Thus, we can not discard the hypothesis that restraining related stress could have some interference on the HRV indexes obtained. Previous works have described blood pressure measurement in conscious rats, allowing the determination of blood pressure variability and baroreflex sensitivity (Ramaekers et al. 2002). We should remark that the present method is only suited for the measurement of ECG, and is not valid if blood pressure recording is also needed.

V. CONCLUSION

It can be concluded from the present study that significant relation was observed in relation to Heart rate, RR interval, QTc, VLF, LF and HF among anaesthetised and non-anaesthetised wistar rats.

REFERENCES

[1]. Konopelski P, Ufnal M. Electrocardiography in rats: a comparison to human. Physiological Research. 2016;65(5).

[2]. Hall JE. Cardiac Arrhythmias and their electrocardiographic interpretation. In: Guyton and Hall Textbook of Medical Physiology. HALL JE, GUYTON AC, SCHMITT W (eds), Saunders, London, 2011, pp 143-153.

[3]. Wagner GS, Macfarlane P, Wellens H, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part VI: acute ischemia/infarction: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. J Am Coll Cardiol 2009;53:1003-1011.

[4]. Farraj AK, Hazari MS, Cascio WE. The utility of the small rodent electrocardiogram in toxicology. Toxicol Sci 2011;121: 11-30.

[5]. Sambhi MP, White FN. The electrocardiogram of the normal and hypertensive rat. Circ Res 1960;8: 129-134.

[6]. Rowan III WH, Campen MJ, Wichers LB, Watkinson WP. Heart rate variability in rodents: uses and caveats in toxicological studies. Cardiovasc Toxicol 2007;7: 28–51.

[7]. Howarth FC, Jacobson M, Shafiullah M, Adeghate E. Long-term effects of type 2 diabetes mellitus on heart rhythm in the Goto-Kakizaki rat. Exp Physiol 2008;93: 362–369.

[8]. Kumar P, Srivastava P, Gupta A, Bajpai M. Noninvasive recording of electrocardiogram in conscious rat: A new device. Indian J Pharmacol 2017;49:116-8.

[9]. Ramaekers D, Beckers F, Demeulemeester H, Aubert AE. Cardiovascular autonomic function in conscious rats: a novel approach to facilitate stationary conditions. Ann Noninvasive Electrocardiol 2002;7: 307–318.