ASSESSMENT OF CARDIORESPIRATORY FUNCTION USING TELEMETRIC JACKET IN RODENTS

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Introduction

In Preclinical safety, Jacketed External Telemetry (JET system) offers a reliable alternative (vs implantable approach) to monitor cardiorespiratory parameters in dogs, primates and pigs [1] during safety endpoints in toxicological studies. "All in one" monitoring of respiratory and cardiovascular parameters on the same animals is advantageous from scientific and ethical points of view.
This methodology does not exist for smaller animals such as rats, guinea pigs or rabbits for which implantation or restraining is still required.

We have developed a multi-sensor Bluetooth jacket (*DECRO*) that simultaneously records : an external ECG, the activity level of the animal (Overall Dynamic Body Acceleration - ODBA) and respiratory volume with inductive plethysmography monitoring (RIP) sensors.

The aim of this study is to validate cardiorespiratory measurements from this jacket in comparison with reference methods : Unrestrained Whole-Body Plethysmograph chamber (UWBP) and an implanted ECG telemetry device (IMP).

(Fig.1) Animal equipped with DECRO connected jacket

Material and methods

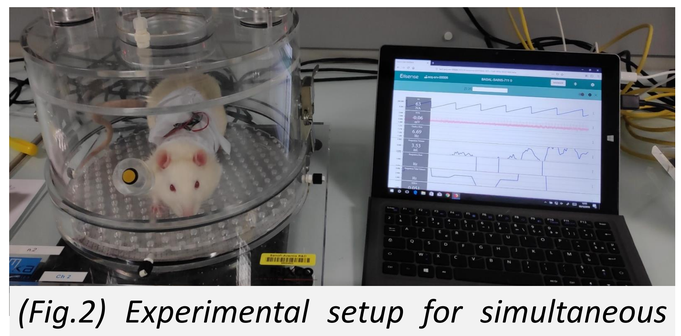
Animal model : 6 telemetered (*DSI*) Sprague-Dawley (505±28 g) males were locally shaved on the left and right flanks to place two external ECG electrodes in lead I position. Animals were dressed with the jacket which also maintains the electrodes and then equipped with a harness containing the Bluetooth Emitter (as visible in Fig.1). This emitter is connected to the electrodes and to the respiratory inductive sensors integrated into the jacket in a way to measure thoracic and abdominal volume variations. It transmits data to an acquisition system located in the same room. Before acquisition, animals had been twice accustomed to experimental conditions.

Physiological recording : The parameters below were recorded twice for 1 hour in rest condition:

- **Cardiac :** Heart rate (HR)
- **Respiratory :** Respiratory Rate (RR), Tidal Volume (TV)
- **Activity :** ODBA (from jacket)

Data from the jacket are analyzed and displayed in real time on a Tablet-PC using LASA software (ETISENSE) (Fig.2).

ECG from IMP is simultaneously recorded and HR calculated using Notocord-hem software. Respiratory measurements from the UWBP are recorded in parallel and processed with IOX software (EMKA).

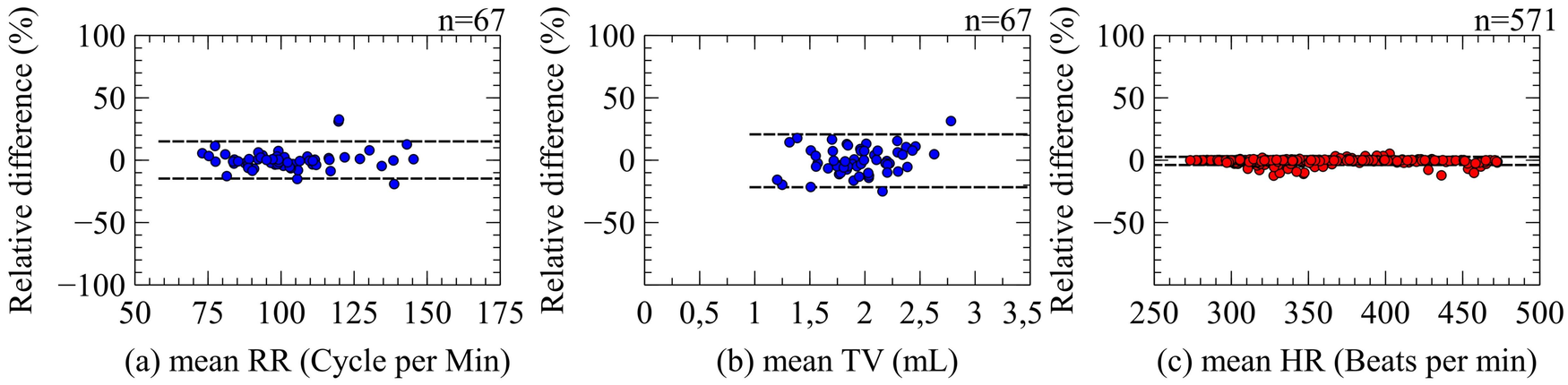


(Fig.2) Experimental setup for simultaneous recordings.

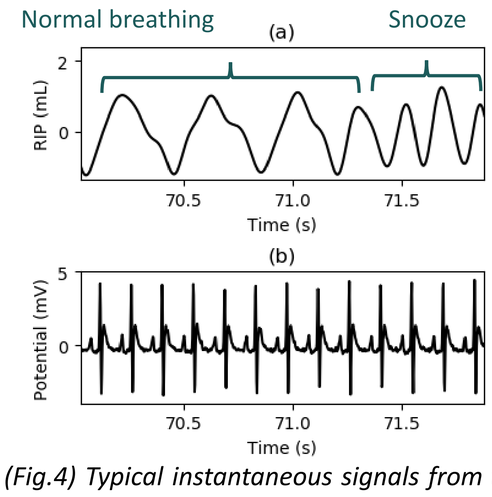
Analysis : For each recording, analysis is performed during ten minute segments to minimize bias due to time shifts between systems. Each segment is averaged. A calibration gain for RIP TV measurements is calculated using the average value of TV given by the UWBP during the last 10 minutes.

Agreement between physiological parameters calculated by the jacket and IMP/UWBP is then evaluated on the whole dataset (merging all animals and all recordings) using the method described by Bland & Altman to calculate 95% confidence intervals on relative differences [2].

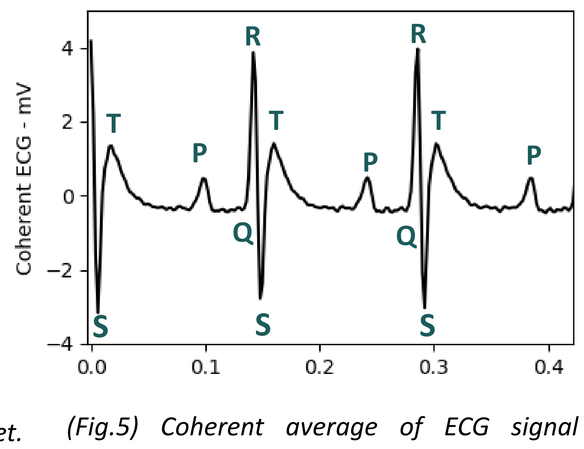
Results



(Fig.3) Agreement between DECRO and the reference measurements on the following parameters : (a) Respiratory Rate (cycle / minutes), (b) Tidal Volume (mL), (c) Heart rate measurement (beats / minutes). Abscissa represents the average value of the two systems and ordinates the average relative difference between the systems. The solid line represents the average difference between the two systems, and the dashed lines limits containing 95% of the differences.



(Fig.4) Typical instantaneous signals from the jacket. (a) Calibrated trunk volume variation from RIP. (b) External ECG recorded.



(Fig.5) Coherent average of ECG signal recorded with the jacket calculated on 5 cardiac cycles. Q,R,S,T,P points marked.

- Jacket is easy to set up and can be worn by the animals for several hours without clinical signs or abnormal behaviors thanks to an acclimation protocol before experimentation
- External ECG traces showed low noise recordings with distinct QRS complex associated with visible P and T waves as shown on Fig4.b and marked in coherent average on Fig.5. Rip recording enable proper respiratory cycle detection and snoozing is well measured as visible on the right part of the RIP signal shown on Fig.4.a
- B&A analysis between methods shows for HR an agreement of ± 3,8% (14bpm), for RR and agreement of ± 15% (19bpm) and TV agreement of ± 21% (0,3 mL) as shown on the Fig.3.b

Conclusions and discussion

- **Monitoring standard cardiorespiratory parameters in freely moving rats using this new connected jacket exhibits high agreement with reference methods (IMPLANT and UWBP).** TV measurements agreement of 21% is comparable to a previous comparison study of the jacket versus invasive pneumotachograph in anesthetized animals that had shown a 20% agreement [3].
- **This new jacket is accepted by the animals and easy to set up. It helps to refine, simplify and fasten procedures.** This non-invasive measuring approach reduces the number of animals required as they can serve in multiple experiments.
- **Non-invasive measurements are equivalent to implantable telemetry and plethysmography to evaluate cardiorespiratory functions in unrestrained rats.** Therefore, this external telemetric system is a valuable tool to monitor physiological parameters and endpoints in safety pharmacology studies as well as to integrate cardiorespiratory endpoint during in toxicological studies.

Références

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