Intrapleural Pressure Monitoring Using Telemetry Implants in Rats: A New Approach for Dynamic Pulmonary Function Assessment.

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Micro-abstract

We validated a novel telemetry-based method to continuously monitor intrapleural pressure and respiratory patterns in conscious rats.
This approach mirrors plethysmography results while eliminating the need for restraint or acclimation.
It enables real-time, longitudinal assessment of respiratory function during both baseline and disease challenge conditions.

Introduction

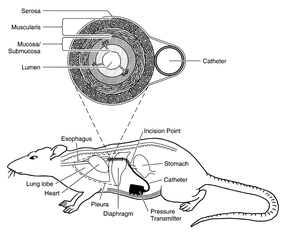
Accurate assessment of respiratory function is critical in preclinical studies for evaluating the potential effects of new therapies on lung function. Traditional methods present significant challenges: Plethysmography requires extensive animal acclimation and offers limited insight into dynamic respiratory pattern changes. In this study, we aimed to address these limitations by utilizing telemetry implants in rats, enabling continuous, non-terminal monitoring of intrapleural pressure and respiratory parameters. This approach parallels plethysmography, and adds the critical dimension of real-time, longitudinal monitoring. Following baseline characterization, we proceeded to multiple challenges to confirm the sensitivity of the method in physiological and pathological conditions.

Methods

Ten (10) male adult Sprague-Dawley rats weighing 250-300 grams were anesthetized using isoflurane, and PTA telemetry probes (EMKA Technologies) were implanted. The pressure catheter was inserted from the abdomen, through the diaphragm and into the thoracic cavity, beneath the esophageal serosa. Post-operative monitoring ensured stable signal quality. Telemetry recordings of intrapleural pressure, heart rate, body temperature, and activity levels were obtained continuously from conscious animals. To validate the sensitivity of the method, parallel plethysmography measured breathing rate and tidal volume. Respiratory patterns were also examined in response to acute respiratory challenges using *E. coli* lipopolysaccharides (LPS), capsaicin, and hypoxia.

Pressure Probe Implantation

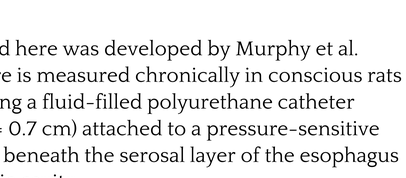
The method described here was developed by Murphy et al. (1998). Pleural pressure is measured chronically in conscious rats by surgically implanting a fluid-filled polyurethane catheter (length = 10 cm; O.D. = 0.7 cm) attached to a pressure-sensitive telemetry transmitter beneath the serosal layer of the esophagus and within the thoracic cavity.



Under isoflurane anesthesia, an abdominal incision is made along the linea alba. The esophagus is isolated approximately 2 cm below the Hiatus oesphagicus (junction with the diaphragm). A 22-gauge needle (1 inch in length with an approximate 90-degree bend) is inserted into the esophagus between the serosa and muscularis layers and the needle is tunneled cranially into the thoracic cavity (see above) to a point approximately 1 cm beyond the diaphragm junction. The fluid-filled catheter from the telemetry transmitter is advanced up the channel.

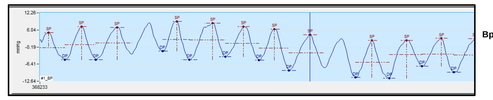
Plethysmography

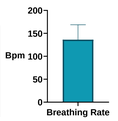
Animals were acclimated to the plethysmography chambers (EMKA) for at least 30 minutes on two separate days prior to data collection. On the day of recording, the rats were placed individually in calibrated chambers maintained at 22–24°C, and pressure transients were continuously recorded for 60 minutes post-challenge with LPS, capsaicin or hypoxia (if applicable). Tidal volume (TV), respiratory rate (RR), and minute volume (MV) were derived. Only periods of stable breathing without grooming or exploratory activity were selected for analysis. Data were averaged over 3-minute segments per animal.



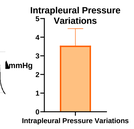
Physiological Monitoring

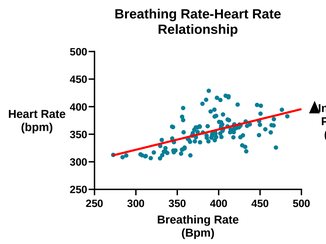
Telemetry signal for intrapleural pressure

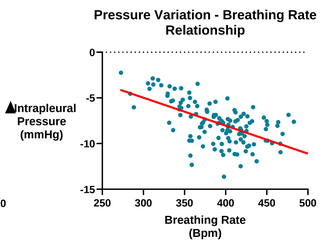




Whole-body plethysmography signal – same animal

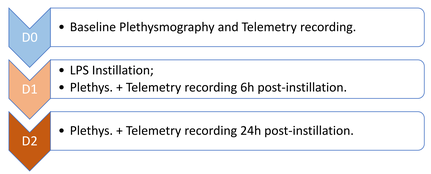


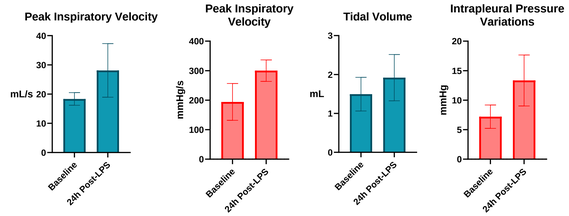




LPS Challenge

Experimental Design:

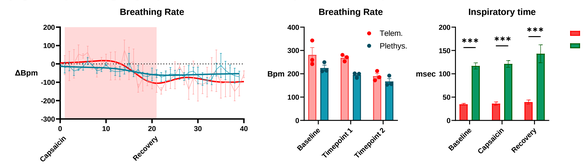




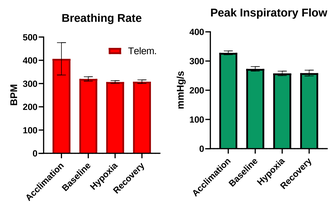
LPS was administered by intratracheal instillation (5 mg/kg). Plethysmography ( ) and telemetry ( )monitoring revealed increases of 36% and 35% in inspiration velocity and increases in tidal volume and pressures.

Capsaicin and Hypoxic Challenges

Capsaicin (30 µM) was administered by nebulization over 10 minutes, following a 10-minute baseline. 10 minutes of recovery were monitored by plethysmography, while telemetry was always on.



Both methods picked up the apparent slowing of the breathing, with longer inspiratory times during recovery. Overall, however, capsaicin did not induce significant changes in breathing in the rats.



Ambient O_2 levels were lowered from 21 to 10% for 1 h, followed by a 1-hr recovery period. Intrapleural pressure telemetry captured significant decreases in breathing rate and inspiratory flow.

Conclusion

Intrapleural implantation of telemetry pressure probes was found to be a reliable modality to monitor changes in breathing rate and general breathing mechanics.

- Variations in intrapleural pressures mirrored the changes in pressure captured by whole-body plethysmography.
- With dual-pressure or pressure + ECG probes, it is possible to monitor the positive correlation between breathing rate vs. heart rate, and the negative correlation between intrapleural pressure and breathing rate.
- Changes in breathing depth (air velocity) and tidal volume are similar when the animals are challenged with LPS.
- Similarly, breathing rate changes caused by capsaicin or hypoxia and captured by telemetry, mirrored those captured by WBD.
- WBD captured respiratory pauses, whereas intrapleural probes did not.

While both techniques are reliable, they are more complementary than a replacement for one another.

REFERENCE: Bouchard, A., Salvail, D. (2024). Respiratory Function as a Safety Concern in Drug Development. In: Hock, F.J., Pugsley, M.K. (eds) Drug Discovery and Evaluation: Safety and Pharmacokinetic Assays. Springer, Cham. https://doi.org/10.1007/978-3-031-35529-5_65