3R Benefits of Using Star-Oddi Micro-HRT for Monitoring Temperature and Heart Rate in Group Housed Laboratory Mice

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PROBLEM

The laboratory mouse is the most common animal model used in scientific research. It has genetic similarities to humans, they can be easily genetically modified, they have short life cycles and fast reproduction. They are cost-effective and manageable with well-established regulatory and ethical framework.

Longitudinally collecting, quantifying, and analyzing cardiovascular (heart rate) and metabolic (temperature) data in group-housed, freely moving, awake experimental mice has been historically challenging. Current technologies (ie., some telemetry) remain very limited in capability due to size constrain not present in larger animals such as NHP and rats and are also often cost-prohibitive.

This study explores the benefits, data quality and practicality of implanting Star-Oddi DST micro-HRT data loggers that were originally designed for laboratory rats into laboratory mice to monitor body temperature and ECG derived heart rate (HR).

The data loggers store all data on-board the loggers and enable users to measure without any housing or group restriction such as metabolic chambers, individually ventilated cages (IVC), transport or even

APPROACH

Animals: Eight (n=8) 10-12 week-old male C57BL/6 mice were used in a series of two trials.

Mice were implanted with Star-Oddi micro-HRT loggers Figure 1 (left) for recording of heart rate and body temperature data, then returned to pair-housed home cage on a 12:12h light cycle.

Physiological recordings were taken every minute at 773Hz over 7 days and at the end of the study the mice received a 1mg/kg isoproterenol injection to elicit a maximum heart rate response Figure 1 (right).

The power spectral density (PSD) of the ECG signal was calculated and compared to previously recorded data from rats to better understand the processing of the ECG data.

Finally, two surgical approaches were tested on 4 animals each, tethering the logger to the skin and subcutaneous implantation without tethering.

Figure 1: (Left) DST micro-HRT (3.3g), (right) example of location of logger, group housed animals that received an Isoproterenol injection in the end of study to elicit maximum heart rate.

OBSERVATIONS

It was possible to record ECG derived heart rate in mice using the DST micro-HRT loggers see Figure 2. The quality of the recordings was assessed using raw ECG data and manual annotation and compared to on-board HR calculations and their associated quality index (QI); 0 (Best) to 3 (Worst) for periods with lights off (active) and lights on (resting). Validated HR ranged from 343bpm to 804bpm see distribution for 1108 manually validated records and 45557 algorithmically calculated records in Figure 3. This data was compared to previously presented data on laboratory rats [1] see Figure 4. In this study recordings with quality index 0 and 1 considered reliable within the HR range of 300-850bpm. No difference was found between quality in sutured vs. non sutured loggers with data retention between 59% to 73%, about 10-15% lower than what is typical in rats. These quality estimations furthermore revealed as expected that accuracy was the greatest during daytime when animals are mostly resting while at night time they are highly active as can be seen in Figure 5.

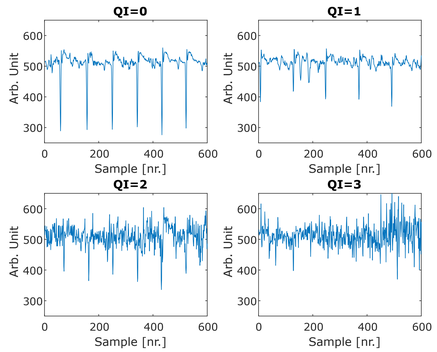

Figure 2: Example of ECG recordings and QI (Quality Index) from one of the loggers

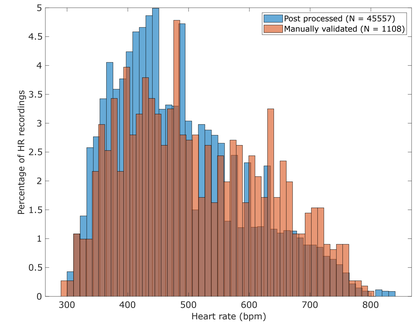

Figure 3: Distribution of the heart rates from both on-board algorithm and manually validated records

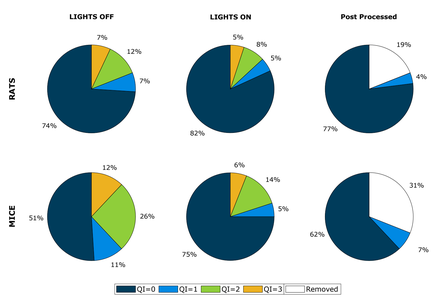

Figure 4: QI distribution from the study compared to a previous study that used the same device on laboratory rats

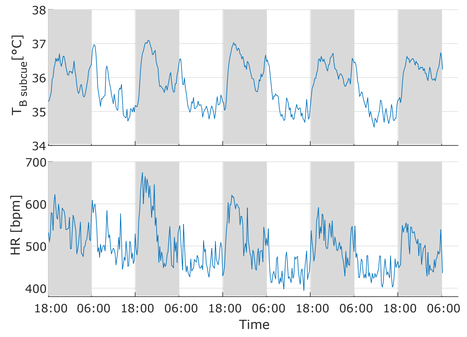

Figure 5: Overview of subcutaneus body temperature and heart rate (HR) for the study. Data is presented as 15min average from all animals (n=8).

The data in Figure 5 is plotted as 15min average and the correlation between heart rate and temperature was calculated and compared to previously recorded data in laboratory rats. That revealed good correlation although slightly lower than in the rats see Table 1 and Figure 6. When adding data from the Isoproterenol experiment (Figure 6 in green) it highlights periods where HR and body temperature are not correlated.

Relationship	R^2 - Lights OFF	R^2 - Lights ON
T vs HR - RATS	0.54	0.77
T vs HR - MICE	0.41	0.46

Table 1: R^2 relationship between 15min average temperature and heart rate

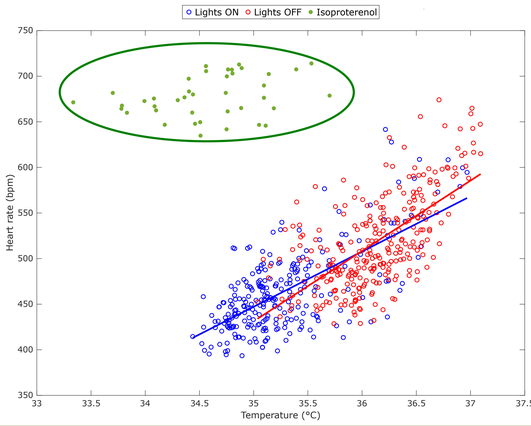

Figure 6: Relationship between 15min average temperature and heart rate (n=8) during lights on (blue) and lights off (red). The data in green is 15min average of individual animals after isoproterenol injection

No significant difference was found between logger types, with average amplitude of the QRS waveform ranging from 13-20% FS. Power Spectral Density (PSD) estimation (Figure 7) revealed high variability between animals that warrants further investigation but also significantly higher frequency content then rats with peak content from 50-120Hz while rats are 20-60Hz.

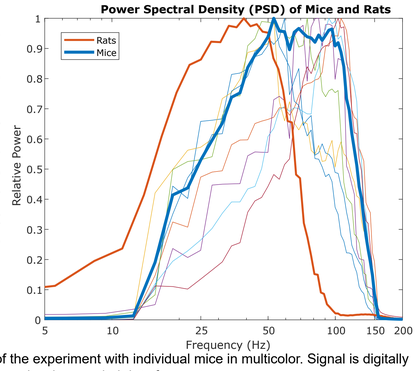

Figure 7: Average Power Spectral Density (PSD) of the experiment with individual mice in multicolor. Signal is digitally bandpass filtered from 30-130Hz and compared to previously recorded data from rats.

CONCLUSIONS

1. It is possible to collect heart rate and body temperature data in group-housed mice using the DST micro-HRT loggers
2. The quality of the ECG and heart rate data needs validation to discover best practices of programming and implanting the device
3. Although quality is considered slightly lower than in laboratory rats, 69 % of HR data is verified as correct
4. Compared to traditional telemetry, the loggers don´t offer continuous ECG collection, however the loggers offer further refinement of reduced surgical duration and invasiveness.
5. Elimination of any restriction with cage type or group-housing creates opportunities for a novel study system.
6. Unexpected events with high HR can be identified through the relationship between temperature and heart rate
7. We found no difference between anchoring the logger to the skin or not

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Citations: [1] Long term measurements of temperature, activity and heart rate in laboratory rats using data loggers as minimally invasive and low-cost screening too. Bjarnason A, Kreuser S, Cunio T, Bernal J. (2022) Society of Safety Pharmacology Annual Conference