Long term measurements of temperature, activity and heart rate in laboratory rats using data loggers as a minimally invasive and low-cost screening tool

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BACKGROUND
Preclinical safety pharmacology and toxicology studies use several tools such as Implantable telemetry and jacketed external telemetry to evaluate 24-h endpoints. There exists a need that enables cardiovascular (CV) screening using minimally invasive and low-cost solutions.

OBJECTIVES
Leashless data loggers from Star-Oddi were explored as an alternative to traditional telemetry for three typical physiological signals: temperature, heart rate and activity for three weeks. Correlation between signals was compared, quality of HR estimated and physiological response to a series of husbandry and protocol-defined activities occurring during light cycle events were evaluated.

METHODS
Data was used from twelve laboratory rats, implanted subcutaneously with two data loggers on the flank of the animal, one on each side. One data logger measures temperature and ECG derived heart rate (DST micro-HRT) implanted on the right side and one measures temperature and accelerometer derived activity (DST micro-ACT), implanted on the left side (see Fig 1). Both devices measured for 20 days with an 8-minute fixed sampling interval (Fig 2). The heart rate measurement is from ECG recording sampled at 700Hz for ~1 sec (Fig 4). The activity measurement is based on an average from 3-axis accelerometer measurement recorded over 1 minute at 1Hz. Animals were individually housed under 12:12 light:dark cycle, in Techniplast cages with food and water ad libitum.

RESULTS
Heart rate recordings were processed based on quality index (QI) and threshold. Recordings with QI=0-2 were eliminated and HR above 600bpm and below 140bpm were deleted from the dataset. This provided an average of 81.5% of all HR data recorded being used (see Fig 3). The logger with the highest quality provided 96% of reliable HR recordings while lowest quality was 42%. Fig 4 shows the QI distribution where QI=0 is the highest quality and QI=3 is the lowest quality ECG recording.

Fig 2: Raw data from a single animal, showing body temperature (top), HR (center) and average activity (bottom) for 20 days. 12h:12h light cycle is showed in gray.

Fig 3: QI distribution for the heart rate recordings, (left) Lights off, (center) Lights on and (right) the post processed data.

Fig 4: Example of the ECG signals recorded and how the QI is reflected for one data logger.

Average daily waveforms (20d) and cosinor rhythmometry was calculated (see Fig 5) from the raw data for the three variables, for all the animals (n=12). The rhythm characteristics are presented in Table 1. HR acrophase was 23:45 followed by temperature at 0:05 and Activity at 0:45.

Fig 5: Average daily waveform (± SD) for all the animals (n=12) of body temperature (°C), heart rate (bpm) and Activity - AvgEA (mg) throughout the experiment. The broken red line shows the cosinor fit.

Table 1: Mesor (the rhythm-adjusted mean), Amplitude (the difference between the peak and mesor) and Acrophase (the timing of peak value reacouring).

FINDINGS & CONCLUSIONS
1. Weak correlation between the variables indicates added information not revealed by heart rate alone.
2. The animals are most active during the dark (Lights OFF) cycle creating a more complex assessment then during the resting light (Lights ON) cycle.
3. Compared to traditional telemetry, the loggers don’t offer continuous ECG collection, however
4. As a CV screening tool the loggers offer further refinement of reduced surgical duration and invasiveness.
5. Extended battery capacity and elimination of any restriction with cage type or group housing creates opportunities for a novel study systems.

Table 2: R² relationship between daily temperature and heart rate, daily temperature and activity - AvgEA and (C) daily recorded Activity - AvgEA and Heart Rate.

Fig 6: Violin plots for all raw heart rate recordings during lights off and lights on (top) and individual violin plots of heart rate for each animal during a study activity that took place during daytime (bottom).

Individual study activities were visualized with violin plots and compared to routine values (Fig 6) while circles represent median values HR (bpm) OFF = 388bpm, HR (bpm) ON = 332bpm. Bottom plot shows a 2.5h time period while the activity took only 45 minutes. Median value for the group was 376bmp with ten out of twelve animals reaching heart rates of 500bpm or more.