Equivalency Validation of a Novel Freely Moving Animal Based Telemetry System versus a Stationary Cage Bound System for Blood Pressure Recordings

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ABSTRACT

- **Equivalency Validation of a Novel Freely Moving Animal Based Telemetry System versus a Stationary Cage Bound System for Blood Pressure Recordings**
- Traditional rodent blood pressure (BP) monitoring required single housing, a known stressor for rodents. We developed a microprocessor based long range wireless telemetry system with large internal memory that allows rodents to live in groups, interact, exercise and be housed in large enriched environments. BP is recorded with a solid-state sensor along with core temperature and 3D axial activity within the implant. The measurement protocol is transmitted once to the programmable implant via a single room antenna mobile base station. The implant becomes an autonomous recording device until contacted again by the base station with an updated protocol. The implanted animals are thus allowed to undergo procedures, leave the room or be subject to other tests while the recording is running. Data can be automatically downloaded periodically within the protocol.
- In order to objectively validate this system we contracted a study with the Michigan State University INVIVO facility. 8 male SD rats of 275g were implanted with a model PTA-M TSE Stellar telemetry implant. After 8 days of recovery the animals entered a crossover study and were dosed with vehicle, 3, 10, and 100 mg/kg L-NAME or Verapamil at t=0 hrs. BP was recorded for 10s hourly for 24hrs sampled at 200Hz following drug administration. The BP responses were compared to a control group of 8 animals implanted with a similar conventional implant from a competitor. Drug responses were qualitatively the same between the groups. Mean arterial pressures (MAP) at +12hrs in the 100 mg/kg LNAME group with the TSE implant increased by 26±11 versus 26±9 mmHg in the control group. MAP in the 100 mg/kg Verapamil group at +12 hrs dropped by 31±9 versus 20±6 mm Hg in the control group. Baseline MAP was significantly elevated to 118±5 versus 92±11 in the control group with the conventional implant which may account for the blunted verapamil response.
- We conclude that there are no significant differences in quantitative blood pressure responses to L-NAME or Verapamil in animals implanted with a TSE Stellar device versus a leading competing device. We also conclude that the short hourly recordings used for the TSE device produced equivalent MAP values while significantly prolonging implant battery life, thus extending possible study length.

Author Disclosure Information:
H. Knot: A. Employment; Significant; TSE Systems Inc. ; G. Miller: A. Employment; Significant; TSE Systems Inc.
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Topic : Blood Pressure Monitoring
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BACKGROUND

Wireless transmission of key physiological parameters such as blood pressure, ECG, activity and body temperature in group housed freely moving animals provides the best possible experimental condition to study regulation of blood pressure including the effect of pharmacological interventions.

Legacy telemetry systems suffer from the limitations of older analog technologies including cross-talk between animals, sensor drift, limited wireless range and expensive hardware infrastructure , often not compatible with modern experimental cage and housing conditions as needed in order to meet or follow current animal welfare regulations.

OBJECTIVES

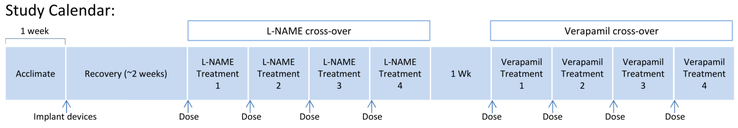
- Develop an economical digital telemetry system for physiological monitoring of (blood)pressure, ECG, Temperature & animal based activity, featuring:
- Larger wireless range, no cage-bound antennas and “out-of-range” data logging” capabilities.
- Unique digital animal specific ID with no possible cross-talk between individuals
- Miniaturization, use of solid-state sensors for pressure readings
- Seamless scalable technology from small rodent to large animals
- Allowing group housing of animals

METHODS

To validate this system, we implanted 8 male Sprague-Sawley rats of ca. 220-250 g BW with a model PTA-M telemetry implant (TSE Systems) followed by a two week recovery period. 2-week post-surgery, baseline hemodynamic data were collected for approximately 2 hours (10 seconds every 10 min). Vehicle (0.5% methylcellulose) or L-NAME was administered at 3, 10, or 100 mg/kg by oral gavage in a dose volume of 10 mL/kg in a cross-over design according to the Treatment Schedule below. A 6-day washout period was allowed between doses. Following the completion of the 4th L-NAME Treatment and washout, an additional 1-week washout was allowed and animals were then administered verapamil by oral gavage (at 0, 3, 10, and 100 mg/kg; dose volume of 10 mL/kg) in a cross-over design according to the Treatment Schedule below. A 6-day washout period will be allowed between doses. In each instance, hemodynamic data were collected for 10 sec every 10 min for 2 hours prior to dosing through approximately 24 hours following dosing.

The blood pressure responses were compared to an equal group of animals implanted with a competitor legacy model BP rodent implant using the same protocol from an earlier study. The competitor implant recorded continuously, sampled at 100Hz and data were averaged per hour.

Study Calendar:



RESULTS

Table: Drug response at 12 hours (TSE: PTA-M; Legacy Rat BP transmitter)

Drug mg/kg	Heart Rate BPM		Mean Arterial Pressure mmHg	
L-NAME	TSE Stellar	Competitor	TSE Stellar	Competitor
0	404 ± 38	413 ± 10	90 ± 16	104 ± 7
3	405 ± 38 (Δ 0)	410 ± 22 (Δ -3)	98 ± 22 (Δ +8)	107 ± 8 (Δ+3)
10	394 ± 30 (Δ -10)	403 ± 45 (Δ -10)	98 ± 16 (Δ +8)	116 ± 13 (Δ +12)
100	345 ± 31 (Δ -59)	383 ± 31 (Δ -30)	116 ± 11 (Δ+26)#	130 ± 9 (Δ +26)#
Verapamil				
0	393 ± 18	396 ± 14	92 ± 11	118 ± 5
3	393 ± 37 (Δ +1)	391 ± 18 (Δ -5)	89 ± 11 (Δ -3)	116 ± 5 (Δ -1)
10	353 ± 40 (Δ -40)	391 ± 29 (Δ -5)	84 ± 20 (Δ -8)	115 ± 5 (Δ -3)
100	363 ± 6 (Δ -30)	373 ± 27 (Δ -23)	61 ± 9 (Δ -31)§	97 ± 6 (Δ -20)§

Drug responses were qualitatively the same between the groups (n.s.).

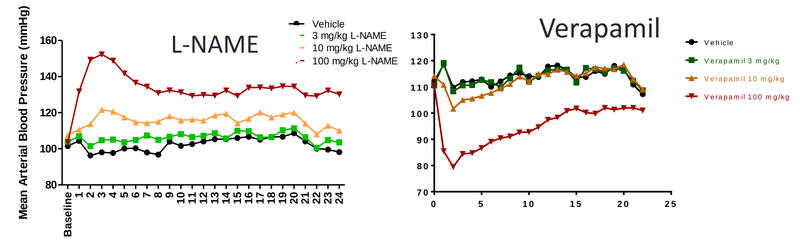
#Mean arterial pressures (MAP) at+12hrs in the 100 mg/kg LNAME group with the TSE implant increasedby 26±11 versus 26±9 mmHg in the control group.

§MAP in the 100 mg/kg Verapamil group at +12hrs dropped by 31±9 versus 20±6 mm Hg in the control group. Baseline MAP was significantly elevated to 118±5 versus 92±11 in the control group with the conventional implant which may account for the blunted verapamil response.

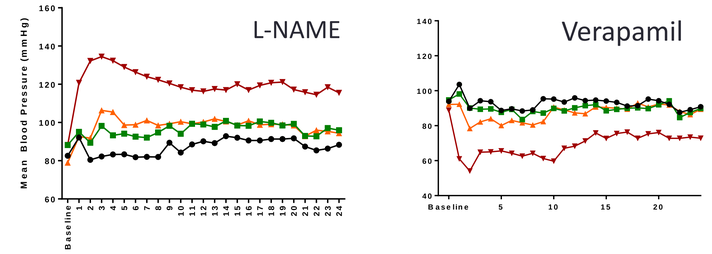
RESULTS

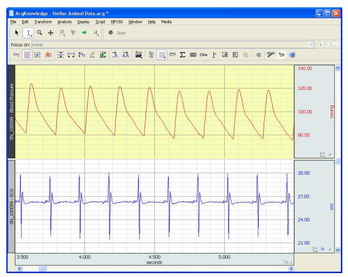
Graph: Mean arterial drug response to increasing dose L-Name and Verapamil during 24 hours (0,3,10,100 mg/kg)

Legacy Rat BP transmitter



TSE Stellar transmitter: PTA-M





- TSE Antenna/Receiver & Stellar transmitter model PTA-M (170g+), SW Screenshot

CONCLUSIONS

We conclude that there are no significant differences in quantitative blood pressure responses to LNAME or Verapamil in animals implanted with a TSE Stellar device versus a leading legacy device.
We also conclude that the short hourly recordings used for the TSE device produced equivalent MAP values while significantly prolonging implant battery life. This greatly extends possible study length at lower operating cost.