Evaluation of Shipping Stress in Surgically Altered Rodents During Commercial Air Transport

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Planes, Trains and Sometimes Automobiles

- When establishing our Global Surgical program, we looked for solutions that would keep projects moving forward.
- A need arose on the west coast for telemeterized animals.
- The strain and model was not available on the west coast.
- There was hesitation to shipping a surgical model over the road.
- Why can't we fly?causes too much stress on the animals.
- How could we measure physiological indicators of stress during shipping?
- Continue our partnership with Charles River (CRL)









Background

- Understanding shipping stress of surgically altered rodents is relevant to animal welfare as well as the science and research that these models support.
- The changes in normal physiological parameters associated with shipment related stress can affect scientific validity and consequently alter study results.
- This study focused on heart rate, which is one of the physiologic parameters previously documented and associated with stress.
- Based upon this assumption, increased heart rates would be correlated with increased stress.
- Many stress evaluation studies include cortisol levels.
 - Cortisol levels were not included in this study because the effects of stress and the associated levels have previously been researched extensively and documented in the literature.
 - Previous publications are used to guide the assessment of the data for our conclusions with respect to cortisol levels.





Background

- Pfizer outsources the production of many rodent surgical models.
 - At this time, the only approved method for shipment is by ground courier due to concerns about the impact of shipping stress on the animals.
 - Transit time can sometimes take up to four days from origin to destination.
- There is limited published information on the duration of physiological stress indicators during the time before, during, and after transportation.
 - Data has never been collected during shipping in rodents.
 - Discovered a novel device that would allow us to focus on physiological data during travel
 - Evaluate stress in rodents following surgery, in relation to time of shipment and acclimation
 - Assist in establishing guidelines for humane shipping post operatively.
- We focused this investigation on the departure from supplier to landing at destination.
 - However, data was collected for 14 days.
 - Future presentations







Star Oddi Device

- Key Features
 - Small size- only 3.3g
 - Long battery life typically over 3 months
 - Depends on data collection
 - Automatic stress-free measurements
 - Leadless, minimally invasive
 - The DST micro-HRT simultaneously measures long term heart rate and temperature in the study animal.
 - The logger has no external wires, which makes it especially simple to implant.
 - Made of unique ceramic housing and epoxy and is hermetically sealed.







Star Oddi Device

- Data collection
 - ECG derived heart rate, including data verification
 - The heart rate is derived from a leadless single channel ECG.
 - The logger takes a burst measurement of ECG at the set time interval and calculates the mean heart rate for each recording.
 - For validation purposes, individual ECG bursts can be saved. In addition each burst is graded with a QI (quality index).
 - Heart rate is recorded every 2 minutes based on a 1 second ECG measurement.







Materials and Methods

- All procedures involving animals were in accordance with regulations, and established guidelines. They were reviewed and approved by Pfizer and CRL's Institutional Animal Care and Use Committee.
- Star Oddi DST micro-HRT data logger devices were utilized to evaluate heart rate and temperature in rodents from the time of surgery to delivery and acclimation.
- Surgical procedures were performed at CRL Raleigh.
- Twelve male, 8-10 week, variable weight, CRL CD Sprague Dawley rats were used.
 - Group A (n=6) control group data logger implants only.
 - Group B (n=6) Surgery group jugular catheter and data logger implantation.





Surgical Description

- Anesthetized with ketamine (75 mg/kg) and xylazine (6.0 mg/kg) administered intraperitoneally and provided buprenorphine (0.02 mg/kg) subcutaneously.
- The jugular vein was isolated and ligatures were placed using non-absorbable suture material.
 - A phlebotomy was made in the jugular vein, a polyurethane catheter was inserted, and secured with ligatures.
 - The data logger was subcutaneously tunneled to the left chest (close to apex of the heart).
 - The extravascular portion of the catheter was tunneled subcutaneously to the dorsal scapular region.
 - The catheter was locked with heparinized dextrose solution and the skin incision was closed using a subcuticular suture.







Post Surgical Activities

Significant events as well as behavioral observations within the housing room were recorded.

- Immediately following surgery, assessments were completed daily as per CRL guidelines.
 - Monitored for pain and healing
 - The behavioral observations recorded evaluated movement, posture, body condition, respirations, and other parameters.
- Day 3
 - Body weight assessment and Physical exam was performed.
 - Animals were packaged for shipment.





Surgery to Packaging

- Animals undergo surgery and recover smoothly
- Animals maintain normal rhythm •

Comparative Medicine

Minor effect on Surgery group





Comparison Surgery to Packaging

- Increased heart rate of surgical group noted
- Body temperatures were similar with no significant differences.





Day 4 Day of Travel



Approximately 29 hours of travel time Packaged 17 hours prior to departure 46 hours of box time



3:41	Depart CRL			
4:41	Processed in at airport (2 hour 30 minute layover)			
7:17	Loaded onto plane			
7:30	Departed for Los Angeles			
9:40 (12:40)	Arrive Los Angeles (5 hours 10 minutes flight)			
10:07 (13:07)	Checked into Los Angeles (4 hour 36 min layover)			
14:43 (17:43)	Loaded onto plane for San Diego			
15:58 (18:58)	Departed for San Diego			
16:12 (19:12)	Arrive San Diego (19 minute flight)			
16:39 (19:39)	Checked into San Diego			
17:15 (20:15)	Arrive at warehouse			
17:16 (20:16)	Checked into warehouse (Held over night 15 hours)			
08:10 (11:10)	Delivered CRL SAN			
(PST) (EST)				





Travel Day







Shipping Departure Raleigh to Los Angeles

- HR begins to increase and reaches peak at 1 hour into flight.
- Body temperature decreases throughout flight





Shipping Departure Raleigh to Los Angeles

- Significant increase in HR During flight
- Significant decrease in body temperature during flight





Surgery Versus Control Group Differences

Surgical group body temperature decreased during the initial shipping period



	Depart CRL to Loadin	Load on plane/travel	Check in at Los Ange	Load in LA travel to
Surgical	-0.55	-1.08	0.05	0.16
	(-1.03, -0.08)	(-1.66, -0.50)	(-0.31, 0.42)	(-0.40, 0.73)

Surgical group showed a 56 bpm increase compared to the control group



Heart Rate : Fitted treatment differences from Vehicle (95% C.I.)

	Depart CRL to Loadin	Load on plane/travel	Check in at Los Ange	Load in LA travel to
Surgical	17.7	55.9	18.5	4.3
	(-47.0, 82.4)	(12.0, 99.8)	(-38.1, 75.1)	(-69.9, 78.4)





Flight Temperatures in Transport Box





Packing for Shipment to Un-Packing at Delivery

- Packaging to unpacking which is 10:00am on 12/18 through 10:00am on 12/20 •
- Increased HR and decreased temperature during flight through unpacking
- Surgery group temperatures are slow to normalize after flight





Receipt to 72 Hours Post Delivery

- Establishing normal rhythm within 24 hours
- Resting heart rate of surgery group remains higher through 72 hours







Surgery to the End of Study (14 days)







Summary

- Behavior
 - All animals appeared normal through the study
 - Normal rhythm observed at 24 hours post delivery
- Body weight
 - Animals met expected weight gain
- Heart Rate
 - Statistically significant increase in HR during flight to LAX
 - Surgical group difference of 55.9 BPM
 - Surgical group maintained a higher peak HR through day 8 post surgery
 - Surgical group resting HR normalized at day 13 post surgery
- Temperature
 - Significant decrease seen during air shipment
 - Synchronized with increased HR
- While Surgical group animals did experience significantly higher heart rates, they did appear to recover quickly after the flight
- No long-term adverse effects were seen with air shipment





References

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