Don't Miss a Beat – Understanding Continuous, Real Time Physiologic Monitoring: Webinar Q&A Report

1. Can DSI sensors be used in human research? *Dusty*

    a. *No, DSI sensors are only intended for, and approved for, use in animals.*

2. Do I need a Faraday Cage for EEG recordings with the telemetry system? *Steve*

    a. *It depends on your recording environment. We've had examples where laboratory study rooms have a great deal of electrical interference and we've had to shield walls. We typically use stainless steel shielding around our rodent cages, but the main purpose is to minimize "cross-talk" between adjacent transmitters rather than to create Faraday-like shielding.*

3. For sleep studies, do you use automated scoring or does someone manually score the data? *Steve*

    a. *We use a combination. Due to the large number of studies we run simultaneously across all species, we've found that automated scoring gives a good balance between accuracy and speed. For studies where the effects might be small and/or there is a higher precision of accurate sleep scoring, we'll hand score sections of the recordings.*

4. Have you evaluated EEG and/or other CV parameters in the evaluation of infectious agents? Any additional consistent trends aside from decreased body temp and increased HR? *Anna*

    a. *Although I have not looked at EEG in the models I've used, I believe this is an important area for future expansion. Many of the viral biodefense agents cause encephalitis or encephalopathy during acute disease or survivor sequalae. This includes the alphaviruses (Chikungunya, as well as EEEV, WEEV, and VEEV), Rift Valley Fever virus, and the arenaviruses (such as JUNV and LASV). This would be particularly interesting for those viral models that may not be uniformly lethal, but have observed/reported neurological signs, as a possible differentiating biomarker. Regarding other parameters, in my experience, blood pressure and respiratory rate also correlate with outcome (decreasing and increasing, respectively).*

5. Is heart rate dysregulation in infected Nonhuman Primates a common feature? What causes it? *Anna*

    a. *Yes, heart rate dysregulation appears to correlate with lethal disease progression in most of these viral disease models. Initially, we see normal diurnal patterns in heart rate (HR)*

and blood pressure (BP). Heart rate begins to increase shortly after fever occurs, and usually remains high until the NHP are euthanized or succumb − HR dysregulation may also be observed in NHP that survive exposure; however, these animals eventually return to a diurnal pattern. Depending on the virus, HR dysregulation may be a direct effect of the viral infection (myocardial infection/viral antigen has been noted; examples include some orthopox models, arenaviruses, and Rift Valley Fever Virus), or an indirect mechanism as the body attempts to compensate for dehydration or fever. Also, there are a number of soluble mediators that can affect cardiac function (such as interleukin 6, nitric oxide, Fas or FasL, etc) that might be stimulated in response to viral infection.

6. What is the negative impact on animal physiology after implantation of transmitter(s) for a long time/duration? *Dusty*

    a. *Several studies have been conducted over the years in small and large animals implanted with DSI telemetry products, including physiology as well as gross and microscopic pathology endpoints. As long as rigorous aseptic surgical techniques are utilized, these effects have been shown to be minimal. Heart rate, blood pressure and body temperature returns to normal, with normal circadian fluctuations, within several days to 2 weeks postoperatively. Histopathology changes are limited to slight arterial endothelial changes at the site of the pressure sensing catheter tip and a thin fibrotic encapsulation of the device body, catheters and wires. Several toxicologic pathologists have stated that these changes aren't problematic, even in nonrodent repeat dose toxicology studies.*

7. Can you provide an example of a cardiovascular research application that would benefit from continuous monitoring of physiologic endpoints? *Dusty*

    a. *Any experiment where there is an interest in short term responses that might be lost by taking only samples of continuous data. Also, the observation of sporadic changes, such as spontaneous arrhythmias that might be lost if only samples of data are acquired. Even if all of the data are not reviewed, they may be retrieved from archival later if a situation arises. This is analogous to pathologists evaluating individual slides and going back to the original fixed specimens to further investigate a suspicious finding.*

    b. *Any experiment where an intervention is required in response to a detected effect. This could be either a trigger to treat in the case of an efficacy study or to ensure timely humane euthanasia in the case of severe adverse effects, whether anticipated or not. These two scenarios are common in biodefense or chemical defense studies, as described by Dr. Honko.*

8. How long can you continuously record sleep data from your research subjects? *Steve*

    a. *For pre-clinical studies we record for 24-hours per day across 2-3 weeks in a cross-over or latin-square dosing paradigm. For clinical research, it depends on the phase. Phase I safety studies typically record for approximately 24-hours for each subject at each dose, while Phase II and III may only record for the duration of the sleep period (8-10 hours) for each subject at each dose.*

9. How do you manage OR what data reduction techniques do you use to manage the large quantities of data you presumably accumulate from multiple channels of EEG/EMG/ECG recorded chronically from all study animals? *Steve*

   a. *For the data directly saved from the DSI equipment, we don't currently have any techniques for data reduction; we bite the bullet and store all of the data on corporate-sized data storage servers. We do then process the data to create smaller binned or grouped data which are more amenable to graphing and statistics applications, so in theory we could then delete the original data. The scenario that seems to pop up from time-to-time, is when a new algorithm, or new analytic technique emerges and without the raw data, there's no way to evaluate it. For this reason, we've kept all of our raw data.*

10. Have you been able to use the real-time telemetry signal to refine euthanasia criteria when dealing with very sick animals? *Anna*

    a. *Yes, telemetry has been central to refining our objective euthanasia criteria, currently we are using body temperature in combination with cageside scoring (but individual investigators should determine using their models). When using telemetry for developing euthanasia criteria, it has been essential that the system is easy to use for both the PI as well as the technician – since these will be rapid paradigm-based decisions that should be as simple as possible to execute. Also, equipment and software should be robust to ensure there will not be failures during critical study phases. For studies where the FDA Animal Rule may be used for approval, the endpoint needs to be related to what the investigator is trying to do – and since this is usually survival for us, using telemetry has given us better defined euthanasia criteria that are less subjective.*

11. When working with bacterial agents, does the way in which you use telemetry to conduct your studies differ (from working with viral agents)? *Anna*

    a. *The telemetry usage is not particularly different – although not discussed in this presentation, real-time telemetry monitoring has played a critical role in the development of animal models for bacterial diseases such as inhalational anthrax (Bacillus anthracis), primary pneumonic plague (Yersinia pestis), and tularemia (Francisella tularensis). Similar physiological parameters are measured, such as fever, heart rate, and blood pressure and these can be applied to the evaluation and approval of antibiotics (for example, the approval of Ciprofloxacin for plague via the FDA Animal Rule).*

If you have additional questions for DSI regarding content from their webinar or wish to receive additional information about their telemetry products and laboratory services please contact them by phone or email:

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