Webinar Q&A Report:

Using Touchscreen Operant Systems to Study Cognitive Behaviors in Rodents

Q: What age of mouse would you recommend for using a task like the 5CSRTT?

JULIE: The literature reports using mice aged from 3 months to 9 months, at the beginning of training. It is recommended to minimize the age range of the cohorts tested to reduce potential age-related variability.

Q: How much time do we have to wait from the end of the session to give them the daily 2h of water?

JULIE: It is recommended to feed and water animals immediately after a session. This way they get to associate being fed with doing the tasks.

Q: Do you know of any researchers who are working with Swiss mice (CD1)?

JULIE: Currently we only know of the strains sited in the webinar presentation.

Q: Are there any webinars being planned specifically about the 5CRSTT task? What resources are available for training and learning?

JULIE: There are no webinars planned specifically on this task at present. At Lafayette, we always provide training paradigms and advise with the tasks. The following paper also gives a lot of information on training the rodents:

Mar AC, Horner AE, Nilsson SR, Alsiö J, Kent BA, Kim CH, Holmes A, Saksida LM, Bussey TJ. **The** touchscreen operant platform for assessing executive function in rats and mice. *Nat Protoc.* **2013** 1985-2005.

Q: Do you have to have the Bussey-Saksida chambers inside isolation chambers?

JULIE: We can provide the chamber without the isolation chambers but research has found animals learn and perform better in the isolation chambers as it limits other distractions.

Q: What kind of pellets can be used for food?

JULIE: Generally we recommend dustless precision pellets for rats. Sucrose dustless pellets are favoured by some researchers. These can be purchased from BioServ or Research Diets. For mice we recommend a strawberry milkshake liquid reward.

Q: Please elaborate on how the touch is actually detected by IR?

MATT: The touchscreen has a series of very thin Infra Red (IR) beams over the surface of the monitor in both the horizontal and vertical directions. When the animal "touches" the screen, it is actually bringing its nose or paw close enough to the monitor to interrupt these beams. The touchscreen detects the location by determining specifically which beams are interrupted in both the horizontal and vertical directions and reports the coordinates for the touch. For the mouse version the IR beam array is stood off from the glass to provide more of a 'nose poke' rather than a 'touch' response thus allowing more natural behavior of the mouse.

Q: How are you doing the set shifting - what are the modalities of the cues?

JULIE: Set-shifting is not a finalised task at present. We know that Cambridge University have done some work on this, but we do not have details at present.

Q: Can you provide references for tests-brain areas please?

JULIE: Yes, please contact us for a current Bibliography

Q: When doing Pavlovian conditioning, it is possible to extract the following dependent variables at the same time: responses to the stimuli (number and duration) and responses to the reward dispenser?

JULIE: Yes our ABET Touch software will record approaches to the screen, touches to the screen and entries into the reward tray. Number and duration of the responses can all be extracted from this data.

Q: Will the screen get scratched while the mouse is touching the screen?

MATT: No, the touchscreen has a glass surface and will not scratch from use with mice or rats

Q: How do you train a rat to touch the screen?

JULIE: Initial training is to get the rodent to associate an image on the screen with reward, by displaying an image and following this with a reward delivery. Once the animal is freely collecting the reward, we move onto a paradigm were the animal must touch the screen to get reward delivery.

Q: I would imagine the temperature within the chambers gets rather high during training. Is it possible to increase ventilation? Any other suggestions for temperature control?

MATT: The sound attenuation chamber has a fan located on one side of the chamber as well as a passive vent on the side opposite. This provides four full air changes per minute. The monitor does produce a small amount of heat, but this is not significant enough to raise the temperature inside the chamber with the standard ventilation and air change over rate provided. Additional ventilation could be added, however, this would compromise the sound and light isolation qualities of the enclosure.

Q: Is it better to train animals on the sPAL task before training them on the dPAL? What is the best order?

JULIE: sPAL is a probe test used to assess whether the animals form specific object-location associations, as opposed to acquiring a set of trial type specific conditional responses. The currently used approach is to run two sessions of sPAL following stable performance on the dPAL. This is detailed in the following paper:

Horner AE, Heath CJ, Hvoslef-Eide M, Kent BA, Kim CH, Nilsson SR, Alsiö J, Oomen CA, Holmes A, Saksida LM, Bussey TJ. The touchscreen operant platform for testing learning and memory in rats and mice. *Nat Protoc.* **2013** 1961-84.

Q: How long does a typical training session take (days/weeks)?

JULIE: This does vary from task to task. Please refer to the table shown in the presentation

Q: Once a group of animals are trained, does it apply for several (other) Testing paradigms?

JULIE: Most of the tasks do have similar training paradigms. It is not necessary to repeat all these stages when moving onto a new task. We would recommend just repeating the last stage of the training with the appropriate mask. When the criteria is met, then move onto the new task.

Q: Can the system be integrated with wireless headstages?

MATT: Yes, the touch chamber can be integrated with wireless headstages. The electrophysiology compatible versions of the touchscreen chambers have noise reducing shielding as well as additional I/O to synchronize with either tethered or wireless recording systems.

Q: Does the food magazine being located on the other side of the chamber risk the animal not looking at the screen for stimuli shown for a short duration?

JULIE: With the Lafayette chambers the food magazine can be either at the rear of the chamber, or in front of the screen. For most of the tasks, however, it is important that the rodent sees all the available images before approaching them, and for that reason most of the tasks have the food magazine situated at the rear. Pre task training gets the animal used to the images appearing when the animal initiates a trial by nose pokes the magazine, so they generally look to the screen straight away. Trial initiate usually occurs when the animal leaves the magazine (i.e. a Nose Poke in to the magazine and then when leaves the magazine).

Q: Can your equipment replace the traditional "Novel Object Recognition" test in mice?

JULIE: Some work has been done to make a touchscreen version of the Novel Object Recognition:

Carola Romberga, Alexa E. Hornera, Timothy J. Busseya, b. Lisa M. Saksidaa, b. A touch screen-automated cognitive test battery reveals impaired attention, memory abnormalities, and increased response inhibition in the TgCRND8 mouse model of Alzheimer's disease. *Neurobiology of Aging* **2013** 731-44.

However, we do not at this stage consider this to be a task good enough to replace the traditional Novel Object Recognition task.

Q: If we intend to integrate a Touch screen system with another system (like optogenetics), what type of resources are available to assist with setup up? Also, is there technical support or training from your company to help integrate these systems?

MATT: The best option for integration may depend on the type and brand of system you are integrating. Tethered optogenetics systems pose a unique obstacle with the delicate fiber optic cable. The length of cabling needs to provide enough slack for the animal to freely move everywhere in the chamber while also not restricting movement or bending too tightly causing the cable to break. The best option is to discuss the integration with the support team at either Lafayette Instrument or Campden Instruments. We can provide instructions for integrating components or quote onsite assistance.

Q: We used wild-type and mutant mice on the C57BI/6 background in most of our studies at Synome and at Charles River. We also used recombinant inbred strains that derived from crossing of C57BI/6 and DBA mice (BxD mice). Is there anything we need to consider as it pertains to the Bussey-Saksida system with these strains?

JULIE: C57BI/6 mice are the most widely used strain with the touchscreen and they perform well. Some work has been done comparing the C57BI/6 and DBA mice in the rCPT task:

Kim CH, Hvoslef-Eide M, Nilsson SR, Johnson MR, Herbert BR, Robbins TW, Saksida LM, Bussey TJ, Mar AC. The continuous performance test (rCPT) for mice: a novel operant touchscreen test of attentional function. Psychopharmacology 2015; 232

Q: During the pre-training period, how should we train animals so that they will not touch the blank screen? This is quite an important step before we can move on to the training of a specific task. Correct?

JULIE: Animals can show some preference for the blank windows in the mask, so training them not to touch these areas does help with the tasks that have blank windows alongside the images. For this reason, many of the tasks have a training period that punishes blank window touches with a timeout period.

Q: How do you compare the speed of training for your 5-CSRT task to the same task implemented in a traditional nose-poke setup? Is 'nose-poking' the touchscreen as intuitive to mice as traditional nose-poking?

JULIE: Having a very sensitive touchscreen and using masks to create individual response areas makes training to the touchscreen very similar to training to nose-poke. It has even been reported that mice train more quickly on the 5-CSRTT in the touchscreen chambers than in nose-poke boxes:

Carola Romberga, Timothy J. Bussey Lisa M. Saksida. Paying more attention to attention: Towards more comprehensive cognitive translation using mouse models of Alzheimer's disease *Brain Research Bulletin* 2013 49-55

Q: Is it possible to distinguish nose pokes from unaware touches (e.g. of the tail during movement inside the chamber)?

MATT: The ABET II Touch software cannot differentiate between nose and tail touches, however, all the prewritten tasks use masks in front of the touchscreen to identify the specific response areas and prevent "unaware touches." The masks prevent nearly all tail touches as the response areas are raised above the floor and would require the animal to direct the tail into the response area like a nose poke. Some of the rat tasks use the upper part of the touch screen thus requiring the animal to rear up to respond, further eliminating the potential for any tail coming in contact with the screen.

Q: Is it possible to add a video camera to the chamber to record the behavior of the mouse?

MATT: Yes, the standard touchscreen systems have an option to include an IR camera for observation in each chamber. The video signals are then sent to a standalone DVR to allow users to record sessions.

Q: In 5CSRTT for mice, can I do more than one session/day to speed up the training?

JULIE: Work at Cambridge found that if you train the rodents twice a day, as opposed to once a day, they will still learn, but they take more sessions to reach criteria. They do not, however, take as many as twice as many sessions, so the time in days to train the rodents can be reduced.

Q: Can rats be trained to hold their nose in one of the touch screen response holes for, let's say 1-3s, before they are allowed to retreat out of the response hole to make another response in another response hole?

MATT: We have worked with researchers who have required a small dwell time at the touchscreen in order for a touch to be classified as correct. These dwell times were around 500 milliseconds. Increasing this dwell time requirement to 1 - 3 sec. would most likely require additional training and would of course be dependent on the rat strain being used.

Q: What is the cost of a system?

JULIE: This does depend on how many boxes are bought and whether you want to integrate with other systems such a video tracking, Optogenetics or Electrophysiology recording. If you would like a price please contact us, so we can discuss your requirements. Most researchers are pleasantly surprised at the price.

If you have additional questions for Julie Gill or Matt Croxall regarding content from their webinar or wish to receive additional information about using touchscreen operant systems to study cognitive behaviors in rodents, please contact them by phone or email:



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