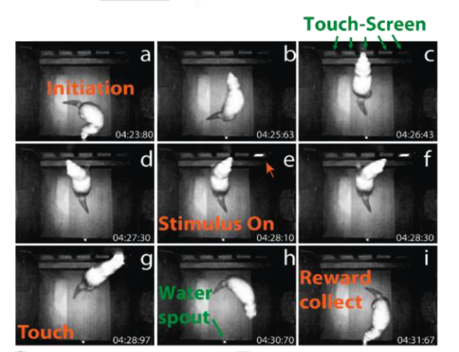
**Introduction**

In the field of neuropsychological testing, Continuous Performance Test (CPT) is commonly used to assess the efficacy of novel medication that treats schizophrenia and attention-deficit/hyperactivity disorder (ADHD).1 A 5-choice serial reaction time task (5CSRTT) is a CPT-like preclinical task developed to investigate attention.2 In the Frohlich Lab, studying the neural substrates of sustained attention is one of the core interests of study. In definition, sustained attention is a process that enables sustained performance on tasks over an extended time.3 Although scientists have investigated sustained attention for a long time in animal models, they cannot conclude its neuronal circuit and relationship to the thalamocortical network. Since that dysfunction of this process is associated with attention deficit and impulsivity in several psychiatric disorders, such as schizophrenia and ADHD,4 it is crucial to explore more about the mechanism of sustained attention. In the Frohlich Lab, a rodent version of 5CSRTT is applied to ferrets to investigate the causal role of higher-order thalamocortical oscillations in sustained attention via temporally-precise rhythmic stimulation. Ferrets are used in this research because they have more similar postnatal cortical folding to a primate, whereas rodents have lissencephalic brains, i.e., “smooth-brains.” Also, ferrets show the same thalamocortical alpha oscillations that are assumed to be defective in some human neuropsychiatric disorders.5 In the 5CSRTT, the animals need to detect short flashes of light that is in a pseudorandom manner and to make a correct nose-poke response to receive the water reward.6

The present version of 5CSRTT in the Frohlich Lab is performed in a behavior box. As shown in figure 1, the box includes five touchable screens on one side of the box. The ferrets are expected to wait on a shelf that is below these screens. The ferrets would wait for the stimulation after the initiation. On the opposite side, there is a spout where the water would come out after the animal making a correct touch. The animal can initiate the next trial by giving a lick on the spout when there is no water left on the spout.

Despite the behavior box has been used for several studies in the Frohlich Lab, there are some limitations and problems that remain unsolved. For instance, one limitation is that the behavior box requires direct human supervision when animal training is in progress. On average, it takes two months to train the animals to do the task before the experimental sessions can take place. To make the training process effective, researchers need to train each animal in the morning and the afternoon. Also, to make sure the animals are thirsty enough to complete as many trials with reasonable accuracy as expected, the researchers have to keep a four-hour leisure period without giving water between the morning and afternoon sessions. Additionally, body position is another problem that needs to be solved. The accuracy depends on the body position of the animal during the stimuli presentation, and the absence of controlling for body position devalues of the interpretation of the reaction time.2 At present, researchers can only determine the animal’s body position by the infrared camera post-recording, and they cannot control the body position during the task.

Figure 1. A paradigm of one training trial in the behavior box. **a** Initiation. **b** Turn around. **c** Wait on the shelf. **d** Look for stimulus. **e** Stimulus on. **f** Go for the stimulus. **g** Touch. **h** Water release. **i** Reward collect. (figure from the Frohlich Lab)

In this independent study, I intend to develop a modified signal detection task (SDT) box. In previous studies, it shows that the SDT reduces the training time.2 Earlier this year, the Frohlich Lab worked on making a prototype of an SDT box.7 In my project, I would modify the SDT box to allow the animals to train themselves to save human effort. Also, I would optimize the SDT for ferret training so that we can fix the animal’s body position and make the distance from the animal to the stimuli isometric so that the analysis of reaction time would be more valuable.

**Specific Aims**

Aim 1: Develop and improve the behavior box to control the animal’s body position.

I will improve the interface based on the animal need, and refine the design of the SDT behavior box for the animal use. The primary purpose of the redesign is to make sure that the distances from the animal’s waiting point to the signals to be isometric. In this way, the reaction time can be analyzed as a dependent variable as an indicator of animals’ attentional level without being confounded by the animal’s position.

Aim 2: Optimize the training system to achieve self-training.

I expect the modified behavior box to save human efforts. In the old 5CSRTT, direct human supervision is necessary because researchers have to make sure that there are at least four hours between each training session, for ensuring that the animals are thirsty to complete enough trials. I will adjust the code to enable the box to decide when to start one session and to end one. The goal is to minimize the level of human effort as much as possible in the training process. To achieve this aim, I would test each adjustment with the ferrets. This process will take time, and problems that have not yet been seen will emerge to the surface. I will fix the problems and make the modified box suitable for the animals to train themselves. Also, I will modify the code so that the box can automatically record the training process once the session begins. I will also make the box be able to identify the animal so that it can tag the animal I.D. to the data automatically.

Completion of these two aims will lead to a reduction of human resources inputs into the training process. It used to take half an hour to train each animal. After the application of the modified SDT behavior box, the researchers can take the time to do other tasks such as data analysis. My project will ensure an efficient environment. Besides, completion of these two aims will also make the reaction time data more valuable because my project will reduce the errors in the reaction time. What is more, we can achieve parallel training since minimal human supervision is needed for each animal. Also, it will be more self-motivated for animals when they are thirsty and mentally ready to do the task, while we decided when it is a good time for the animal to be trained before.

**Methods and Plans**

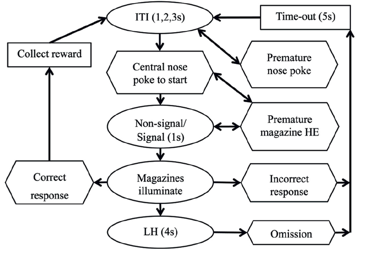
****The modified SDT behavior box is developed based on the standard SDT protocol (Figure 2). It is essential to review and improve the training aspect for the refinement of animal research.8 Instead of giving the animal signals and water reward on the opposite of the box (5CSRTT), I will reduce the range of motion for the animal that is required to complete the trial, not only for less time but also for better control of the animal’s position, easy learning of the task, and less miss trials due to animal turning back. To make the animals to train themselves, I will apply the knowledge of electronics, statics, and coding in the box-developing process. The prototype of the box has been made. In the process of polishing the box for the animal use, the mountings and non-electronic parts will be either made by a laser cutter or a 3-D printer. On the prototype, the animal would need to initiate the trial by pushing a button. It reduces the chance that the animal is not looking at the front panel when the stimulation is on. However, whether or not the animal is capable of pushing the button for a default time is unknown. The method to check the specification of the box is to test it with the ferrets. If it indicated that the ferrets were unable to put much force on the button, I would make an alternative of the button to meet the two requirements: to make the distances to the signals to be isometric and to make the animal always face the front panel. A lever system will be a solution to this problem. As discussed above, to make sure that the animals complete enough trials in one training session, there must be at least four hours between each session. This interval is one of the reasons why the old 5CSRTT requires direct human supervision. The optimization of the function of the behavior box will primarily be reflected in the code. The electronics in the box are all connected to an Arduino Mega 2560. The codes for training levels are pre-prepared, but I will write a code to let the box decide which code needs to be run based on each animal’s training progress and automatically send a message to the researcher to inform the researcher when the training starts/ends and information about the overall performance. Optimization of the SDT box will be an 8-month project. In the first three months, I will improve the mechanism of the box. In the fourth month, I will write a written report illustrating the design of the box, and I will write a user manual so that the box is standardized and reproducible to sure that every researcher can easily use my device to train animals. In the later period of my project, I will focus on code writing. I will infuse fundamental artificial intelligence knowledge to the box, and I expect the box to recognize the animal, to train, and to record automatically.

Figure 2. standard SDT protocol. The inter-trial interval (ITI) can be adjusted in the code on the basis of the research need. Limited hold (LH) refers to the time after which, if there was no response, counts as an omission. 2

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