

# Prefrontal Cortex Is Essential for Working Memory but Not Sensory Stimulus Discrimination

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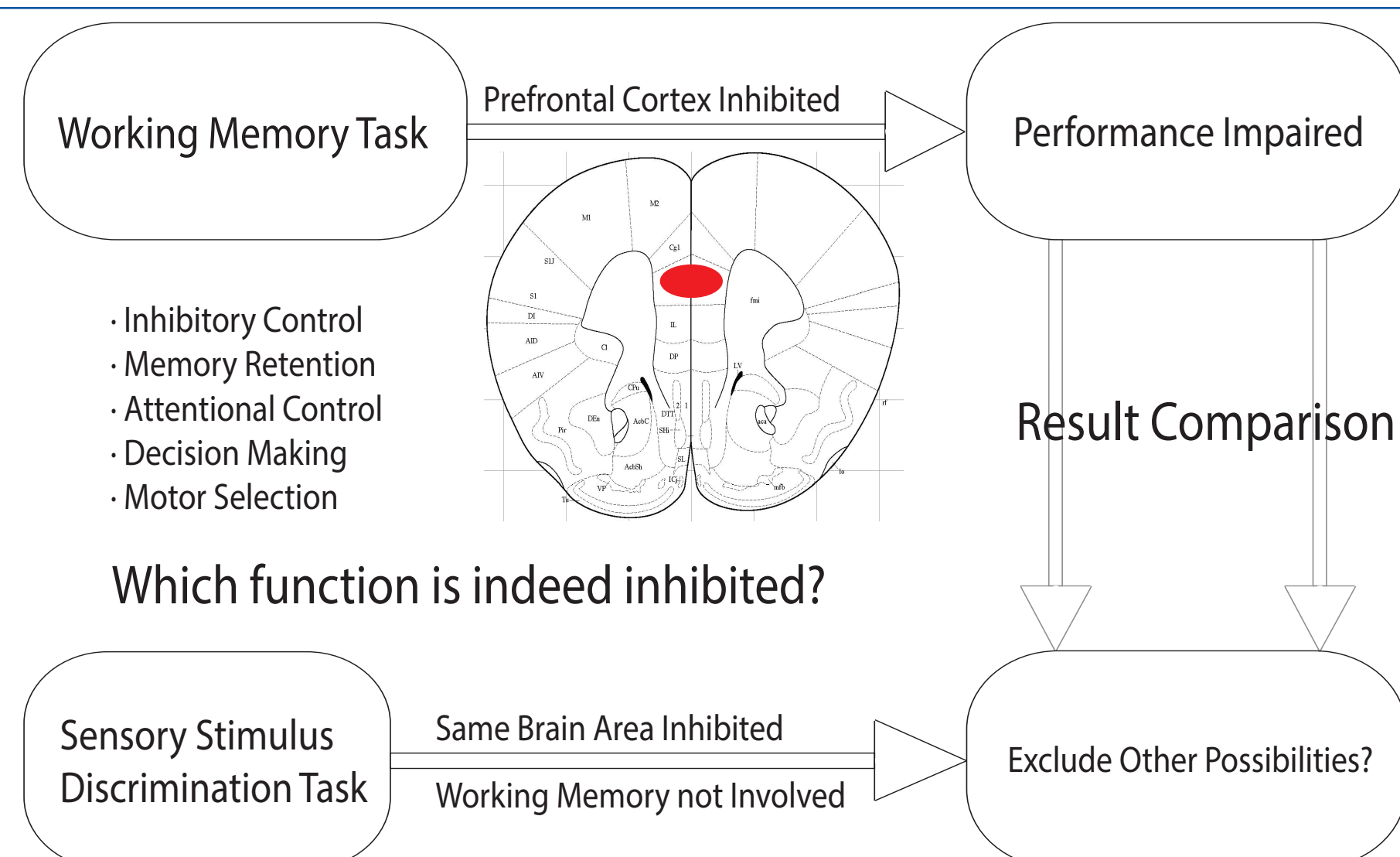
## Background

**Working Memory** A limited capacity memory that combines temporary storage and manipulation of information in the service of cognition.

**Prefrontal Cortex** is proposed to have the functions of: inhibitory control, memory retention, attentional control, decision making, motor selection.

**Previous study** has shown that inhibition of the prelimbic area within the medial prefrontal cortex in mouse brain impairs animals' behavior in designed working memory tasks, but whether the prelimbic area is essential for working memory or sensory stimulus discrimination remains unclear.

## Hypothesis

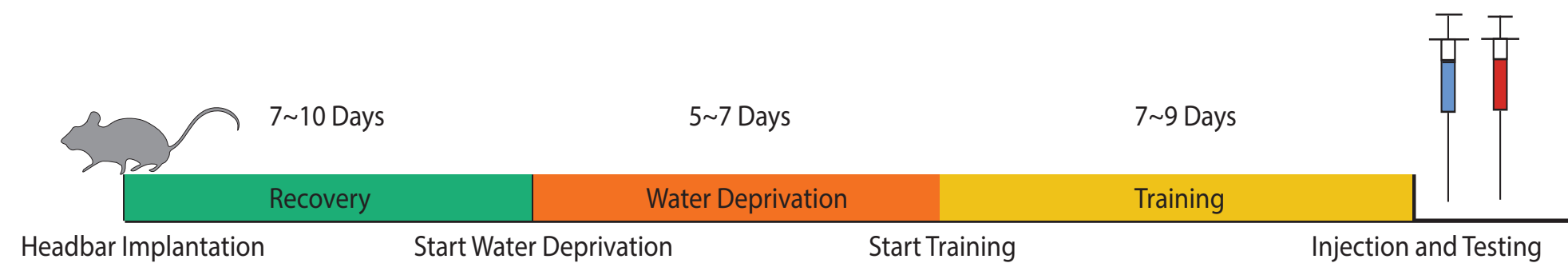


If the Sensory Stimulus Discrimination Task with no Working Memory involvement gives the same results, other functions might take place in the prefrontal cortex.

If the Sensory Stimulus Discrimination Task turns out that performance will not be impaired, the prefrontal cortex is essential for Working Memory processing.

## Methods

### Surgeries & Training Time-line



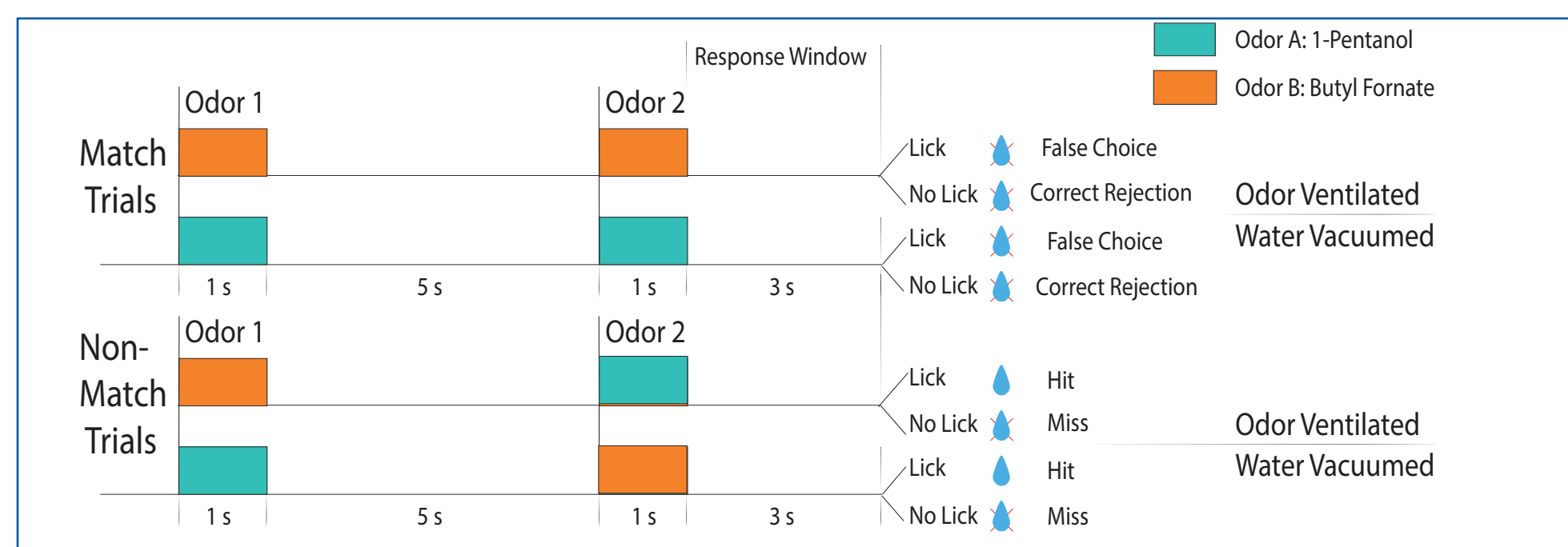
- Water Deprived Animals: water is presented as reward in tasks
- Training: animals are trained until tasks are completely learned
- Testing: performance is tested when the prefrontal cortex is inhibited

### Experiment Setup

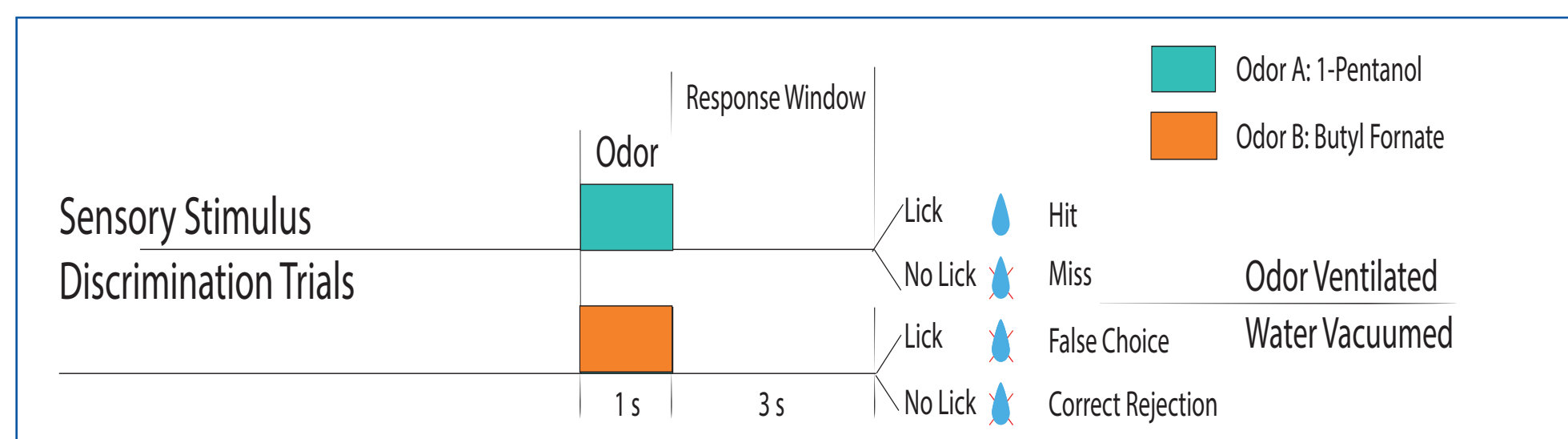


- Training and testing with the same setup
- Odors and water presented automatically according to task settings
- Quiet environment and good ventilation guaranteed

### Behavior Tasks



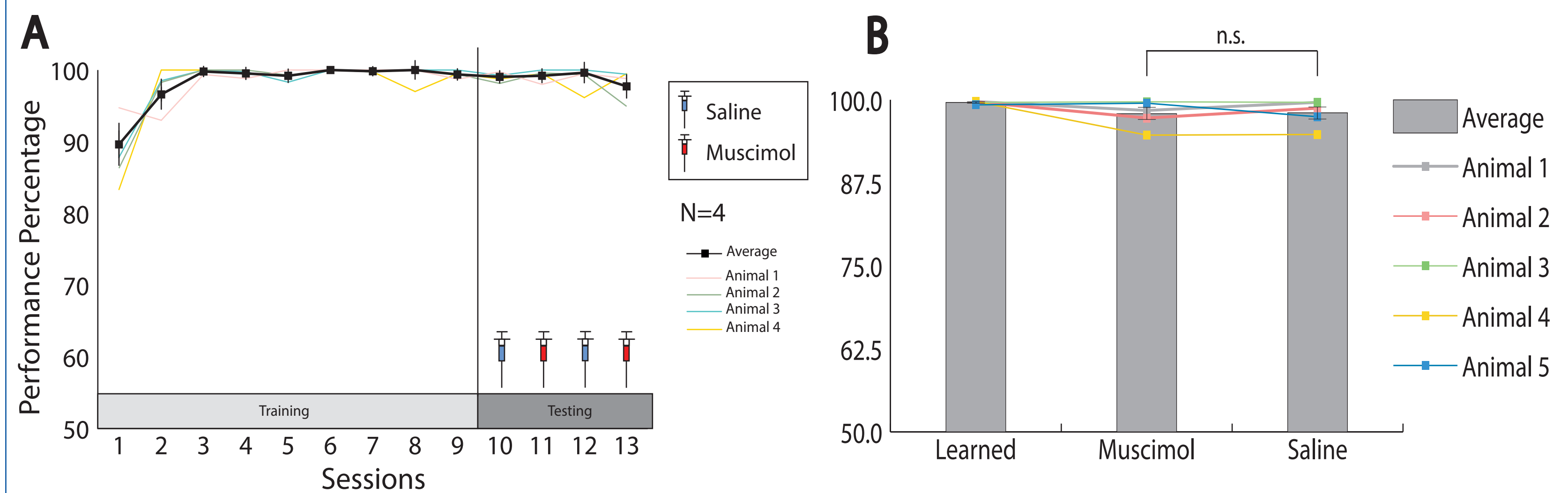
**Working Memory Task:** Animals are trained to lick only in non-match trials, water presented as reward for 'Hit' performance. Working memory is involved in these tasks.



**Sensory Stimulus Discrimination Task:** Animals are trained to lick only in odor A trials, water presented as reward for 'Hit' performance. Working memory is not involved in these tasks, but other cognitive and behavioral processing is maintained.

## Results

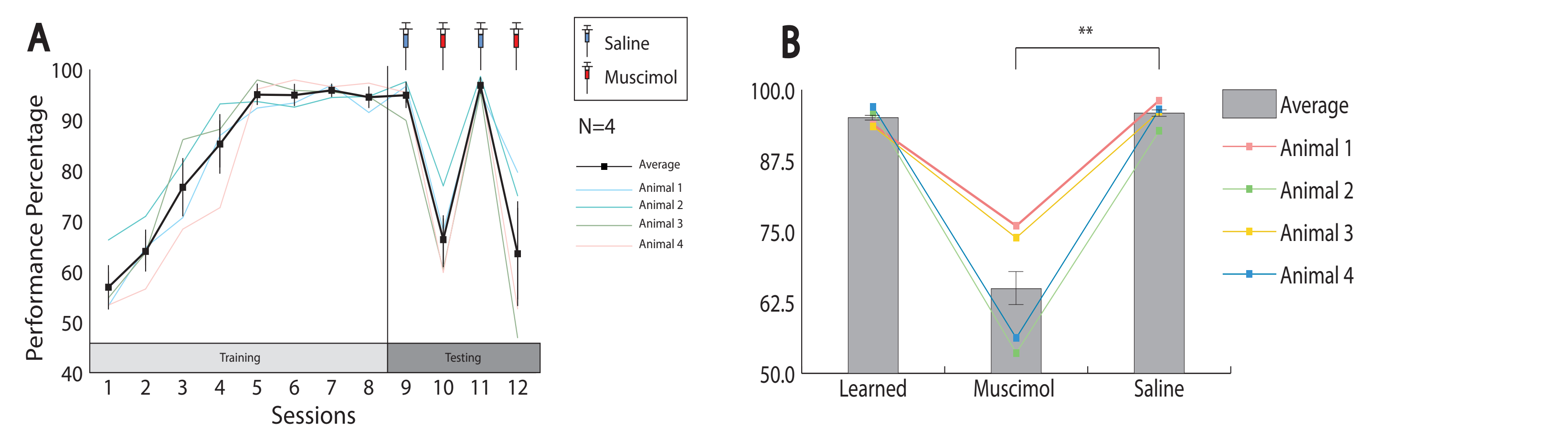
### Performance in Sensory Stimulus Discrimination Task



A. Performance of tested animals (n=4) in sensory stimulus discrimination task. In the first two sessions of training, only odor A is presented; in the following training sessions, animals are trained with two-odor sensory stimulus discrimination task (See Methods). In the testing sessions, the prefrontal cortex is injected with either Muscimol or Saline.

B. Comparison of animals' performance under different conditions (Learned: when sensory stimulus discrimination task is well-learned at the ending of training; Muscimol: animals are injected with Muscimol; Saline: animals are injected with Saline in the prefrontal cortex). No significant performance difference with the injection of Muscimol and Saline (p= 0.8407).

### Comparison of Performance in Working Memory Task and Sensory Stimulus Discrimination Task



A. Performance of animals (n=4) from previous study in working memory task. Inhibition of the prefrontal cortex impairs behavior (Red as Muscimol injection and blue as Saline injection).

B. Comparison of animals' performance under different conditions (Learned: when working memory task is well-learned at the ending of training; Muscimol: animals are injected with Muscimol; Saline: animals are injected with Saline in the prefrontal cortex). Significant performance difference with the injection of Muscimol and Saline: p= 0.004418.

C. Performance comparison between working memory task(WMT) and sensory stimulus discrimination task (SSDT).

D. & E. Anatomy of the prefrontal cortex with injection locations marked. (D. Prelimbic area of the pfrontal area (PrL) 1: Animal 1&3&4, +2.46AP, ±0.25ML, 0.60DV; E. PrL2: Animal 2&5, +1.98AP, ±0.50ML, 0.72DV. Orange dots: locations)

## Conclusion

Inhibition of the prefrontal cortex in mice impairs performance in working memory task, but not sensory stimulus discrimination task. Therefore, we confirmed that the prefrontal cortex is essential in working memory but not sensory stimulus discrimination.

## Future Directions

- Use cell type specific methods to target responsible neurons for processing working memory
- Use optogenetic tools to transiently manipulate the activity of the prefrontal cortex and look for the temporal window of working memory processing
- Look for the circuit basis and mechanisms of the prefrontal cortex in working memory processing

## References

- A. D. Baddeley, Working Memory (Oxford Univ. Press, Oxford, 1986)
- J. M. Fuster, The Prefrontal Cortex (Academic Press, London, ed. 4, 2008)
- D. Liu, et al, Medial prefrontal activity during delay period contributes to learning of a working memory task.Science 2014;346:458-463