Introduction

• Current attentional and decision-making literature uses reductionist methods to model neural mechanisms by which primates and rodents accumulate sensory evidence to make informed decisions
• Mante et al. uses a more complex task that required macaque monkeys to flexibly select and integrate visual information to make a decision
• Mante et al. had limitations, i.e. long training times and small sample sizes that are addressed in this thesis study with a high-throughput, computer-automated procedure to train rats more efficiently

Objective

• To understand the pathways by which realistic, complex decisions are made in the rat brain, with a particular focus in previously unexplored brain areas, i.e. FEF, striatum, and mPFC
• To compare rodent findings with parallel clinical tasks done with humans to expand our understanding of psychiatric conditions that require individuals to be flexible in shifting attention, e.g., autism, ADHD, Asperger's, and dementia

Surgical methods

• Animals: Adult male rats kept on a 12-hr reversed light-dark cycle, free access to food. Water access was limited each day to the rat’s training reward, in addition to 1 hour of free water after end of training
• Surgeries were performed under isoflurane anesthesia using standard stereotaxic technique. Rats were placed in an isoflurane induction chamber in which the isoflurane concentration was raised to 4%. Injections of ketamine (10 mg) and buprenorphine (0.006 mg) were given to provide analgesia and assist in induction. Hair over the skull was shaved, and rats were moved to a stereotax where 1.5-2% continuous isoflurane was delivered through a nose cone.
• Scalp was scrubbed with three rounds of betadine and ethanol, and subcutaneous lidocaine was injected at multiple locations across the skull. A midline incision was made to expose the cranium, which was then cleaned of all overlying tissue. A partial-depth hole was made using a Piezoelectric surgery system to secure a bone anchor screw. A separate full craniotomy was made to allow a silver ground wire to be inserted between the dura and the bone. Craniotomies and durotomies were made bilaterally above FOF

Multidimensional Paradigm

On each trial, rats will get 1s long visuo-auditory cue to discriminate either the prevalent frequency or location of a series of auditory pulses After cue, rats poke their noses into a wall hole. Trains of pulses of 5 ms are played for 1.3 s with both a frequency and location component
• Low-frequency (6.5 kHz) vs high-frequency (14 kHz)
• Played from left or right of the rat’s head
Rat receives water reward for selecting correct port depending on the trial cue and stimuli

Questions

• To what extent do frontal cortical regions, specifically the FOF, mPFC and the striatum, play a causal role in flexible decision-making tasks?
• Characterize the neural representation in the FOF, mPFC and striatum to understand how these areas independently select and integrate sensory information. In addition, there may be overlapping interactions amongst these regions as there are mutual neural connections that may form an unknown circuit for flexible behavioral outputs.
• To what extent are our rodent mechanistic findings comparable and applicable to parallel human paradigms?

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