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Current Biology

Dorsal Raphe Serotonergic Neurons Control Intertemporal Choice under Trade-off

Highlights

- Mice performed a novel odor-guided intertemporal choice task
- Manipulations of DR serotonergic neurons at the decision point regulated impulsive choice
- Effects of manipulations were most prominent under trade-off conditions
- The nucleus accumbens is a target for DR serotonergic neurons in regulating choice

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In Brief

Xu et al. optogenetically interrogate dorsal raphe serotonergic neurons in a novel odor-guided intertemporal choice task. They found that serotonergic neuronal manipulations bidirectionally regulated impulsive choice at decision point under choices involving delay-size trade-off.

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Dorsal Raphe Serotonergic Neurons Control Intertemporal Choice under Trade-off

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SUMMARY

Appropriate choice about delayed reward is fundamental to the survival of animals. Although animals tend to prefer immediate reward, delaying gratification is often advantageous. The dorsal raphe (DR) serotonergic neurons have long been implicated in the processing of delayed reward, but it has been unclear whether or when their activity causally directs choice. Here, we transiently augmented or reduced the activity of DR serotonergic neurons, while mice decided between differently delayed rewards as they performed a novel odor-guided intertemporal choice task. We found that these manipulations, precisely targeted at the decision point, were sufficient to bidirectionally influence impulsive choice. The manipulation specifically affected choices with more difficult trade-off. Similar effects were observed when we manipulated the serotonergic projections to the nucleus accumbens (NAc). We propose that DR serotonergic neurons preempt reward delays at the decision point and play a critical role in suppressing impulsive choice by regulating decision trade-off.

INTRODUCTION

Intertemporal choice is decision about future outcomes that are differently delayed. Impulsive choice, the preference for more immediate but smaller rewards, is associated with a number of maladaptive behaviors [1–4] and psychiatric disorders [5–8].

Serotonin has been well studied in intertemporal choice paradigms with lesion and pharmacological methods and is thought to promote the choice for larger, more delayed reward [9–11]. Due to the low temporal resolution of such techniques, it has been difficult to pinpoint how serotonin performs this function. We reasoned that, since many intertemporal decisions are carried out before action or outcome materializes, and are often prompted by conditioned stimuli (CSs), neuronal activity causally driving decision making should occur at cue. Indeed, recordings of optically tagged dorsal raphe (DR) serotonergic neurons in a Pavlovian task showed that some of them fired phasically to reward-predicting cues [12]. We, therefore, hypothesized that this phasic activity of serotonergic neurons could be used to direct choice at the decision point with the presentation of a CS.

To test our hypothesis, we needed a behavioral task that isolated a clearly defined decision point [13]. To this end, we devised a novel odor-guided intertemporal choice (OGIC) task that randomizes reward delay contingencies trial by trial, in the fashion of existing odor-based rodent decision tasks [14–16]. Randomizing reward contingencies ensures that a decision has to be made on every trial, and the use of odor cues allows the isolation of a decision period for temporally precise neural manipulations. We then systematically tested mouse subjects on decisions between a large reward and a small one that were differently delayed while optogenetically activating or suppressing DR serotonergic neurons during the decision period in a random subset of the trials. Our findings suggest that serotonergic neuronal activity suppresses impulsive choice at the decision point under trade-off conditions, possibly via action in the nucleus accumbens (NAc), another structure-implicated impulsive choice [17–20]. We propose that serotonergic neurons play a crucial role in resolving reward delay and size trade-off under decision conflict.

RESULTS

Mice Can Use Odor Cues to Choose Sooner or Larger Rewards

We conducted the task in a custom-designed operant chamber with a center odor port and two side reward ports. Subjects initiated each trial by nose poking into the odor port and sampled a mixture of two odors. After cue sampling, mice could respond by choosing to nose poke in either reward port (Figure 1A). After a reward delay, a water reward was delivered in the chosen side port. A predetermined trial duration was set to the same length, regardless of the chosen reward option, so that subjects could not perform more trials over a given period of time by choosing the less delayed reward. All