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Research article

Neural representation of cost-benefit selections in medial prefrontal cortex of rats

Hua Tang[a,b], Xuan Sun[a,b], Bao-Ming Li[b], Fei Luo[b,*]

[a] School of Life Sciences, Nanchang University, Nanchang, 330031, China
[b] Center for Neuropsychiatric Diseases, Institute of Life Science, Nanchang University, Nanchang, 330031, China

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ABSTRACT

Decision making refers to the process that subjects use to choose between competing courses of action based on the expected costs and benefits of their consequences. However, few studies have addressed the neuronal mechanisms behind the processes of how costs and benefits influence decision making. Here we investigated the neuronal representation of costs and benefits towards a goal-directed action under a differential reward schedule by training rats to perform a "Do more, get more" (DM-GM) task utilizing a nosepoke operandum, where longer nosepoke durations resulted in correspondingly larger rewards. Our results showed that the cost a rat pays can be expected from the activity of neurons located in the medial prefrontal cortex (mPFC). These findings indicate that mPFC activity is predictive of the subjects' costs and benefits, providing mechanistic insights on this mental calculation.

1. Introduction

Decision theory proposes that subjects decide what to do in a given situation by assessing the relative value of each possible response. Accordingly, each course of action is perceived as having its specific advantages and disadvantages. For e.g., a larger or more palatable reward may be gained only after a longer time elapsed or a greater effort invested. Subjects must learn to evaluate the costs and benefits of potential actions and bias choices toward more valuable options for optimal survival [27,34]. Recently, neuro scientists have elucidated aspects of the mechanisms through which benefits or rewards influence decisions [29]. Conversely, behavioral ecologists are interested in the effect of different costs, including delay, effort and risk on decision making in humans and animals [20,40]. To date, however, few studies have addressed the neuronal mechanisms through which such costs and benefits influence decision making.

Neuropsychological studies of human and animals have implicated multiple sub regions of the prefrontal cortex (PFC) in mediating certain decision making processes [2,9,13]. Some reports suggest that lesions of the orbitofrontal cortex (OFC) increased the percentage of time the small immediate reward was chosen, thereby influencing how long rats decided to wait for rewards [18,21]. Additionally, another study reported that destruction of the anterior cingulate cortex (ACC) biases rats' decision making so that they are cost-averse, choosing smaller rewards with smaller efforts [36].

There are also several reasons to believe that rats' mPFC might also be important in motivating cost-benefit decisions. Firstly, mPFC lesions or in activation shifted the animals' decision criterion [8,37] and decreased the willingness to expend cognitive effort [12,31]. Secondly, single-unit recordings have shown neuron responses in this region that differentiate between high and low reward sizes [14,26]. A series of studies showed that neural activity in the mPFC reflects stimulus detection, action timing, and outcome monitoring [15,16,19]. Thirdly, accumulating evidence suggests that a cortico-limbicstriatal circuit that involving the mPFC, basolateral amygdala (BLA) and nucleus accumbens (NAc) is involved in decision making [5,32,40]. These structures are regulated by major dopaminergic and serotonergic afferents, and pharmacological manipulations of these systems affect decision making in rats [3,17,30,33]. However, it is uncertain what, if any, role mPFC plays in cost-benefit decision making task.

The current study was set out to address these questions by employing a self-paced behavioral paradigm called DM-GM task. The animals were required to initial a freely-timed nosepoke response and consequently obtain a water reward proportional to the nosepoke duration at the reward site. The duration of nosepoke depended solely on the animal and was not specifically aligned to any external motivation. In our previous study, we revealed that there is a "balance point" of cost and benefit that exists in the valuation system of rats [34]. In the present study, we have examined how neuronal activity in the mPFC represent cost and benefit in DM-GM task.

* Corresponding author.
E-mail address: luofei@ncu.edu.cn (F. Luo).

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2. Materials and methods

2.1. Subjects

Twenty 5-week-old male Sprague-Dawley rats weighing 140–160 g were used as subjects. They were randomly grouped and individually housed at 21 °C in a 12 h light/dark cycle (lights on at 7:00) climate-controlled vivarium, and experiments were conducted between 9:00 and 17:00. All rats were handled, 5 min/day/rat, for 7 days before the training began. Water was restricted to ~85% of their ad libitum body weight gradually following the handling process. During the experiment period, every subject was free to drink for 10 min after performing the daily task, and their body weights were monitored daily. All procedures were conducted in accordance with the *Guiding Principles for the Care and Use of Laboratory Animals* (NIH, 1996). All experiments were approved and monitored by the Ethical Committee of Animal Experiments at the Institute of Life Science, Nanchang University.

2.2. Behavioral apparatus

The rats were trained in the apparatus shown in Fig. 1A. The DM-GM arena is a gray plastic chamber (70 cm × 25 cm × 25 cm) with an open top. There is a semi-circular hole with a diameter of 2.5 cm at 10 cm height of one wall. Outside the hole, there is a pair of infrared detection devices. Once a rat poked its nose into the hole, the infrared ray would be interrupted and 10 cm away from the nosepoke wall, there is a pair of infrared detection devices on both sides of the training apparatus 3 cm above the floor that the rat must pass through. At the bottom center of the opposite wall, there is a reward receptacle, connected with a valve through a tube. Once the rat arrives at the reward receptacle and interrupts the infrared ray, the appropriate amount of water would be delivered.

2.3. Behavior protocol

2.3.1. Pre-training stage 1

A group of three to four water restricted rats were placed in the chamber and allowed to explore freely. Once one of the subjects probed its nose into the nosepoke hole for more than 30 ms,a slight tone with gradually increasing frequency will sound and the apparatus would deliver 100 μl water instantly. Each session was terminated once every subject completed an average of 64 trials. Once a subject was observed to be able to probe its nose into the hole and turn back to drink water immediately, it would be introduced to the next stage.

2.3.2. Pre-training stage 2

This stage was basically as same as the previous stage except that subjects were placed in the chamber individually. Each subject needed to complete 64 trials every day. The subject would be transferred to the next stage on ceit was able to accomplish this task for two consecutive days.

2.3.3. Training

Each rat was required to probe its nose into the nosepoke hole and stay for at least 800 ms. Once a subject withdrew its nose from the hole, it must move to the opposite end of the chamber within 5 s to be rewarded. The volume of the water delivered was directly proportional to the nosepoke duration (Fig. 1C).

2.3.4. Performance criteria

Rats that reached the following two criteria were considered as reaching stable performance: 1) its success rate (the percentage of successful trials in a session) had to be above 85% for three consecutive days; 2) all main task variables, including success rate, single-attempt rate (the percentage of successful trials with a single-attempt nosepoke) and locomotion time (the time between nose withdrawal and reward delivery) had to show no significant differences for at least three consecutive days. Further details were mentioned in our previous study [34].

2.4. Surgery

Rats were anesthetized using sodium pentobarbital (40 mg/kg, i.p.). Microelectrode arrays (MEA) were constructed with 16 microelectrodes (formvar-insulated nichrome wires, 35 μm in diameter) in a 2 × 8 configuration with a 200 μm inter-electrode interval. The impedance of each microelectrode was 0.5–1.0 MΩ measured at 500 Hz. Each rat was implanted with one MEA in the mPFC (AP 2.5–4.5 mm, ML 0.3–0.8 mm and 2.0–2.5 mm below the cortical surface). The MEAs were fixed in

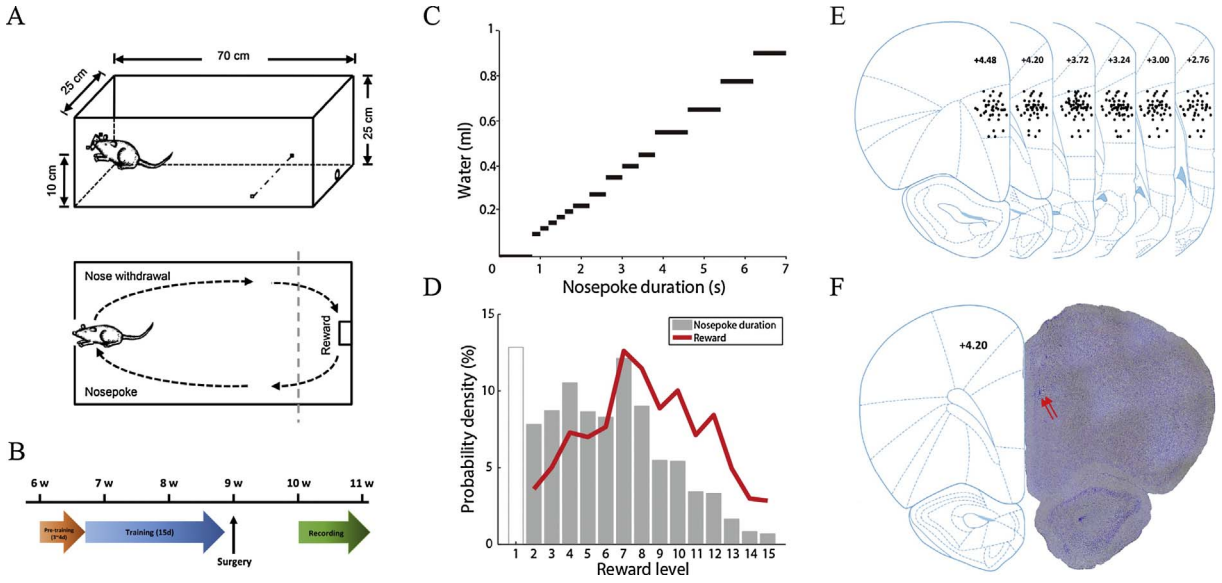

Fig. 1. Behavioral task and recording sites.
(A) Side view (up) and top view (down) of the training apparatus. (B) A schematic diagram of experiment protocol. It consists of pre-training, training, surgery and recording stages, where "w" means week. (C) The cost-benefit diagram between the length of nosepoke duration and the amount of reward. (D) The probability density of nosepoke duration and reward acquired for different reward levels during the recording stage. Hollow bar represents error trials. (E) The placement site of the electrodes in the mPFC. (F) Two electrode placement sites in the mPFC, as indicated by the arrow.