Neuroscience Research 88 (2014) 28–38

Contents lists available at ScienceDirect

Neuroscience Research

journal homepage: www.elsevier.com/locate/neures

Small effect of upcoming reward outcomes on visual cue-related neuronal activity in macaque area TE during conditional associations

Kaoru Ohyama[a,b], Yasuko Sugase-Miyamoto[b,*], Narihisa Matsumoto[b], Chikara Sato[a,c], Munetaka Shidara[a,b,d]

[a] Comprehensive Human Sciences, University of Tsukuba, Tsukuba 305-8577, Japan
[b] Human Technology Research Institute, National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba 305-8568, Japan
[c] Biomedical Research Institute, AIST, Tsukuba 305-8566, Japan
[d] Faculty of Medicine, University of Tsukuba, Tsukuba 305-8577, Japan

ARTICLE INFO

Article history:
Received 27 March 2014
Received in revised form 8 August 2014
Accepted 11 August 2014
Available online 20 August 2014

Keywords:
Ventral visual pathway
Perirhinal cortex
Memory
Electrophysiology in monkeys
Single unit

ABSTRACT

Area TE sends dense projections to the perirhinal cortex in macaque monkeys, an area in which we previously observed flexible signals regarding upcoming reward outcomes during a conditional-association cued-reward task. To investigate neuronal processing during the generation of information on upcoming reward outcomes, neuronal activities in area TE were examined. In the task, a color stimulus as Cue 1 and a pattern stimulus as Cue 2 were sequentially presented. Each pattern stimulus indicated both rewarded and unrewarded outcomes depending on the preceding color stimulus. In the activities during Cue 2 presentation, two-way analysis of variance revealed the effect of the interaction between Cue 1 and Cue 2, i.e., reward conditions, in 19 out of 133 neurons recorded in area TE. Of the 19 neurons, 12 also represented a response delineating a specific cue sequence, i.e., a trial-type activity. The latency of the reward-condition dependence in 7 neurons without the trial-type activity was indistinguishable from the latency in neurons without a trial-type activity in the perirhinal cortex. These results suggest that the effect of upcoming reward conditions is small in area TE and that the representation of reward conditions arises in areas beyond the ventral visual pathway, including the perirhinal cortex, during conditional associations.

1. Introduction

Area TE comprises the final stage in the ventral visual pathway that processes visual objects in macaque monkeys. Its connections with areas that are important for reward related information processing, including the perirhinal cortex (Kravitz et al., 2013; Lavenex et al., 2002; Saleem and Tanaka, 1996; Stefanacci et al., 1996; Suzuki and Amaral, 1994), the amygdala (Freese and Amaral, 2005; Webster et al., 1991), and the basal ganglia (Middleton and Strick, 1996; Saint-Cyr et al., 1990) suggest a role of this area in visual stimulus-reward association, and its role in visual habit formation in which animals gradually learn stimulus-reward pairings has been shown by an ablation study (Phillips et al., 1988). A recent electrophysiological study has shown that responses of area TE neurons to visual stimuli are affected by associated reward conditions when the relationships between visual stimuli and reward outcomes are stable (Mogami and Tanaka, 2006).

Our previous electrophysiological study has shown that neurons in the perirhinal cortex represent the meaning of a visual stimulus, namely, upcoming reward outcomes, during a conditional-association cued-reward task, in which a visual cue is conditionally associated with both rewarded and unrewarded outcomes depending on the context set by another visual cue (Ohyama et al., 2012). To elucidate how such flexible representation of upcoming reward outcomes depending on context is achieved in the two processing stages, i.e., area TE and the perirhinal cortex, neuronal activities in area TE were examined. We sought to determine whether or not the upcoming reward outcome affects activities in area TE when the relationship between a visual stimulus and a reward outcome is flexible, and if so, we ask whether or not there is a time difference between the onset latency of an upcoming reward-condition signal in area TE and that in the perirhinal cortex. If conversion of a visual cue signal to a reward-condition

Abbreviations: Mgnta, magenta; Cyn, cyan; Ptrn, pattern.

* Corresponding author at: Systems Neuroscience Group, Human Technology Research Institute, AIST, Tsukuba Central 2, 1-1-1 Umezono, Tsukuba, Ibaraki 305-8568, Japan. Tel.: +81 29 861 5843; fax: +81 29 861 5849.
E-mail address: y-sugase@aist.go.jp (Y. Sugase-Miyamoto).

http://dx.doi.org/10.1016/j.neures.2014.08.004
0168-0102/

signal depending on context occurs progressively from area TE to the perirhinal cortex, the reward-condition signal in area TE would be observed earlier than that in the perirhinal cortex.

During the conditional-association cued-reward task, two visual stimuli, a color stimulus as Cue 1 followed by a pattern stimulus as Cue 2, were sequentially presented to a monkey. Each pattern stimulus was conditionally associated with both rewarded and unrewarded outcomes depending on the preceding color stimulus. Our results showed that, during Cue 2 presentation, a small proportion of neurons in area TE encoded the associated reward conditions. The reward-condition signal was almost simultaneously represented both in area TE and in the perirhinal cortex. These results suggest that the effect of upcoming reward outcomes is small in area TE and that the upcoming reward-condition signal arises in areas beyond the ventral visual pathway.

2. Materials and methods

2.1. Subjects and experimental apparatus

Subjects were two adult male rhesus monkeys (*Macaca mulatta*) weighing 8 kg and 10 kg (monkeys S and T, respectively) supplied by a local provider (Hamri Co., Ltd., Ibaraki, Japan), the same monkeys that were used in the previous study (Ohyama et al., 2012). All experiments were approved by the Animal Care and Use Committee of the National Institute of Advanced Industrial Science and Technology (AIST) and were performed in accordance with the Guidelines for the Care and Use of Animals of AIST. The experimental apparatus has been previously described in Ohyama et al. (2012). Briefly, the monkeys were seated in a primate chair positioned in front of a monitor (16 × 13 inch, GDM-F520, SONY, Tokyo, Japan) on which visual stimuli were displayed. Behavioral control and data acquisition were performed using the REX real-time data-acquisition program adapted to the QNX operating system (Hays et al., 1982).

2.2. Behavioral task

2.2.1. Initial training

The monkeys were initially trained to detect when a red visual target changed to green (details in Ohyama et al., 2012). Each trial began when the monkey touched a touch-sensitive bar that was mounted on the chair. A white square (visual angle, 0.7° × 0.7°; brightness, 13.30 candela/m^2) was displayed at the center of the screen ("Fix On"). Next, a red target ("Wait" signal, 0.7° × 0.7°, 2.59 candela/m^2) was presented. After a random interval of 300–900 ms, the target color turned green ("Go" signal, 9.38 candela/m^2). If the monkey released the bar within 150–1000 ms after the "Go" signal onset, the target turned blue ("Correct" signal, 1.49 candela/m^2) for a period of 200 ms, and a drop of juice was delivered as a reward from a drinking spout positioned in front of the mouth of the monkey. Otherwise, an error was registered and the monkey had to repeat the trial from the beginning. A black and white random-dot background covered the whole screen.

2.2.2. Conditional-association cued-reward task

In the conditional-association cued-reward task, the monkeys did not make an explicit choice. The behavioral requirement was to perform red-to-green color discrimination as in the initial training and to fixate on the center of the screen. The prediction of the animal as to whether it would or would not be rewarded was determined by licking behavior.

In each trial, two additional visual cues consisting of Cue 1 and Cue 2 were sequentially presented (Fig. 1A). Cue 1, i.e., a color stimulus, was a magenta square (Mgnta, 5.6° × 5.6°, 3.97 candela/m^2) or a cyan square (Cyn, 5.6° × 5.6°, 10.80 candela/m^2). Cue 2, i.e., a pattern stimulus, was one of two black-and-white Walsh patterns (Ptrn 1 or Ptrn 2; black, 50%, white, 50%; Richmond et al., 1987). Each pattern stimulus was conditionally associated with both rewarded (R) and unrewarded (NR) outcomes depending on the preceding color stimulus (Fig. 1B). Juice as a reward was provided after a correct response in trials with Mgnta-Ptrn 1 (Mgnta-Ptrn 1-R trial type) and Cyn-Ptrn 2 (Cyn-Ptrn 2-R trial type) presentation, but not in trials with Cyn-Ptrn 1 (Cyn-Ptrn 1-NR trial type) and Mgnta-Ptrn 2 (Mgnta-Ptrn 2-NR trial type) presentation.

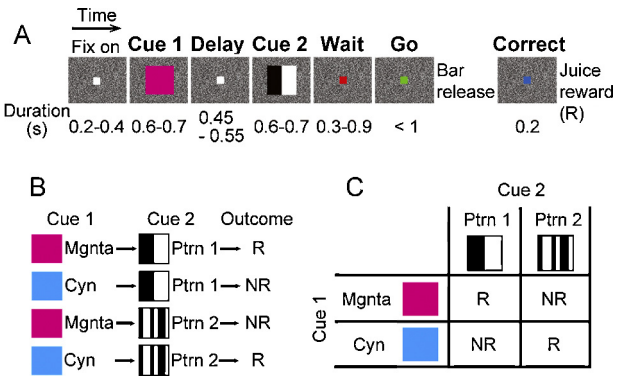

Fig. 1. Conditional-association cued-reward task. (A) Timing and sequence of trial events. A white square (Fix on) appeared when the monkey touched a bar. After the monkey fixated on the white square, Cue 1 and Cue 2 were presented sequentially, with an intervening delay. A red target then appeared in the center of the screen at the beginning of a wait signal period after which the target turned green. When the monkey detected the green target, it had to release the touch bar to complete the trial. Behavioral data were analyzed during six trial events, namely, Cue 1, Delay, Cue 2, Wait, Go, and Correct signal presentations, and neuronal data were analyzed during three trial events, namely, Cue 1, Delay, and Cue 2 presentations. The six periods are indicated by bold letters. (B) Four trial types. Cue 1 is a magenta square (Mgnta) or a cyan square (Cyn). Cue 2 is one of two black-and-white patterns (Ptrn 1 and Ptrn 2). R, a rewarded outcome; NR, an unrewarded outcome. (C) Factors for two-way ANOVA. The leftmost column shows the two levels of the Cue 1-identity factor (Mgnta or Cyn). The top row shows the two levels of the Cue 2-identity factor (Ptrn 1 or Ptrn 2). Interaction between the two factors corresponds to the reward conditions, i.e., whether the current trial was a rewarded or unrewarded trial.

A trial began when the monkey touched the bar and the white target appeared. After the monkey fixated on the white target, Cue 1 and Cue 2 were presented sequentially, separated by a delay (450–550 ms). After Cue 2 disappeared, the monkey was required to perform red-to-green color discrimination. In unrewarded trials, a disconnected solenoid was activated to produce a click sound after the disappearance of the "Correct" signal. This sound was similar to the sound produced by juice delivery in rewarded trials. The inter-trial interval (ITI) was 1500–2200 ms following unrewarded trials. In rewarded trials, the ITI was 2600–3500 ms to allow for the jaw movements associated with taking the reward to abate before the beginning of the next trial. Each of the four trial types appeared two times in every eight trials in a pseudo-random order.

Eye positions were measured using a magnetic search coil technique (Judge et al., 1980; Robinson, 1963) for monkey T and an infrared pupil-position monitoring system (i_rec, http://staff.aist.go.jp/k.matsuda/eye/) for monkey S. The window size for eye fixation was 5.6° × 5.6° at the center of the screen for monkey T and 14.0° × 14.0° for monkey S.

Licking behavior was monitored using a touch sensor attached to a drinking spout. The tip of the spout was placed 7 mm (monkey T) and 11 mm (monkey S) from the upper front teeth of the monkey.

Error trials included bar-release errors and fixation-break errors. Bar-release errors referred to any bar release occurring outside of the 150–1000 ms period after the "Go" signal onset. A fixation break occurring between the "Fix on" and "Wait" signal presentation was counted as an error. If the monkey made an error,