Neuroscience Research 105 (2016) 2–18

Contents lists available at ScienceDirect

Neuroscience Research

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

Characteristics of fast-spiking neurons in the striatum of behaving monkeys

Hiroshi Yamada[a,b,c,d,*], Hitoshi Inokawa[a], Yukiko Hori[a,e], Xiaochuan Pan[f,g], Ryuichi Matsuzaki[h], Kae Nakamura[h,i], Kazuyuki Samejima[f], Munetaka Shidara[c,d], Minoru Kimura[a,f], Masamichi Sakagami[f], Takafumi Minamimoto[a,e,i]

[a] Department of Physiology, Kyoto Prefectural University of Medicine Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto 602-8566, Japan
[b] National Center of Neurology and Psychiatry, 4-1-1 Ogawa-Higashi, Kodaira, Tokyo 187-8502, Japan
[c] Division of Biomedical Science, Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki 305-8577, Japan
[d] Graduate School of Comprehensive Human Sciences, University of Tsukuba, Tsukuba, Ibaraki 305-8577, Japan
[e] Department of Molecular Neuroimaging, Molecular Imaging Center, National Institute of Radiological Sciences, Chiba 263-8555, Japan
[f] Brain Science Institute, Tamagawa University, 6-1-1, Tamagawa-Gakuen, Machida, Tokyo 194-8610, Japan
[g] Institute for Cognitive Neurodynamics, East China University of Science and Technology, Shanghai 200237, China
[h] Department of Physiology, Kansai Medical University, Shin-machi, Hirakata city, Osaka 570-1010, Japan
[i] Precursory Research for Embryonic Science and Technology, Japan Science and Technology Agency, 4-1-8 Honcho Kawaguchi, Saitama 332-0012, Japan

ARTICLE INFO

Article history:
Received 25 December 2014
Received in revised form 6 October 2015
Accepted 7 October 2015
Available online 23 October 2015

Keywords:
Basal ganglia
Inhibitory interneuron
Monkey
Reward

ABSTRACT

Inhibitory interneurons are the fundamental constituents of neural circuits that organize network outputs. The striatum as part of the basal ganglia is involved in reward-directed behaviors. However, the role of the inhibitory interneurons in this process remains unclear, especially in behaving monkeys. We recorded the striatal single neuron activity while monkeys performed reward-directed hand or eye movements. Presumed parvalbumin-containing GABAergic interneurons (fast-spiking neurons, FSNs) were identified based on narrow spike shapes in three independent experiments, though they were a small population (4.2%, 42/997). We found that FSNs are characterized by high-frequency and less-bursty discharges, which are distinct from the basic firing properties of the presumed projection neurons (phasically active neurons, PANs). Besides, the encoded information regarding actions and outcomes was similar between FSNs and PANs in terms of proportion of neurons, but the discharge selectivity was higher in PANs than that of FSNs. The coding of actions and outcomes in FSNs and PANs was consistently observed under various behavioral contexts in distinct parts of the striatum (caudate nucleus, putamen, and anterior striatum). Our results suggest that FSNs may enhance the discharge selectivity of postsynaptic output neurons (PANs) in encoding crucial variables for a reward-directed behavior.

1. Introduction

The activity of various classes of interneurons regulates the information flow in the brain subserving cognition and volition. Striatum, an input stage of the basal ganglia, is involved in a wide range of reward-directed behaviors, and its output has been suggested to be under the control of various classes of interneurons (Kawaguchi et al., 1995). Cholinergic signal mediated by cholinergic interneurons has been shown to modulate the activity of the striatal output neurons (Goldberg et al., 2012; Schulz and Reynolds, 2013). Activity of the output neurons and cholinergic interneurons in behaving animals has been well examined in relation to learning and performance in reward-directed behaviors (Aosaki et al., 1994a; Balleine et al., 2007; Cai et al., 2011; Garenne et al., 2011; Jog et al., 1999; Kawagoe et al., 1998; Lau and Glimcher, 2008; Morris et al., 2004; Samejima et al., 2005; Schultz et al., 2003; Yamada et al., 2004, 2007), while the medium spiny projection neurons (output neurons) and the cholinergic interneurons have been electrophysiologically characterized as PANs and TANs (tonically active neurons), respectively (Apicella et al., 1991; Inokawa et al., 2010; Kimura, 1990). Little is known, however, about how the striatal inhibitory interneurons organize the striatal outputs in behaving animals, especially in close primate relatives to human, macaque monkeys.

* Corresponding author at: Division of Biomedical Science, Faculty of Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8577, Japan.
Tel.: +81 29 853 6013; fax: +81 29 853 6013.
E-mail address: h-yamada@md.tsukuba.ac.jp (H. Yamada).

http://dx.doi.org/10.1016/j.neures.2015.10.003

Beyond these two classes of striatal neurons, parvalbumin-containing GABAergic interneurons have been identified in vitro based on their histochemical properties and morphologies (Kawaguchi et al., 1995). This class of interneurons has been electrophysiologically characterized as FSNs in rodent slice preparation (Tepper et al., 2004; Wilson, 2007). FSNs possess perisomatic synapses with a powerful inhibitory influence on medium spiny projection neurons (Koos and Tepper, 1999). Neuronal activity of FSNs in reward-directed behaviors has been examined in small number of rodent studies, suggesting that they represent information for actions and outcomes (Gage et al., 2010; Lansink et al., 2010; Schmitzer-Torbert and Redish, 2008). However, to the best of our knowledge, no study has examined the role of FSNs in organizing striatal outputs during reward-directed behaviors in monkeys. It is largely because FSN constitutes a minority of cell classes in the striatum (Kawaguchi et al., 1995), and thus, only tiny amount of sample data could be obtained in a single study. Given this limitation, it is challenging to elucidate the inhibitory mechanism of FSNs on the regulation of striatal outputs, which are presumably embedded across distinct functional territories of the striatum.

In the present study, we aimed to understand how FSNs organize striatal outputs during reward-directed behaviors in monkeys. To overcome the above-mentioned difficulty, we accumulated and analyzed single neuron activity in four independent experiments, in which activity of PANs has already been reported under various behavioral contexts. We differentiated FSNs from other neurons based on the spike shapes recorded extracellularly in the striatum of behaving monkeys. We addressed the two critical issues to examine the role of FSNs in organizing striatal outputs: (i) How are FSNs in the striatum of behaving monkeys involved in guiding their actions toward reward outcomes? And (ii) How is the activity of FSNs distinct from that of PANs, while the striatal output would be shaped by inhibition of FSNs? We asked these questions in distinct parts of the striatum in view of cortico-basal ganglia functional loops (e.g., the motor loop, associative loop, and limbic loop). Our results suggest that FSNs may enhance the discharge selectivity of postsynaptic output neurons (PANs) during reward-directed behaviors.

2. Materials and methods

The data obtained from the four independent experiments were used in the present study. Table 1 is the summary of the experiments including their reference numbers (#1 to #4), behavioral task used, the number of monkeys, recording sites, and paper in which the results of PANs have been reported. In this study, we briefly describe each experiment in terms of behavioral task, recording methods, and the specific data analysis used. Other details have been described previously (see references in Table 1). All experimental procedures were carried out in accordance with the Guide for the Care and Use of Laboratory Animals (National Research Council of the National Academies in the USA) and were approved by the Animal Care and Use Committee of the Kyoto Prefectural University of Medicine (Exps. 1 and 2), Tamagawa University (Exp. 3), and Kansai Medical University (Exp. 4).

2.1. Subjects and behavioral tasks

2.1.1. Experiment 1

Single neuron activity was recorded from the caudate nucleus and putamen of two monkeys (monkeys RO and TN), while they performed a task using the arm contralateral to the recording hemisphere to obtain multiple rewards through a series of choices. All details regarding analyses of the monkeys' behavior and activity of the PANs ($N = 292$) have been reported previously (Yamada et al., 2011). Here we analyzed the activity of 280 PANs for which spike shape data were available. The activities of FSNs and TANs in this experiment have not been reported elsewhere.

Multistep choice task. The monkeys performed multistep choice tasks using a trial-and-error approach. After illumination of the start light-emitting diode (LED), the monkeys depressed the illuminated start button. Then, three target LEDs were turned on; the monkeys were required to keep the start button depressed for another moment until the small, red Go LED was turned off (GO), release the start button, and depress one of the three illuminated target buttons within 3 s. If a reward target button was depressed, a high-tone beep (1 kHz) sounded with a delay of 0.9–1.0 s as positive feedback, and reward water was then delivered. If a no-reward target button was depressed, a low-tone beep (0.3 kHz) sounded as negative feedback and no reward was given.

If the monkeys chose the no-reward target in the first step, the second step of the search trial began with the illumination of the start LED 5 s (inter-trial interval; ITI) after the end of the first step. The three targets were illuminated again and the monkeys chose the target. The monkeys remembered the no-reward target chosen during the first step and made another choice between the two remaining target buttons in the second step. If they depressed another no-reward target button, the negative feedback beep sounded and the third step started. They then had to remember the previous two no-reward targets and depress the remaining single target button. Once the monkeys depressed the reward target button in any step of the search trial, the same button was used again as the reward target button in the next repeat trial. The monkeys received a water reward once during the search trials, and once (monkey RO) or twice (monkey TN) during the repeat trials. To instruct the monkeys of the termination of a single series of choices, all four green LEDs were simultaneously flashed for 1 s at 2 s after the end of the final repeat trial.

2.1.2. Experiment 2

Single neuron activity was recorded from the putamen while one monkey was engaged in a task using its arm to obtain rewards. All details regarding analyses of the monkeys' behavior and activity of the PANs have been previously reported (Hori et al., 2009). The activities of FSNs and TANs during this task have not been reported elsewhere.

GO–NOGO button-press task with asymmetric rewards. The monkeys faced a panel in which a rectangular hold button and two instruction buttons were embedded. When the monkey depressed the hold button for 0.2–0.6 s, one of the two instruction buttons was illuminated yellow as a cue stimulus. After some delay, its color turned to either green or red, instructing GO or NOGO action, respectively. After the GO instruction, the monkey released the hold button and depressed the illuminated target button within 3 s. After the NOGO instruction, the monkey kept depressing the hold button for another moment. Combinations of either a large water reward (0.3 ml, +R) after the successful GO trials and a small water reward (0.1 ml, −R) after the successful NOGO trials or vice versa were run in single block of 60–120 correct trials. The occurrence of large- and small-reward trials was not predictable (the average probability was 0.5). A high (1 kHz) or a low (0.3 kHz) tone was sounded after a correct behavioral reaction, which was followed by a large reward (LR) or a small reward (SR), respectively.

2.1.3. Experiment 3

Single neuron activity was recorded from the anterior part of the striatum while one monkey was engaged in an eye movement task to obtain rewards. All details regarding analyses of the monkey's behavior and the activity of PANs have been reported previously (Pan et al., 2014). TANs were classified online but were