Functional connectivity between prefrontal cortex and striatum estimated by phase locking value

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Abstract The interplay between the prefrontal cortex (PFC) and striatum has an important role in cognitive processes. To investigate interactive functions between the two areas in reward processing, we recorded local field potentials (LFPs) simultaneously from the two areas of two monkeys performing a reward prediction task (large reward vs small reward). The power of the LFPs was calculated in three frequency bands: the beta band (15–29 Hz), the low gamma band (30–49 Hz), and the high gamma band (50–100 Hz). We found that both the PFC and striatum encoded the reward information in the beta band. The reward information was also found in the high gamma band in the PFC, not in the striatum. We further calculated the phase-locking value (PLV) between two LFP signals to measure the phase synchrony between the PFC and striatum. It was found that significant differences occurred between PLVs in different task periods and in different frequency bands. The PLVs in small reward condition were significant higher than that in large reward condition in the beta band. In contrast, the PLVs in the high gamma band were stronger in large reward trials than in small trials. These results suggested that the functional connectivity between the PFC and striatum depended on the task periods and reward conditions. The beta synchrony between the PFC and striatum may regulate behavioral outputs of the monkeys in the small reward condition.

Keywords Prefrontal cortex · Striatum · Phase-locking value · Beta band · Gamma band

Introduction

The prefrontal cortex (PFC) and striatum are two important brain regions. Anatomically, they are tightly connected (Alexander et al. 1986). Particularly, the striatum receives direct projections from the PFC (Haber et al. 2006), and its outputs project to thalamus through direct or indirect pathways, and the signal is feedback from the thalamus to the PFC, forming a closed loop (Yin and Knowlton 2006). The anatomical connections between the PFC and striatum suggest that the two areas may have close relations in functions. Many studies have reported that they are involved in some cognitive functions, such as, learning, attention, reward processing, category representation and behavior controlling by different neural mechanisms (Antzoulatos and Miller 2011; Asaad and Eskandar 2011; Deserno et al. 2015). One hypothesis held that the PFC controls the behavior for subjects using mode-based learning approach, while the striatum controls the habitual behavior using mode-free learning method (Daw et al. 2005). Accordingly, in animals' electrophysiological and humans' fMRI experiments, it has been found that the striatum utilized the temporal difference learning algorithm to select behaviors (O'Doherty et al. 2003; Samejima et al. 2005; Lee et al. 2014), while the PFC built a corresponding model to achieve cognitive functions (Glascher et al. 2010; Lee et al. 2014), such as, encoding abstract rules (Genovesio et al. 2005), planning behaviors (Rushworth and Behrens 2008), and decision making (Barraclough et al. 2004).

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Although individual functions of the PFC and striatum were well demonstrated in learning and behavior controlling processes (Rangel et al. 2008; Hikosaka and Isoda 2010), their interactive functions remain elusive in cognitive processes. A recent study showed that the fronto-striatal circuit was involved in category learning (Antzoulatos and Miller 2014). In the experiment, Antzoulatos and Miller trained their monkeys to learn a new shape classification task and recorded local field potentials (LFPs) in the PFC and striatum simultaneously. The results showed that the synchronization of LFPs between the two areas significantly increased in beta band after the monkeys had learned the classification task, and before the classification, there was no synchronization between the two areas, which suggested that the formation of category depended on the functional loop of the two brain regions. In literature, it has been reported that the impairment of functional connectivity between the PFC and striatum was associated with some mental disorders (McConathy and Sheline 2015), such as depression (Heller et al. 2009; Tadayonnejad et al. 2015), schizophrenia (Yoon et al. 2013), alcohol dependence (Courtney et al. 2013). Together, these results demonstrated that the interaction between the PFC and striatum may play a great role in high-level cognitive processes.

Some studies have reported that both the PFC and striatum were involved in reward processing (Hollerman et al. 1998; Samejima et al. 2005; Hikosaka et al. 2014; Pan et al. 2014). Single neurons in the two areas were able to encode reward information related to the reward type, amount and availability that was indicated by conditioned visual stimuli (Watanabe 1996; Kawagoe et al. 1998; Kobayashi et al. 2006). It remains elusive, however, the role of interaction between the two areas in reward processing. To investigate this issue, LFPs were simultaneously recorded in the PFC and striatum of the monkey performing a sequential paired-association task using an asymmetric reward schedule (Pan et al. 2008). We first analyzed spectral power of LFPs to examine whether PFC and striatal LFPs encoded reward information or not. We then calculated the phase-locking value (PLV) of LFPs to estimate the strength of phase synchronization between the PFC and striatum in three frequency bands: the beta, the low and high gamma bands. We found that the beta power of LFPs were significantly different in both the PFC and striatum, indicating reward information was represented in the LFPs. The PLVs in small reward trials was significantly higher than that in large reward trials in beta and low gamma bands, but significantly lower in high gamma band. The results suggested that the functional connectivity between the PFC and striatum was modulated by reward conditions.

Materials and methods

Subjects

Two Japanese monkeys served as subjects in this study (Monkey A, 8.9 kg; Monkey B, 6.5 kg). A detailed description of the experimental procedure and behavioral task can be found in the previous reports (Pan et al. 2008, 2014). Briefly, before the experiment, a head holder and 2 recording chambers (one in each hemisphere) were implanted for each monkey under aseptic techniques with ketamine (4.6–6.0 mg/kg by intramuscular injection) and sodium pentobarbital anesthesia. The size of the chamber was 40 mm (length, anterior–posterior) × 30 mm (width, lateral–medial) and each was implanted with its center located near the end of the principal sulcus, which allowed us to record neural activity in the lateral PFC (LPFC) and striatum simultaneously from the same chamber. All surgical and experimental protocols were approved by the Animal Care and Use Committees at Tamagawa University and were in accordance with the National Institutes of Health's Guide for the Care and Use of Laboratory Animals.

During experimental sessions, the monkey was seated on a primate chair (with its head fixed) and was put inside a completely enclosed, sound and electric shielded room. A 21-inch CRT display (FE220; NEC, Japan) with 60 Hz refresh rate was set at a distance of 60.0 cm in front of the monkey for the presentation of visual stimuli. Eye movements of the monkey were monitored by the Eyelink2 system (SR Research, Canada) with 500 Hz sample rate. All the stimulus presentation and behavioral procedures were controlled by the TEMPO system (Reflective Computing, USA).

Sequential paired-association task with asymmetric reward schedule

The two monkeys were required to learn two associative sequences (Fig. 1a) in a sequential paired-association task (Fig. 1b). Six discriminable icons were used as visual cues counterbalanced across the two subjects (a blue question mark and a draw of a tower were denoted as A1 and A2; red and green patches as B1 and B2; a white cross and a white circle as C1 and C2). The two correct sequential associations were as follows: A1 → B1 → C1 and A2 → B2 → C2. Each sequential paired-association trial (SPAT; Fig. 1b) started with the onset of a white fixation spot (0.21° of visual angle) presented at the center of the monitor. The monkey had to fixate on the spot for a random duration (800–1200 ms). Subsequently, the first stimulus cue (e.g., A1) was presented for 400 ms at the center of the

Fig. 1 The illustrative sketch of the reward predicting task. **a** The two associative sequences (A1 → B1 → C1 and A2 → B2 → C2) learned by the monkeys. **b** Time events in a sequential paired-association trial (SPAT). The monkeys made two saccadic choices (the first choice from **a** to **b** and the second choice for **b** to **c**) in each trial. The yellow arrows indicate saccadic eye movements (not shown in the real experiment).

c Sequential paired-association trials with an asymmetric reward schedule. Reward instruction trials and SPATs were arranged in a block. The monkeys first learned the stimulus-reward association in reward instruction trials, and then performed the SPATs with the asymmetric reward rule. The yellow arrows indicate saccadic eye movement and are not shown for this experiment. (Color figure online)

display. After a variable delay period (700–1200 ms), the fixation spot disappeared and at the same time the second cues (B1 and B2) were presented pseudo-randomly at the left and right positions of the CRT. If the monkey made a saccade to the target cue (e.g., B1) which was denoted as the first correct choice. Immediately after the correct choice, the distracter (e.g., B2) was removed from the monitor and the monkey continued fixating on the target cue (B1) for another 600 ms. After the disappearance of the target cue (B1), the third cues (C1 and C2) were simultaneously displayed pseudo-randomly to the left and right of the position of B1. In the second choice, the monkey made a further saccade eye movement to the correct target cue (e.g., C1). After the two correct choices, the monkey received a drop of water as a reward. During the fixation, the cue and the delay periods, the monkey was required to fixate on the spot. If the monkey shifted its fixation away from the spot (out of a virtual window centered at the fixation spot), this trial was rejected as a fixation break. In addition, when the monkey made an erroneous stimulus choice, this trial was considered as an error one. Either in the fixation break trial or in the erroneous one, the monkey could not get any water but a high tone of 4 kHz. After the monkey made two choices for the targets, it received a correct tone of 1 kHz and water as reward.

Through the SPAT training, the two monkeys learned the two correct associative sequences, A1 → B1 → C1 and A2 → B2 → C2.

After the learning of the two sequential associations was completed, we introduced an asymmetric reward schedule using reward instruction trials (Fig. 1c). In reward instruction trials, the monkey learned which stimulus (C1 or C2) was paired with a large reward (0.4 ml), and which stimulus (C2 or C1) with a small reward (0.2 ml). Reward instruction trials and SPATs were arranged in one block, first reward instruction trials (3 trials) then followed by SPATs (8–10 correct trials) (Fig. 1c). The procedure of each SPAT was the same as shown in Fig. 1b, except for the difference of the amount of reward. In a given block, if C1 was paired with the large reward and C2 with the small reward in reward instruction trials, then the A1 → B1 → C1 sequence was followed by the large reward and the A2 → B2 → C2 sequence was followed by the small reward in SPATs. In another block, if C1 was paired with the small reward and C2 with the large reward, then the A1 → B1 → C1 sequence was followed by the small reward and the A2 → B2 → C2 sequence by the large one. The asymmetric reward schedule between blocks was pseudo-randomly assigned.

Data acquisition

Extracellular recordings were conducted using linear-array multi-contact electrodes (U-probe, Plexon, USA) to obtain LFPs. Each electrode contained 8 recording contacts (impedance, 0.3–0.5 M Ω at 1 kHz) with an inter-contact spacing of 150 or 300 μ m. Neuronal activity was measured against a local reference that was close to the electrode contacts (a stainless guide tube or the tube of U-probe). Data amplification, filtering, and acquisition were done with a Multichannel Acquisition Processor (Plexon, USA). The signal from each contact (channel) was passed through a head-stage and then split to separately extract the spike and the LFP components. For LFP recordings, the signals were filtered with a passband of 0.7–170 Hz, further amplified, digitized at 1 kHz and saved in Plexon files for further analysis. In each recording session, two U-probe electrodes were inserted simultaneously, one into the LPFC and the other into the striatum. Once the two electrodes reached the target positions, we did not move the electrodes any more throughout the session. After about 1 h for stabilization, we started collecting data.

Data analysis

Off-line analysis was performed using custom-made MATLAB (The MathWorks) programs on a PC. The behavioral performance (correct rate) of the first choice in SPATs was calculated in large and small reward trials, respectively. For the analysis of neuronal data, we used only those in correct trials. Before analyzing the LFPs, the line noise (50 Hz) was removed from the original LFP data by the function of *rmline* in Chronux toolbox (<http://chronux.org/>). In this study, we concentrated on neuronal activity in three time epochs: the fixation period (500 ms before the first cue onset), the cue period (400 ms after the first cue onset) and the delay period (400–900 ms after the first cue onset). During the cue period, the first cue stimulus (A1 or A2) was presented, which could induce an event-evoked potential (ERP) in the LPFC and striatum. The ERPs evoked by the first cue stimulus simultaneously in the LPFC and striatum may influence the synchronization of the two areas. To remove any effect of stimulus-evoked potentials on ongoing LFP activity, the average time-locked LFP signal (aligned at the first cue onset) across trials in each channel was subtracted from each trial's LFP in that channel. In this study, we focused on the neuronal activity in the beta (15–29 Hz), the low (30–49 Hz) and high (50–100 Hz) gamma bands. During the recording experiment, the monkey started its mouth movements to anticipate the reward just after the presentation of the first cue stimulus (A1 or A2). The monkey had more mouth movements in the large reward trials than in the small

reward trials. The signals in the theta and alpha bands might be affected by the mouth movement. In the current analysis, we did not analyze the LFPs in the lower frequency band than the beta band.

The power spectrum of LFP

To examine whether the LFPs of the LPFC and striatum coded reward information, we analyzed the power spectrum of LFPs in the two reward conditions. A fast Fourier transformation (the function of *fft* in MATLAB) was used to estimate the power spectrum of LFPs in the fixation, the cue and delay periods, respectively. The power in each frequency was calculated based on the LFP in each trial from each channel, and then was averaged across trials in that channel. During the fixation period, the LFP signals did not contain any reward information. The monkeys knew the reward condition in current trial only after the presentation of the first cue stimulus (A1 or A2). We were interesting in the change power before and after the first cue onset. The percentage change in power was defined as the following equation:

$$\text{power change} = 100 \times \frac{\text{activity} - \text{baseline}}{\text{baseline}}$$

where baseline indicated the power in the fixation period in each channel, and activity indicated the power in the cue period or the delay period in that channel.

Phase-locking value (PLV)

The functional connectivity between two areas can be tested by examining synchrony between oscillations of their LFPs (Friston et al. 2013). If the phases of oscillations of two brain regions are relevant, we claim that the phases of two signals synchrony. For example, the potential of area “A” get to the peak, meanwhile, the potential of area “B” also get to the peak. Phase synchronization is a fundamental and common neuronal mechanism (Engel et al. 2001; Juergen and Axmacher 2011). Phase locking value is usually used to be an important index of phase synchronization, by which the degree of phase variance between two signals can be measured. Unlike other methods, such as, traditional spectral coherence, PLVs separate the phases of signals from the amplitudes, and can explain the functional connectivity problems of the brain areas. Therefore, we adopted this method to calculate the value of phase synchronization of LFPs in different reward conditions and frequency bands.

The phases of the two signals are extracted by the Hilbert transform and signed as ϕ_a and ϕ_b . Then PLVs are determined as follows (Xu et al. 2013):

$$PLV = \left| \frac{1}{N} \sum_{j=1}^N \exp(i[\phi_a(j\Delta t) - \phi_b(j\Delta t)]) \right|$$

where N stands for the length of time series and $1/\Delta t$ is the sampling frequency. The formula takes the average of phase angle differences between the two signals over time. The PLVs has values within $[0, 1]$, where 0 represents no phase synchrony and 1 the full phase synchrony.

We had 8 channels of LFP data from the LPFC and 8 channels of LFP data from the striatum. In total, there were 64 pairs of channels (in every pair, one channel from the LPFC and the other from the striatum) in each recording session. The PLV was calculated for each pair of channels in every large and small reward trials separately. Then PLVs were able to be averaged across trials, channel pairs and sessions that had the same reward condition. However, in fact, the external reward factors may bias the PLVs. For instance, the power of LFP in the LPFC and striatum increased, as well as the oscillation of them in certain reward condition, which made the PLV larger. The enhancement of PLVs was not caused by the inner synchronization of the two regions (Antzoulatos and Miller 2014; Cohen 2014). To remove the bias, for each paired channels, the PLV was calculated based on randomly shuffled trials between the two reward conditions, which now had no correspond relation in same reward condition. The same procedure was repeated 200 times and the averaged $PLV_{shuffle}$ was obtained. Obviously, the observed PLV was always greater than the shuffled PLV. All PLVs used in our analysis were bias corrected by subtracting this shuffled PLV from the observed PLV, as shown in the following equation: $\Delta PLV = PLV_{observed} - PLV_{shuffle}$. In this study, we calculated the PLV in the three frequency bands, the beta, the low and high gamma bands, respectively. Several studies have observed the neuronal activity in the beta and gamma bands in both the LPFC and striatum (Berke 2009; Kalenscher et al. 2010; Antzoulatos and Miller 2014). We designed a window-based finite response bandpass filter using the MATLAB function of `fir1` with the Blackman window. The LFP signal from each trial was filtered in both the forward and reverse directions using the `filtfilt` function to obtain the signals in the three frequency bands. The instantaneous phase was obtained by Hilbert transform for each filtered signal, and then the PLV was calculated in each frequency band.

Results

We recorded LFPs simultaneously in the LPFC and striatum using two U-probe electrodes while the monkeys were performing the sequential paired-association task with the

asymmetric reward schedule (Fig. 1, see “Materials and methods” section). In total, we recorded 28 tracks (sessions) of LFP data from Monkey A and 25 tracks from Monkey B. We first examined whether the monkeys could correctly predict the reward amount associated with the first cue stimuli. Generally speaking, the behavioral performance would be better in larger reward trials than in small reward trials if the monkeys correctly predicted the reward amount. We calculated correct rates of the first choice (the selection of B from A) in SPATs and found that the accuracy in large reward condition was significantly higher than that in small reward condition (Mann–Whitney U test, $P < 0.01$) (Fig. 2), which demonstrated that the monkeys were able to correctly predict the reward amount for the first cue stimuli (A1 and A2).

The power spectrum of LFP

We examined whether the LFPs in the LPFC and striatum encoded reward information or not by comparing their power in the two reward conditions. We calculated the percentage change of power in the cue and delay periods relative to the power in the fixation period in the three frequency bands (beta, low and high gamma bands, see “Materials and methods” section), respectively. Figure 3a–d display the data from Monkey A and Fig. 3e–h illustrate the results from Monkey B. The two monkeys showed consistent results. During the cue period (Fig. 3a, e), the LPFC showed significant decrease of the beta power in large reward trials than in small reward trials (paired t test,

Fig. 2 The behavioral performance of the two monkeys modulated by the reward amount: **a** Monkey A and **b** Monkey B. The correct rates (the ratio of correct trials divided by total trials) of the first saccadic choice in SPATs were calculated in the large and small reward conditions, respectively. The orange bars indicate the correct rates in the large reward trials while the blue bars represent the correct rates in the small reward trials. *** $P < 0.001$ (Mann–Whitney U test). Error bars s.e.m. (Color figure online)

Fig. 3 The change in power of LFPs before and after the first cue presentation for the two monkeys. **a** The percentage of LPFC power change in the cue period relative to the fixation period in the three frequency bands for Monkey A. **b** The percentage of LPFC power change in the delay period relative to the fixation period in the three frequency bands for Monkey A. **c, d** The percentage of LFP power change in the striatum for Monkey A in the cue period (**c**) and in the delay period (**d**). **e–h** The percentage of power change for Monkey B: **e** the data from the LPFC in the cue period, **f** the data from the LPFC in the delay period, **g** the relative power from the striatum in the cue period and **h** the relative power from the striatum in the delay period. The *orange bars* indicate the data in the large reward trials while the *blue bars* indicate the data in the small reward trials. The *positive values* show the power in the cue period or in the delay period was larger than the power in the fixation period. The *negative values* indicate the reverse relation. The statistical significance was examined by paired *t* test. *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$, n.s.: no significance. Error bars s.e.m. (Color figure online)

$P < 0.001$). The relative change of power did not significantly differ between the two reward conditions in the low gamma band (paired *t* test, $P = 0.12$ in Fig. 3a and $P = 0.88$ in Fig. 3e). In the high gamma band, the power in the two reward conditions increased relative to the baseline power. Moreover, the power in the large reward condition was significantly higher than that in the small reward condition (paired *t* test, $P < 0.001$). In the delay period (see Fig. 3b, f), we observed that the power in the LPFC beta band increased relative to the baseline power, and the relative power was significantly higher in small reward trials than in large reward trials (paired *t* test, $P < 0.01$ in Fig. 3b and $P = 0.03$ in Fig. 3f). There was no significant difference between the two reward conditions in the LPFC low gamma band (paired *t* test, $P = 0.15$ in Fig. 3b and $P = 0.51$ in Fig. 3f). In the high gamma band, the power in the two reward conditions decreased relative to the baseline power, and the percentage changes were significantly different between the two reward conditions (paired *t* test, $P < 0.01$). In the striatum, we also observed significant beta power differences between the two reward conditions in both the cue (Fig. 3c, g, paired *t* test, $P < 0.001$ in Fig. 3c and $P = 0.005$ in Fig. 3g) and delay periods (Fig. 3d, h, paired *t* test $P < 0.01$). In addition, the power of large reward condition in the cue period decreased and the power in the delay period increased relative to the baseline power in the fixation period. The power in the low gamma band or the power in the high gamma band did not show significant difference between the two reward conditions either in the cue period or in the delay period. The results suggested that the recorded LFPs in the LPFC encoded reward information in beta and high gamma bands, and the LFP in the striatum represented reward information only in the beta band, not in the higher frequency band.

Phase synchronization estimated by PLVs

We calculated the PLVs between the LPFC and striatum on the basis of simultaneously recorded LFPs in the two areas in the three frequency bands for the two monkeys (Fig. 4, see “Materials and methods” section), respectively. A two-way ANOVA (two factors: period (fixation, cue and delay) and reward condition (large, small reward amount)) was applied to check the statistical significance of PLVs in these different conditions. The PLVs in the beta band had significant main factors of period and reward ($P < 0.01$), also significant interaction between the two main factors ($P < 0.01$) for the monkeys (Fig. 4a, d). The results of the two-way ANOVA revealed that the PLVs in the low gamma band had significant main factor of period ($P < 0.01$), no significant main factor of reward ($P = 0.1625$ for Monkey A and $P = 0.2347$ for Monkey B). However, the interaction between the two factors was significant ($P < 0.01$) for the both monkeys (Fig. 4b, e). In the high gamma band, the PLVs had only significant interaction between the period and reward conditions ($P < 0.01$, Fig. 4c, f). The two main factors were not significant (Monkey A: $P = 0.5412$ for the period factor and $P = 0.1784$ for the reward factor; Monkey B: $P = 0.191$ for the period factor and $P = 0.2597$ for the reward factor).

We were interested in PLV differences between the two reward conditions in each period. Further post hoc tests with Bonferroni correction were applied to examine the statistical significance of the PLVs between the two reward conditions in each period, respectively. During the fixation period before the first cue stimulus was presented, the monkeys did not know the reward condition in current trial. The PLVs in this period showed no significant difference between the reward conditions in either frequency bands ($P > 0.05$). In the cue period, we did not observe significantly different PLVs between the two reward conditions in either of the frequency bands ($P > 0.05$), although the monkeys knew the reward amount in current trial and some LPFC and striatal neurons encoded reward information in this period (Pan et al. 2014). During the delay period, the PLVs in the small reward trials were significantly higher than the PLVs in the large reward trials in both the beta and low gamma bands ($P < 0.01$). In contrast, the PLVs in the high gamma band were significantly smaller in the small reward condition than in the large reward condition. In short, these results indicated that the phase synchronization between the LPFC and striatum was modulated in the reward condition, in the task period and as well as in the frequency band.

Fig. 4 Phase-locking values (PLVs) between the LPFC and the striatum calculated separately in the three frequency bands and in the two reward conditions. **a–c** PLVs computed on the basis of LFPs in the three task periods for Monkey A in the beta band (**a**), the low gamma band (**b**) and the high gamma band (**c**). **d–f** PLVs calculated

based on LFPs in the three task periods for Monkey B in the beta band (**d**), the low gamma band (**e**) and the high gamma band (**f**). The *orange curves* indicate PLVs in the large reward trials and the *blue curves* represent the data in the small reward trials. ****** $P < 0.01$. *Error bars* s.e.m. (Color figure online)

Discussion

In this study we examined the power of LFPs recorded in the LPFC and striatum and the PLV between the two areas in the two reward conditions. The LFPs encoded reward information in both the LPFC and striatum, consistent with previous reports from single-unit and fMRI studies that neuronal activities in the LPFC and striatum were modulated by the reward amount (Pan et al. 2008, 2014; Hikosaka et al. 2008; Garrison et al. 2013). We found significant power differences between the two reward conditions in the beta band in both the LPFC and striatum during the cue and delay periods. The reward-modulated neuronal patterns, however, were different in the two periods. In the cue period, the relative beta power to the fixation period decreased more in the large reward trials than in the small reward trials. In contrast, the relative beta power in the delay period increased more in the small reward condition comparing to the large reward condition (Fig. 3). The stimulus presented in the cue period but not in the delay period might be one of the factors that affected the beta

activity patterns in the two periods. It has been hypothesized that the beta band activity was linked to the maintenance of the current cognitive status (Engel and Fries 2010). According to this hypothesis, the band oscillation would be expressed more strongly in maintained states than in changed states. In the cue period, the stimulus cue (A1 or A2) was presented and LPFC and striatal neurons responded to it. It was a changing processing, and the beta activity in the two areas would be reduced in this cue period. However, the LPFC and striatum held the stimulus information during the delay period, which might enhance the power of the beta activity. In addition, the LPFC encoded reward information in the high gamma band, showing the higher power in large reward condition than in the small reward condition in the cue period (see Fig. 3a, e). It has been reported that the higher gamma signals in the LFPs was positively correlated with spike activities of single neurons (Ray et al. 2008). The high gamma power differences in the LPFC might reflect the reward information encoded by spike activity. A recent study has also reported that beta oscillation exhibited significantly higher power in

unrewarded trials than in rewarded trials (Lega et al. 2011), consistent with our findings that the beta power was more in small than large reward conditions.

The reward-dependent phase synchrony of LFPs between the LPFC and striatum was observed in the delay period (Fig. 4). The PLVs in small reward trials were significantly higher in the beta and low gamma bands but lower in high gamma band compared to that in large reward trials. It was reported that selective behaviors were accompanied with the enhancement of gamma rhythm which might promote stimulus selection or behavior preparation (Pascal 2009). Increased gamma synchronization with spatial and feature attention has been observed in visual (Siegel et al. 2008), somatosensory (Bauer et al. 2006), frontal (Gregoriou et al. 2009) and parietal (Saalmann et al. 2007) cortices. It has been noticed that, gamma frequency enhancements were observed in tasks that required a relatively long sustained attention period suggesting that expectation and anticipation might be crucial factors for the emergence of gamma frequency synchronization (Gregoriou et al. 2015). In the case of large reward trials in our study, the monkeys paid more attention to the stimulus associated with the large reward and anticipated the large amount of reward at the end of trials. The higher PLVs in large reward trials might be related to more attention to and expectation for the large reward before the first choice (the selection B from A), which may enhance the behavioral performance of the monkeys in large than small reward trials (see Fig. 2). The high gamma activity was also related to spike activity (Ray et al. 2008). The higher PLV in the high gamma band might reflect more overlap of reward-related spike activity in the LPFC and striatum during large reward trials relative to small reward trials.

The beta oscillation and coupling in the beta band have been observed in both the PFC and striatum (Courtemanche et al. 2003; Pesaran et al. 2008; Swann et al. 2009). It has been suggested that the beta activity and its coupling played a role in long-range communication between multiple brain areas (Pavlidou et al. 2014), particularly involved in endogenous top-down attentional control processes (Buschman and Miller 2007). Phase synchrony between the LPFC and striatum in the beta band may serve communication each other (Fries 2015). The stronger synchronization implied the more effective information transmission between the two areas (Fries 2005). We found the small reward PLVs were significantly higher than the large reward PLVs in the delay period, which suggested that more information was transferred from the LPFC to the striatum in the small reward trials relative to the large reward trials. Consistently, it has been reported that the beta synchrony between the PFC and striatum was enhanced during the category performance, suggesting the synchrony could serve to communicate the categorical

decision from the PFC to the striatum (Antzoulatos and Miller 2014). However, it was still unclear what the functional role of the transferred information was and how it modulated the neuronal activity in the striatum. Our hypothesis was that the information from the PFC would enable the striatum to reduce the possibility of choosing the large reward distracter (the preferred stimulus for the striatum due to its large reward amount) in small reward trials (where the correct target was the stimulus with the small reward amount). The information from the PFC might regulate or inhibit the output of the striatum in the small reward trials to obtain better performance. Further investigations are needed to clarify precise function roles of the fronto-striatal circuit.

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