Transient striatal γ local field potentials signal movement initiation in rats

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Sponsorship: This work was supported by NSF IGERT #9870633 (B.M., N.C.S.-T.), NIH MH68029 (B.M., N.C.S.-T., A.D.R.), University of Minnesota IRCSA grant (B.M., J.K.), and by an NSF fellowship (N.C.S.-T.).

Received 25 September 2005; revised 17 October 2005; accepted 18 October 2005

Transient coherent neural oscillations, as indicated by local field potentials, are thought to underlie key perceptual and cognitive events. We report a transient, state-dependent 50 Hz oscillation recorded from electrodes placed in the striatum of awake, behaving rats. These coherent oscillations, which we term γ_{50}, occurred in brief (150 ms) events co-incident with the initiation of movement. On navigation tasks, the animal's speed increased dramatically at the precise moment of the γ_{50} event. This synchronous oscillation may provide a key to understanding striatal function, as well as basal ganglia pathology, which often impairs the control of voluntary movements. *NeuroReport* 16:2021–2024

Keywords: local-field potential, motor control, striatum

Introduction

In many neural structures, transient, synchronous oscillations in the local field potential (LFP) are correlated with distinct behavioral states. These events are thought to reflect organized neural firing patterns that have implications for information processing [1–5]. We have developed a method for identifying fundamental frequencies within LFPs [6]. When applied to LFP data in which the key oscillation frequencies have been determined from conventional filtering analysis, our method readily identifies those frequencies. When applied to LFPs recorded from the dorsal striatum, it identified 48–58 Hz as an important oscillation frequency [6]. For simplicity in the rest of the paper, we will refer to this oscillation as γ_{50}. Using classical filtering techniques, Berke *et al.* [7] have also recently reported the presence of LFP power at a similar 50 Hz frequency in the striatum of awake rats. While other basal ganglia oscillations have been reported to have behavioral correlates in normal animals [7–9], the behavioral significance of γ_{50} is not known. Here, we report that the γ_{50} oscillation occurs in transient ~150 ms events that are co-incident with the initiation of movement on spatial tasks.

Methods

Our primary data came from rats running two behavioral tasks (a sequential spatial navigation task, Multiple-T (n=7 rats) or a sequential nonspatial task, Take-5 (n=5 rats)). Owing to noise present in our early recordings that overwhelms standard filtering methods, specific event times could only be identified on four of the seven Multiple-T rats. Therefore, data from seven rats were used for correlation analyses (Fig. 1), while data from four of those seven were used for speed analyses (Fig. 3). In each of these tasks, rats ran daily sessions (40 min duration) in which they worked for food rewards while recordings were taken from the striatum. All recordings were taken from well-trained rats. All procedures were approved by the Institutional Animal Care and Use Committee at the University of Minnesota and were in accordance with National Institutes of Health guidelines.

Rats (male, FBNF-1, Harlan, Indianapolis, Indiana, USA; age 9–15 months) were pretrained on the task in question and then implanted with 14-electrode microdrives. Briefly, animals were anesthetized with sodium pentobarbital (Nembutal, 50 mg/kg, intraperitoneally) and then placed on a stereotax. During surgery, anesthesia was maintained with isoflurane (0.5–2% isoflurane vaporized in medical grade oxygen). DualCillan (0.2 cm^3, given intramuscularly; Phoenix Pharmaceutical Inc., St Joseph, Michigan, USA) and Baytril (0.1 cm^3, 2.27% enrofloxacin, given subcutaneously; Bayer Corp., Shawnee Mission, Kansas, USA) were used to help prevent infection. See [10] for surgery details.

After surgery, electrodes were advanced to the striatum over the course of 1–2 weeks. Two electrodes were left in the corpus callosum to serve as references for common-noise rejection. LFPs were recorded using 16 channels of a Cheetah recording system (Neuralynx, Tucson, Arizona, USA). All electrodes have been histologically verified to lie in the striatum. See [10] for additional histological details.

Multiple-T

The Multiple-T task consisted of an elevated sequence of T choices (3–5 T) arranged sequentially (each T was 30 cm long

with a 37 cm crossbar). The last choice led to a pair of return rails running parallel to the sequence. Food was provided at two sites on each return rail. On any specific day, only one pair of sites (i.e. the right or left return rail) was active and provided the food reward. The other pair of feeders remained in their usual positions on the track, but did not provide the reward. The sequence of choices remained constant within a day, but changed between days. Rats were allowed to run for one 40-min session each day [10–12].

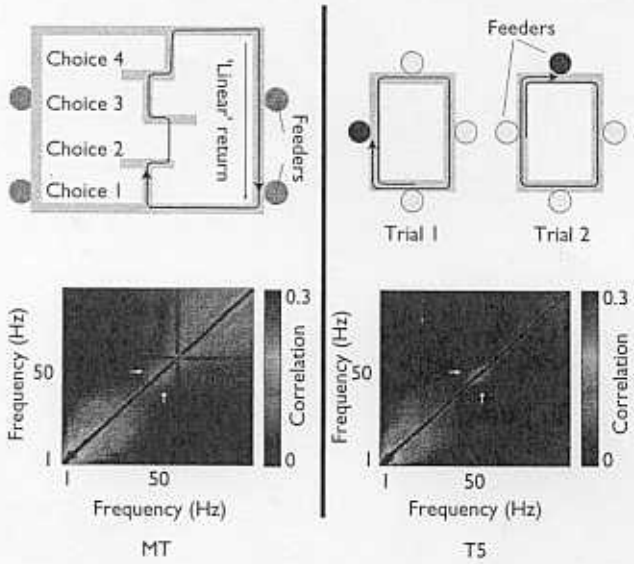

Fig. 1 (Top) Tasks used. Multiple-T (MT): general maze layout. The animal runs a continuous one-way loop. The navigational sequence can change daily. Either the right-side feeders or the left-side feeders are active on a given day, providing a fourth choice to the navigational sequence. Take-5 (T5): two laps around the rectangular track. In order to receive food, the animal must run 5/4 around the track. (Bottom) Cross-frequency self-correlation. Correlations were averaged across tetrodes within each animal, and then across animals. Important frequencies are indicated by blocks of high correlation surrounding the diagonal. Note the clear signal at 48–58 Hz (white arrows). The zero correlation crossbars at 60 Hz are due to electrical line noise and do not contribute to other correlations (MT: seven animals, T5: five animals).

Take-5

In the Take-5 task, four feeders were placed around a rectangular track (90 cm × 60 cm), one feeder at the center of each side. In order to receive food, rats had to run 5/4 around the track in a clockwise direction. Thus, if a rat received food at the west feeder, it had to make one full circuit around the track, returning to the west feeder, and then continue on to the north feeder in order to receive food. Rats were allowed to run for one 40-min session each day [11,13].

Data analysis

Calculating speed

For all experiments, position was sampled at 60 Hz via a camera in the ceiling tracking light-emitting diodes on the headstage of the animal (Cheetah, Neuralynx). On both tasks, the overall motion was essentially angular around a skewed circle. Thus, only the angular components around the pseudocenter of the track were included in the speed calculations. Speed was calculated using the adaptive windowing procedure proposed by Janabi-Sharifi *et al.* [14]. This algorithm provides for both accurate speed estimates and an accurate estimate of the time of speed change. Speed estimates received from the Janabi-Sharifi *et al.* [14] algorithm were subsequently smoothed with a 300-ms Hamming window.

Detecting fundamental frequencies with correlations

A complete discussion of detecting fundamental frequencies with correlations can be found in [6]. Spectrograms were computed with 0.5 s nonoverlapping windows. A standard correlation coefficient was then computed between all pairs of frequencies. Areas of high correlation that appear on the main $x=y$ diagonal are probably due to a single neural process [6].

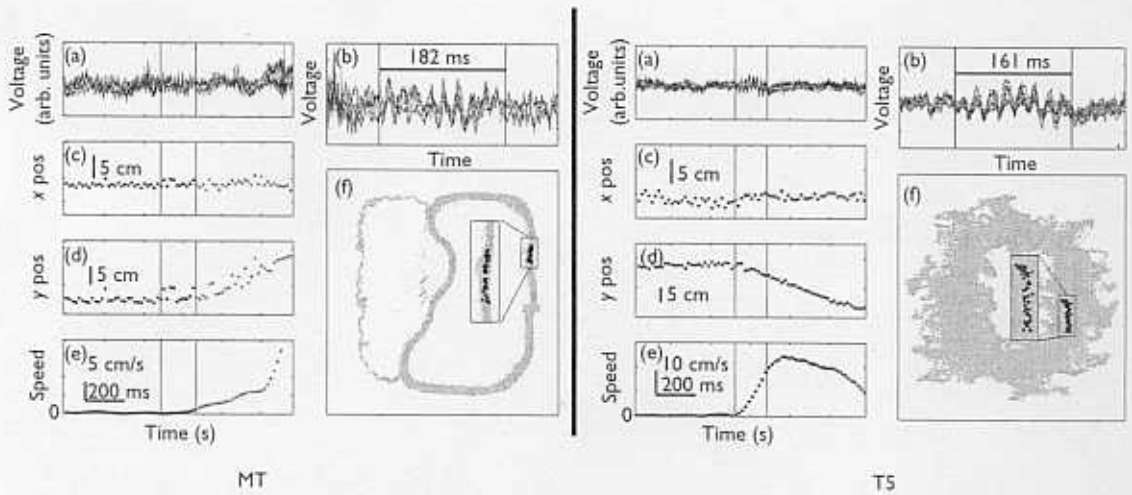

Fig. 2 Example γ_{50} events from the two tasks. (a) Raw local field potential (LFP) data. The two vertical lines indicate the identified γ_{50} event. (b) Raw LFP data zoomed in to show the transient synchrony. (c, d) *x* and *y* position of the animal. (e) Speed of the animal. (f) Position of the animal just prior to and just after the γ_{50} event. Individual lines in panels a and b are raw LFP signals recorded from different electrodes in a single animal. Panels a and c–e are aligned in time. (Left) Multiple-T (MT) – event occurred just as the animal left the first feeder (R018-2002-09-28)]. (Right) Take-5 (T5) – event occurred just as the animal left the east feeder (R032-2003-05-30).

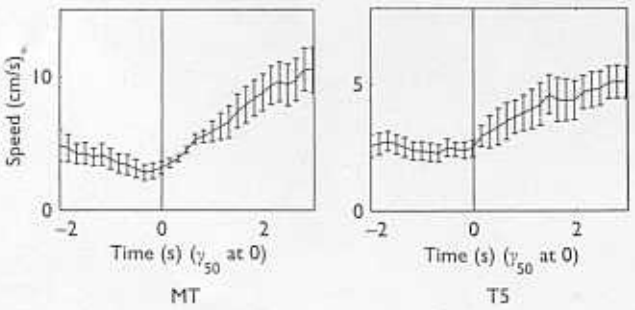

Fig. 3 Speed relative to time of γ_{50} event. Specific γ_{50} events were identified as described in the Methods section. Speed measurements were aligned to the time of the γ_{50} event and averaged first within session (Multiple-T (MT): 88 ± 43 events per session; Take-5 (T5): 94 ± 117 events per session), then within animal (MT: 8.7 ± 6.9 sessions per animal; T5: 6.4 ± 1.8 sessions per animal) and finally across animals (MT: four animals; T5: five animals), producing a peri-event histogram. Error bars indicate SE measurements across animals.

The procedure in [6] for isolating oscillators within LFPs makes use of a frequently overlooked property of the correlation coefficient function. As any peak in the spectral density corresponding to the characteristic frequency of a rhythmic oscillation will have a finite, nonzero width (owing to its transient nature and variability in the oscillation's frequency), it can be identified by the finite cross-correlations with neighboring frequencies, even if it does not interact with other oscillations. The nonstationary, small amplitude aspect of these oscillations would ordinarily be buried in the background noise in a traditional average spectral density. In contrast, uncorrelated positive and negative coefficients cancel out in correlations, while a true correlated signal remains undiluted and is thereby readily detected.

Detecting times of γ_{50} events

Specific events characterized by an increase of power in the 45–55 Hz band were identified using conventional filtering methods [15]. For a given session, all LFPs were filtered individually at both 35–45 and 45–55 Hz. Times when the signal power exceeded 7σ above the mean amplitude for the 45–55 Hz band but not the 35–45 Hz band were identified. As these γ_{50} oscillations appear across the striatum, only high-power epochs occurring in LFPs from two or more electrodes were included.

Results

The within-time series, cross-frequency correlation plot showed a fundamental frequency in the 48–58 Hz range that was clearly distinct from activity at surrounding frequencies (Fig. 1). While every frequency in a power spectrum is trivially correlated with itself (producing a correlation of 1 on the $x=y$ line), transient coherent oscillations hidden within the spectral density are revealed by their nonzero correlations with frequencies adjacent to the center frequency of the oscillation [6,16]. The zero correlation crossbars occurring at 60 Hz (Fig. 1) were due to electrical line noise and do not contribute to other correlations. As can be seen in Fig. 1, our correlation analysis also indicates oscillatory activity in other ranges, such as theta and beta, which is consistent with other observations in the rodent striatum [7,9]; however, we will concentrate on the γ_{50} signal here.

To test the hypothesis that this oscillation was associated with a particular behavioral state, we analyzed data from the rats performing the Multiple-T task (seven animals) [10,12]. In this task, the rat typically runs smoothly through the navigation sequence and stops at the feeders to eat and to groom itself. After remaining at the feeder for a variable length of time, the rat leaves the feeder to initiate a new lap. Rats typically remained at the second feeder for a long time [average wait time at the second feeder was 27 s, 95% confidence interval (CI)=9–45 s], but once they left the feeder they ran at a stereotyped velocity on a stereotyped path through the navigation sequence (average total lap time from leaving the second feeder to arriving at the first feeder, traveling nearly 4 m, was 16 s, 95% CI=10–22 s) [10,12].

The task was divided into behaviorally significant regions such as the navigation sequence and the return rails. The 50 Hz correlation block (Fig. 1) was found to be significantly suppressed during the navigation sequence ($P<0.05$, Wilcoxon paired signed-rank test, $n_{rat}=7$), but not on the return rail portion ($P=0.47$, Wilcoxon paired signed-rank test, $n_{rat}=7$). Rats typically ran smoothly through the navigation sequence, while they engaged in a wide range of behaviors on the return rail, including running, grooming, feeding, resting and transitions between these activities.

Clinical evidence has long suggested that the basal ganglia are involved in volitional movement and, specifically, the initiation of movement [17–20]. This led us to focus on motor activity for further analysis. Figure 2 shows typical examples of a γ_{50} oscillation from each task. These events were found primarily (but not exclusively) at the feeders, closely tied to the instant the animal left the feeders. As shown in panel e of Fig. 2, the animal's speed increased dramatically at the precise moment of the γ_{50} oscillation.

Once the times of specific events had been identified, classical behavioral neuroscience methods (such as peri-event time histograms) could be used to analyze behavior based on those times. Given the hypothesized relationship between the basal ganglia and movement initiation, and the observation that many individual events occurred at the time of feeder departure, we hypothesized a relationship between the γ_{50} signal and movement initiation. To test this hypothesis, we constructed a peri-event time-histogram, measuring the speed before and after the signal, aligned with the start-time of the signal. As shown in Fig. 3, speed increased dramatically at the moment of the γ_{50} event.

Short duration, frequency-focused LFP events, characterized by synchrony across large spatial areas, have been associated with periods of motor activity and visual perception [2,4,9,21]. The γ_{50} event described here is phenomenologically similar in that it is characterized by transient oscillatory activity at 48–58 Hz, with a duration of 100–150 ms and showing synchrony across a relatively large spatial scale (>1 mm). It is possible that the γ_{50} event may arise from the striatal neural activity involved in the self-initiation of a movement, particularly a well-trained, ballistic movement. This transiently synchronous signal may provide a key to understanding striatal function. As diseases of the basal ganglia involve aberrant oscillatory states [8,22,23], striatal oscillations in normal animals may shed light on the changes in information processing that accompany changes in the oscillatory activity in basal ganglia diseases.

Conclusion

An oscillatory LFP event (γ_{50}) has been identified in the striatum. It is characterized by transient oscillatory activity at 48–58 Hz, with a duration of 100–150 ms and showing synchrony across a large spatial scale (>1 mm). A strong increase in speed was found to occur at the moment of these events on rats running multiple tasks.

Acknowledgements

We thank Jadin Jackson for extensive discussions and comments on earlier drafts of this paper. We thank Pratibha Aia, Mallika Arudi, Deborah Bang, Dan Bernal, Chris Boldt, Giuseppe Cortese, Maniezheh Firouzi, Mandy Huber, Adam Johnson, Sarah Jutila, Monica Kumar, Morgan Little, Susan Nwoke, Josh Puhl, Saumya Rao, Patrick Rothwell, Kelsey Seeland, Tim Singewald and Jon Waataja for help in running experiments and for helpful discussions.

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