Chapter 4

Increased cortico-striatal synchronization over hemispheres in the hemiparkinsonian rat
ABSTRACT

In Parkinson’s disease (PD), changes in oscillatory brain activity occur over a wide range of cortical regions and in the basal ganglia. However, it is unknown how dopamine depletion in the 6-OHDA lesioned rat model of PD affects the oscillatory brain activity within and the synchronization of this activity between different cortical areas and the basal ganglia. In the current study, we performed multielectrode recordings in a freely moving rat model of parkinsonism to explore changes in local synchrony of oscillatory brain activity and synchronization between brain regions. Local field potentials were recorded simultaneously from 12 cortical areas and the left and right striatum. Serial recordings were performed in awake, behaving rats before and after a unilateral 6-hydroxydopamine injection into the medial forebrain bundle. We computed spectral power and synchronization between brain regions using the Phase Lag Index in two behavioural conditions: at rest and during locomotion. Our recordings revealed an increase in relative beta power over a wide range of areas at rest, and in a limited number of areas during locomotion. Synchronization between brain regions was moderately increased in the beta frequency band. In addition, we observed excessive gamma band synchronization between many of the recorded brain regions in the resting condition. Our results demonstrate that the changes in local oscillatory brain activity and in the synchronization between brain regions in hemiparkinsonian rats are in many ways similar to the changes observed in PD patients.

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INTRODUCTION

A large body of literature reports altered synchronous oscillatory brain activity in Parkinson’s disease (PD) (for reviews see [1–5]). Evidence shows increased coupling between various cortical areas and also between cortex and subcortical structures. In vivo recording of brain activity from the basal ganglia is possible in patients undergoing functional neurosurgery as treatment for PD, providing an opportunity to investigate the pathophysiological processes involving the cortex-basal ganglia loops. Numerous studies demonstrated increased coupling between basal ganglia and cortex and also interhemispheric coupling at the level of the basal ganglia [6–12]. Whether these detected changes are related to PD or are linked to physiological processes is not clear in human subjects, considering the restrictions of patient studies such as: limited possibility to interrupt chronic treatment (which might affect the detected neurophysiological patterns) or the difficulties in selecting control subjects in the case of intracranial recordings. Animal models may offer a more controlled approach to increasing our understanding of the pathophysiological mechanisms involved in PD.

Experiments in the hemiparkinsonian rat model have revealed similar neurophysiological changes to those seen in PD patients both in resting state and in movement-related signals [13]. The local oscillatory activity in the beta band was shown to be increased both in cortex and in basal ganglia. Furthermore, cortico-basal ganglia coupling is shown to be increased, echoing patient findings [14–18]. The rodent model also provides the opportunity to record from basal ganglia sites beyond the ones investigated in patients. The striatum plays a pivotal role in motor functioning, its function is perturbed in movement disorders: models of PD demonstrated disturbed local and cortico-striatal neurophysiological patterns [19–22]. Interhemispherical cortico-striatal connectivity have been described both in structure and function [23, 24], a pathway that might be involved in the increased interhemispheric coupling patterns detected in movement related signals both in experimental and human parkinsonism [18, 25]. Taken together, these observations indicate that cortico-striatal processes are disturbed in the parkinsonian brain involving both hemispheres and are possibly are modulated by motor activity. However, how bilateral cortico-striatal connectivity patterns alter by dopaminergic cell loss during motor activity, remains to be determined.

In the present study we aim to characterize the functional connectivity patterns in multiple cortical and striatal brain regions in the hemiparkinsonian model at rest and during movement. To enable a more direct comparison with human studies, we selected our methods to be the closest possible to studies using electroencephalography (EEG) and magnetoencephalography (MEG) recordings in PD patients. To attain this, we recorded local field potentials (LFP) from 14 symmetrical cortical and striatal brain areas in awake, unrestrained, behaving rats injected with 6-hydroxydopamine (6-OHDA) in one
hemisphere. To assess changes in both local oscillatory brain activity and synchronization between brain regions, we computed local power at different frequencies for the 14 brain regions recorded from, and the functional connectivity between brain regions using the Phase Lag Index (PLI [26]) both at rest and during locomotion.

**METHODS**

**Animals**

The experiments were conducted in five male Wistar rats (approx. 300g, Harlan; The Netherlands). Animals were kept under standard housing conditions (constant temperature (22+/−1 °C) and humidity (relative, 56%), 12-hour reverse light–dark cycle (daylight period 19:00-7:00), food and water available ad libitum. Behavioural experiments were performed during the dark phase, at the same time of the day. The study was approved by the Animal Ethical Committee at the VU University of Amsterdam and it was conducted in accordance with Dutch (Wet op de Dierproeven, 1996) and European regulations (Guideline 86/609/EEC).

**Recording device and surgery**

Details of the recording device and the implantation procedure are described in more details previously in Chapter 3. Briefly, a custom designed electrode holder was developed to allow chronic, simultaneous LFP recordings from in total 14 brain areas (target coordinates given relative to Bregma, dorsoventral relative to dura surface in mm: AP/ML/DV based on Paxinos and Watson [27]: frontal motor areas (M1: 4.0/2.5/2 ), medial prefrontal cortex (mPFC: 3.2/0.7/3.5), secondary motor areas for whiskers (M2wh: 2.0/1.5/2), primary motor areas for forelimbs (M1FL: 1.0/2.2/2), dorsolateral striatum (Strt: 1.0/3.0/3.9), primary motor areas for hind limbs (M1HL: -1.8/1.6/2) and primary somatosensory areas for hind limbs (S1HL: -1.8/3.0/2). The device and the 6-OHDA injection cannula (targeting the medial forebrain bundle under 18° antero-posterior angle, AP -7, ML 1.9, DV 7 mm from dural surface) were implanted under inhalation anaesthesia.

**6-OHDA lesion procedure**

Under a short inhalation anaesthesia 8 µg 6-OHDA (Sigma, Germany) in 3 µl 0.9% saline NaCl stabilized with 0.05% ascorbic acid was injected to the medial forebrain bundle through the implanted guide cannula, described in more details in [18].
**Multi-electrode recordings in behaving animals**

LFP-s were recorded under two behavioural conditions: at rest and during walk in the active period of the day. Rest related signal was acquired while the rats were placed in a home cage, with the possibility to freely explore the environment. Walking related signals were recorded after a 3-6 session long training period in a simple task (Fig. 1A) where the animals were rewarded with sucrose food pellets at both ends of a 1 meter long corridor to encourage locomotion [18].

Serial recordings were performed before, and at least 14 days after the neurotoxin injection in freely moving, behaving animals. Experimental sessions consisted of 20 minutes in the home cage: resting (sitting) condition, followed by maximum 20 minutes in the behavioural task: walking condition. Signal was recorded from the same neuronal population throughout the course of experiments as the electrodes’ placement was not changed over time. The registered signal was amplified 20-times (HST/16V-G20), followed by a pre-amplifier (PBX/32sp-r G50/16fp-G50, Plexon Inc., TX, USA) with 50x gain. The signal was band-pass filtered to generate LFP-s (0.7-170 Hz). Video recordings (Cineplex, Plexon Inc., USA) and behavioural data (MEDPC), both synchronized with the LFP-s were stored for offline analysis. Data fragments corresponding to the two behavioural states (rest and walk) were selected using Cineplex Markup software (Plexon Inc., USA) [Chapter 3].

**Histology and 6-OHDA lesion verification**

Postmortem histological analysis was performed to validate electrode placements and quantify the extent of neurotoxin induced dopaminergic cell loss (Fig. 1 C), described in details in [18]. The animals were euthanized, the brains were processed for further analysis. Coronal brain sections (40 µm) of electrode placements (AP: -3.5 to -4.0 mm) were stained for cresyl violet to validate their localisation, sections from the substantia nigra (AP:-6.6 to -4.5 mm) were immunostained for tyrosine hydroxylase (TH) for quantitative assessment of dopaminergic cell loss (Fig. 1C). This was determined by 5-point scale through series of TH sections to assess microscopically the number of dopaminergic cell bodies present in ventral tegmental area (VTA) and substantia nigra at the end of the experiment.

**Data analysis**

Data was pre-processed by custom made MATLAB script (B. Jávor-Duray) and the Fieldtrip toolbox [28]. Data was visually screened and cleaned from possible artefacts (movement, etc.). The available LFPs, selected for a given behavioural condition were divided in segments of 2.1 seconds. The 50 Hz line noise artefact was removed from the data by fitting a 50 Hz sinusoid to the data and subtracting this [29]. Then, the power
spectral density was estimated for every segment, with a spectral spectral resolution of 2 Hz in signal from the sitting condition, and 6 Hz in case of the walking condition (where fewer behaviour specific fragments were available, therefore we used a coarser frequency resolution). To facilitate the comparison with observations in patients, we defined the beta frequency as: 15-30 Hz. In patients, this is the frequency band in which changes in local oscillatory brain activity and cortico-basal ganglia coherence have been observed [30–34]. However, in the rodent model of PD, changes in power and functional connectivity are often found at higher frequencies, with a spectral peak at ~30 Hz [15, 16, 18]. Therefore we defined an additional ‘beta30’ band ranging from 20-40 Hz to capture the model-specific parameters with the best possible accuracy. These considerations resulted in the definition of the following six frequency bands: 6-10 Hz (‘theta’), 10-15 Hz (‘alpha’), 15-30 Hz (‘beta’), 30-60 Hz (‘high gamma’), 60-90 Hz (‘high gamma’) and 20-40 Hz (‘beta30’). Relative power values were calculated for each frequency of interest for each recorded brain area. The 6-OHDA lesion-induced changes were tested using a two sampled t-test over ‘pre’ and ‘post’ lesion sessions.

To calculate the functional connectivity changes induced by dopamine cell loss, epochs of 2048 samples (sample frequency 1000 Hz) were imported into the BrainWave software package (version 09.117, available from http://home.kpn.nl/stam7883/brainwave.html). Phase Lag index (PLI, [26]) was then computed for randomly selected epochs, in total 100/80 seconds of data processed per recording session in sitting and walking conditions, respectively. This resulted in a 14 x 14 connectivity matrix per epoch per frequency band. To simplify statistical analysis, the 14 brain regions were grouped into “regions of interest” as enlisted in Table 1. The connectivity matrix was transformed to an 8x8 matrix depicting coupling within and between these groups of areas. Statistical analysis of the changes in functional connectivity between regions of interest was performed by a nested, mixed multilevel model (MLWIN 2.22, Centre for multilevel Modelling University of Bristol) per behavioural condition with the extent of dopaminergic cell loss as a covariate.

<table>
<thead>
<tr>
<th>Region code</th>
<th>Included brain areas</th>
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<tbody>
<tr>
<td>ctx</td>
<td>frontal M1; M2 whiskers; S1 hind limb</td>
</tr>
<tr>
<td>Mctx</td>
<td>M1 fore limb, M1 hind limb</td>
</tr>
<tr>
<td>mPFC</td>
<td>Medial prefrontal cortex</td>
</tr>
<tr>
<td>striatum</td>
<td>dorsolateral (motor) subsegment of striatum</td>
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Table 1. Regions of interest
RESULTS

Electrode placement and dopaminergic cell loss

Post mortem histological analysis was performed to validate electrode placement and neurotoxin effects. Placement varied within 5-600 µm from target coordinates, with most cortical electrodes in layer V (range: IV-VIa). Data from electrodes identified with coordinates beyond these criteria were discarded from further analysis. Quantification of cell loss showed an average score of 3 in VTA in three out of five cases, meaning that less than 50% of the dopaminergic cell bodies was still present. In two cases more cell bodies

Figure 1. Experimental setup and 6-OHDA lesion effects and example LFP signal. A) Schematic drawing of the walking task behavioural setup. The pellet dispenser areas had a cue light (filled grey circles) switched on when a reward was presented in the food cup (black rectangle). B) Electrode, injection cannula placements on the rat skull. Approximate location of the 14 electrodes are indicated by black dots, the cannula is indicated by a hexagon C) Representative coronal section immunostained for tyrosine hydroxylase (TH) at the level of the substantia nigra. Note the absence of TH immunopositive cells in the right substantia nigra (SN) and ventral tegmental area (VTA). D) Example of band-pass filtered (20-50Hz) resting state LFPs 21 days after the 6-OHDA injection
were preserved (average scale 1.2, 1.3) in VTA. In all cases, the substantia nigra was virtually depleted of tyrosine-hydroxylase immunopositive neurons (Fig. 1C). Agreement between the two independent observers as calculated using Cohen’s kappa measure, was 0.467 for substantia nigra (p=0.020) and 0.7 for VTA (p=0.001).

**Behaviour**

After the 6-OHDA injection, the animals spent more time resting. However, neither the total time (sit: 556±320 s vs 703±239, p=0.151; walk: 163±27s vs 164±52s, p=0.9448, all values are expressed as mean ± standard deviation, all behavioural parameters tested with two sampled t-test) nor the relative time (e.g. time spent walking relative to the length of the recording session; sit: 0.477±0.248 vs 0.583±0.1966, p=0.188; walk: 0.188±0.082 vs 0.159±0.093, p=0.332, two sampled t-test) spent in the monitored behaviour was significantly different between pre-, and post-lesion (>14 days after 6-OHDA injection) sessions. Walking speed decreased significantly (p=0.009) after the lesion (0.335±0.134 m/s vs. 0.440±0.075 m/s: pre versus post-lesion, respectively). Task performance decreased significantly for number of pellets collected (baseline: 33±9; lesioned: 18±16 pellets, p=0.0004) but not for task duration (16.636±4.690 s vs. 16.620±5.338 s: pre- versus post-lesion, respectively; p=0.992). For the functional connectivity analysis, whenever a recording session provided less than 100/80 seconds of data for sit and walk, respectively, PLI results were pooled for recordings from consecutive days. This resulted in the inclusion of 716±144 s / 598±151 s of data obtained from each animal for both pre- and post-lesion conditions during sitting and walking, respectively.

![Figure 2](image.png)

**Figure 2.** Relative spectral power in the primary forelimb motor area of the right (lesioned) hemisphere: before (black) and >14 days after (red) 6-OHDA injection. Shading indicates SEM. Black bar indicates significant differences over sessions (p<0.05, two sampled t-test). Blue lines, grey shading (20-40 Hz) delineate frequency bands selected for further analysis based on baseline, lesion induced characteristics of power.
6-OHDA lesion-induced changes in relative power spectra

The overall power spectral analysis showed an increase in relative beta power after the 6-OHDA lesion (Fig. 2.). The relative power spectrum per area is depicted in Figure 3. Lower frequencies (<15 Hz) showed decreased relative power after the dopaminergic cell loss in both resting and walking conditions. In the resting condition, a conspicuous and slightly asymmetric increase of relative power was present in the lesioned animals with the most widespread changes in the 20-40 Hz band. During walking, in general, the differences between the pre- and post-lesion conditions were much less significant. Relative power between 20-60 Hz increased significantly only in the more frontal cortical motor areas of the lesioned hemisphere, once corrected for multiple comparisons. Interestingly, we observed a decrease in relative power for the 60-90 Hz frequencies. In summary, nigrostriatal dopaminergic cell loss induced power increments in the beta frequencies that were modulated by the behavioural state of the animals.

6-OHDA lesion-induced changes in functional connectivity

To assess how functional connectivity changes in response to the 6-OHDA injection, we computed PLI. At rest, PLI (functional connectivity) between the different recorded brain regions (Fig. 4A) was reduced for the 6-10 Hz and the 15-30 Hz frequency bands in the post-lesion condition (Fig. 4B). By contrast, at higher frequencies (above 20 Hz) functional connectivity increased after the 6-OHDA lesion. This effect was strongest in the 60-90 Hz range. Furthermore, we detected increased interhemispheric coupling at the level of cortex (20-40 Hz, 30-60 Hz and 60-90 Hz) and between the cortex and striatum at high gamma frequencies (Fig. 4B). In comparison to the resting condition, post-lesion alterations in functional connectivity above 10 Hz during walking were in general less conspicuous (Fig. 4C). At lower frequencies (6-10 Hz), all possible connections between brain regions showed increased coupling after the lesion. Between 20-40 Hz, we detected an increase in coupling among the cortical and striatal sites within the lesioned hemisphere (Rctx, RMctx, Rstr). In the 30-60 Hz range we detected a similar coupling pattern that extended towards the contralateral cortical areas. Functional connectivity related to the mPFC above 10 Hz showed less lesion induced alterations during walking than at rest, although most of the detected differences did not survive correction for multiple comparisons. To summarize, we found a lesion-induced increase in beta band coupling in hemiparkinsonian rats both at rest and during walking, and an additional increase in functional connectivity over a wide range of brain regions at rest in the high gamma frequency band and during locomotion in the low frequencies.
Figure 3. Relative power changes by dopaminergic cell loss per frequency band and behaviour. Significant relative power changes in the 14 measured brain areas per area, frequency band in sit (upper row) and walk (lower row). Significant increase (red), decrease (blue) per frequency of interest (p<0.05, light color fill), Bonferroni corrected for multiple comparisons (p<0.0083, dark color fill).
DISCUSSION

In the current study we investigated the local synchrony and the synchronization between distributed brain regions of oscillatory brain activity in multiple cortical and striatal areas. The findings showed significant changes in the synchronization patterns between brain regions, particularly in the higher frequency bands. These changes were consistent across different movement conditions, suggesting a robust translational approach to understanding connectivity patterns.

Figure 4. Changes in synchronization between brain regions (PLI) induced by the 6-OHDA lesion. A) Connectivity matrix indicating type of connections. Significant PLI changes per frequency band in sit (B) and walk (C). Significant increase (red) and decrease (blue) per frequency of interest (p<0.05), Bonferroni corrected for multiple comparisons (p<0.0083).
brain areas in the awake, behaving hemiparkinsonian rat. The major findings are a widespread increase in relative beta power and increased functional connectivity in the high gamma band in the resting condition. By contrast, during locomotion the power spectral changes were less widely distributed and increases in functional connectivity were present at theta and low gamma frequencies. The presented findings illustrate the similarities in the lesion-induced changes in local and long-distance neuronal synchronization in the unilateral 6-OHDA rat model compared to the changes that have been reported in PD patients.

We detected an increase in local oscillatory brain activity for a wide range of areas in the beta30 band in unilaterally dopamine-deplete rats. Changes in synchronization between brain regions, i.e. functional connectivity, were present in only a few combinations of brain regions recorded from. The power changes described in the present study are consistent with previous studies that reported increased beta activity in motor cortex and basal ganglia of rodents [15–18, 20, Chapter 3], moreover, in the present study we extend these findings to more cortical areas. These patterns were only moderately present during locomotion, in accordance with findings suggesting that motor activity is associated with reduced beta power [25, 34]. One possible explanation for the contrast between the resting and walking conditions may come from the frequency boundaries applied in this study. We selected these frequency bands with the aim to optimally characterize the changes induced by the dopaminergic cell loss. The additional 20-40 Hz band was introduced based on our previous findings in the same model [18], which suggested that the neurophysiological changes in this frequency band might be a specific trait of dopaminergic degeneration in the rat model. However, in the (hemiparkinsonian) rodent model motor activity related peaks both in power and coherence measurements occur at slightly higher frequencies than at rest [14, 35, 36]. Therefore it is likely that the increased connectivity involves also higher frequencies than the here defined beta30 band and may take part in the synchronization changes detected in the low gamma frequencies, especially in the movement related functional connectivity.

An increase in beta band coupling between cortex and basal ganglia has been described both in experimental and human parkinsonism [14–16, 31, 32, 37] and is shown to be modulated by motor activity [6, 18, 38]. Human studies measuring basal ganglia (STN) and cortical activity revealed that specifically signals from the motor cortex show coherence with basal ganglia activity [8, 39]. The current findings demonstrate that this is not the case with respect to the striatum, the activity of which was coupled to the activity in cortical areas involved in various functions. This may not be totally unexpected, given the position of striatum in the basal ganglia cortical loop systems, where it serves as a way station for pathways related to diverse functions [40, 41]. In brief, in the present model of PD we detected increased beta30 activity both at the level of local synchronized oscillatory activity
and both in synchronization between brain regions, although the altered synchronization patterns were not restricted to the beta frequencies.

Functional connectivity analysis revealed remarkable changes in response to nigrostriatal dopaminergic cell degeneration in two additional frequency bands. First, we detected increased coupling in the high gamma band in the resting condition after the 6-OHDA lesion. Gamma band synchronization has been demonstrated both in physiological and pathological states in association with motor activity [2, 5, 42, 43]. The absence of abundant differences in gamma synchronization during walking in the present study is compatible with the association of gamma band synchronization with motor activity, as the animals were performing seemingly similar locomotor activity before and after the 6-OHDA lesion. However, this does not explain the observed post-lesion increase in coupling in the high gamma frequencies in the resting condition. In our previous experiments in the same model, we did not detect any significant changes in high gamma coupling between the motor cortices of the two hemispheres after dopaminergic degeneration in either walking or resting conditions [18]. The difference between the two studies might be explained by the divergent analytical approaches: in our previous study we compared two single brain areas, whereas in the present study several cortical areas were grouped together for the analysis, which may have produced a better segregation of the effects related to motor and non-motor functions. It is important to note that gamma band synchronization may also be associated with the level of arousal [2, 30]. Although our experiments were conducted under controlled conditions (and no sleep spindles were detected), the arousal level of the animals was not specifically measured, therefore fluctuations in alertness with a potential effect on neurophysiological parameters cannot be excluded. In brief, we detected increased gamma band coupling within and between hemispheres in the resting condition, indicating that gamma coupling might have a dopamine-dependent component in the resting state.

Further increased coupling was noted at a lower frequency range, often referred to as theta in rodents based on oscillatory patterns detected in healthy animals [44]. Theta rhythms have been described in cortex, striatum and hippocampus of rats, usually with a ~8 Hz peak. Theta activity in rats is associated with behaviours like: freely exploring the environment, or the execution of a well-practiced motor task [44, 45], similar to the experimental conditions in the current study. Furthermore, in the latter studies these low frequency oscillations were found to be coherent between hippocampal, striatal, thalamic and cortical brain regions. Whether the increased theta coupling observed in the hemiparkinsonian rat model is related to task performance, the movement itself or related somatosensory processes, remains to be determined. Considering the widespread nature of the low frequency connectivity and the regions where these rhythms typically occur in the brain (e.g. in the hippocampus, thalamus), it not unlikely that other brain areas, beyond the ones recorded in the present study are also involved in these processes.
The present study revealed similarities in the changes of local oscillatory brain activity and synchronization between brain regions observed in the rodent model and the changes known to occur in PD patients. The relative power changes in our rat model are in line with human findings showing increased beta power in cerebral cortex and basal ganglia of PD patients [31, 34, 39, and 46]. Excessive interhemispheric beta band synchronization has been described in the resting state in PD patients [7, 12, 47–49]. Also, combined recordings of cortical and basal ganglia activity have demonstrated altered synchronization patterns in PD patients both in the alpha and beta frequencies [8, 9]. In our study, changes in resting-state functional connectivity below 30 Hz were only modest; the most conspicuous changes were present in the high gamma frequencies, which are often linked to movement associated activity patterns [6, 37].

When comparing our observations in the hemiparkinsonian rat with the results of human studies some additional issues need to be considered. Although some of the neurophysiological changes in the rat model are considerably comparable to those in PD patients [13], there are obvious differences as well, namely the complex neuropathology in PD patients compared with cell degeneration (mostly) restricted to the dopaminergic system in the 6-OHDA model. The increments in beta and upper gamma oscillatory activity detected in the rat may be representative of the same activity that occurs in patients. However, considering that these rhythms are present in the healthy animals as well, comparisons between species should thus be drawn with caution [2, 50–52], especially since some researchers suggest that the frequencies involved in the pathophysiology of parkinsonism may vary from one species to another [36, 53]. Furthermore, recording conditions also might differ considerably: ranging from bipolar electrodes in the basal ganglia through cortical surface measurements using MEG in human subjects up to single cell detection and the recording of signals from dural surface. Lastly, there may be substantial differences in the type and magnitude of movements ranging from a single finger button press to freely moving animals.

In conclusion, our findings revealed remarkable neurophysiological similarities between the hemiparkinsonian rat model and PD patients. We demonstrated that the increased synchronization between distributed brain areas – between hemispheres or between cortex and basal ganglia – in the hemiparkinsonian rat may reflect some of the changes observed in patients. A further characterization of the model should include response to dopaminergic treatment in order to enable an even more accurate comparison between experimental and human parkinsonism.
REFERENCES


43. van der Meer MAA, Redish AD: Low and High Gamma Oscillations in Rat Ventral Striatum have Distinct Relationships to Behavior, Reward, and Spiking Activity on a Learned Spatial Decision Task. Front Integr Neurosci 2009, 3:9.


