

The basal ganglia is a subcortical network of nuclei whose dysfunction is associated with numerous prevalent pathologies such as movement disorders (Parkinson and Huntington disease, Tourette syndrome) and cognitive disorders (addiction, obsession). Despite an impressive body of experimental, clinical and theoretical works, the exact function of the basal ganglia is still highly debated. The understanding and treatment of basal ganglia dysfunctions require a better understanding of its normal function. Furthering this understanding was the general aim of this project.

The specific objective of this project was to understand how neuronal populations in the basal ganglia contribute to the execution of well learned motor sequences (motor skills or habits). Reaching this objective implied to optimize two challenging technical aspects. On the one hand we needed to use electrophysiological tools capable of recording simultaneously the spiking activity of ensemble of striatal neurons. Using low impedance custom-made tetrodes array and Neuralynx NLX9 microdrive we succeeded in simultaneously recording up to 80 striatal neurons which is, to the best of our knowledge, the maximum number of striatal cells ever recorded (see figure 1) in a freely moving animal. On the other hand, we needed to establish a behavioral paradigm in which rats would learn to repetitively perform a motor skill. Importantly for our question, this paradigm had to allow an exhaustive and precise quantification of the kinematics of the movements performed during skill execution. We therefore designed a running task in a treadmill. In short, to obtain reward and optimize their efforts, rats were trained to control their running speed in a timely, precise, and stereotyped manner (**Fig. 1**). This original behavior paradigm combines two main advantages. First, it focuses on a simple and natural motor command which is well known to be under the control of the basal ganglia: the locomotion. Second, a treadmill allow the use of lateral cameras and sensors (like accelerometers) that can fully capture the dynamics of locomotion over several seconds.

The main results derived from those major technical efforts are as follow.

We recorded ensemble of striatal neurons in rats over-trained to perform the running task. Each recording session consisted in 50 to 100 trials. During each trial, which lasted about 7 seconds, the rats run in stereotyped manner changing their running speed in a time- and space-dependent manner (**Fig. 1**). When we analyzed our large-scale neuronal dataset during execution of this locomotor skill we found that spiking activity of striatal ensemble covered the entire execution of the task (**Fig. 2**). Specifically the spiking pattern of individual cells were timely tuned to specific task-relevant sensory cues and kinematic aspects of the locomotor skill (**Fig. 2**, e.g., running speed).

The impact of the results generated by this project is fundamental for our understanding of the role of the basal ganglia in motor control during skill execution. Indeed, only a limited number of studies have so far directly related patterns of spiking activity of striatal neurons and skill execution. Those studies have generated a view of the role of the basal ganglia in skill performance as an "abstract" traffic light disengaged from movements execution itself. The data gathered during this project completely challenge this view and suggest that striatal ensemble continuously influences skill execution rather than generates abstract task-invariant initiation and termination signals. This result is in agreement with slowness of movements observed in Parkinsonian patients.

**Original behavioral task:
Running speed control
in a computarized treadmill**

**After learning, the running
trajectories and speed patterns
of the rats become stereotyped**

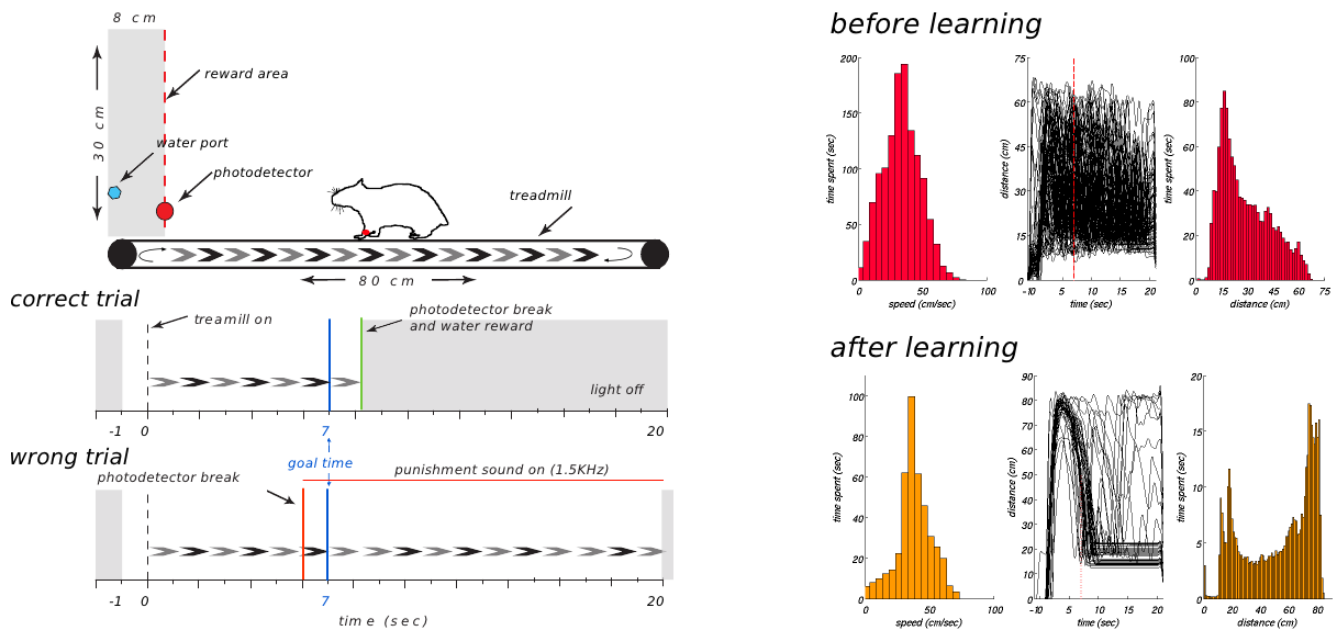


Figure 1
The left part of the figure shows the behavioral apparatus and illustrates a correct and incorrect trials. The right part of the figure shows speed distribution, trajectories and positions distribution of the animal during two behavioral sessions taken before and after learning of the task.

70% of the striatal cells recorded displayed strong task modulation of their firing rate

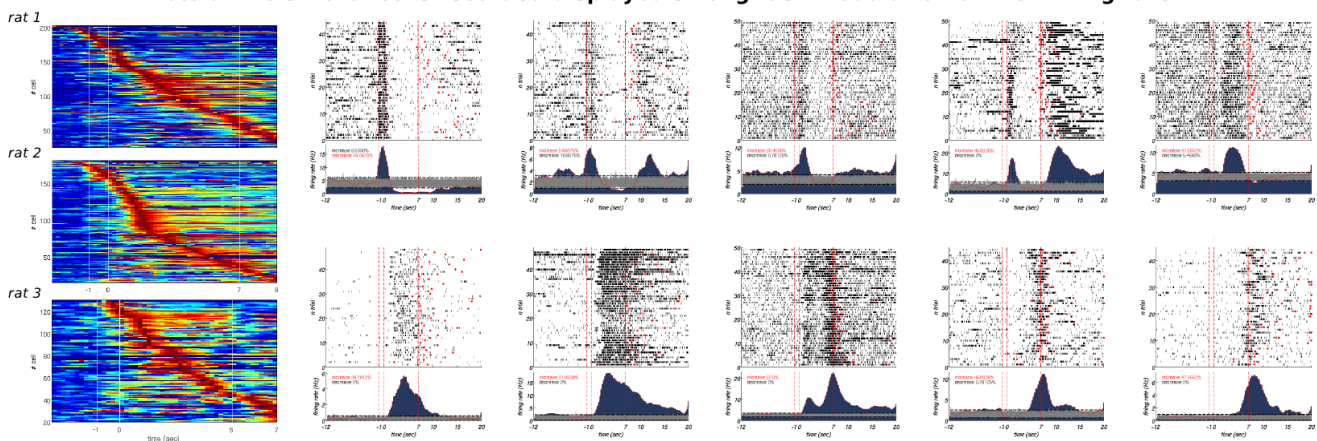


Figure 2
The left part of the figure shows the modulation of the firing rate of ensemble of striatal neurons (normalized Z score sorted in time) recorded in three rats performing the running task. The right part of the figure shows rasters and peri-event histograms of 10 exemple cells.