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Animals perform thousands of daily decisions, some requiring assessment of risks, future gains/losses, while many others simply rely on habits. Decision-making deficits are a common feature of many neuropsychiatric diseases as obsessive-compulsive disorder but can also manifest in chronic pain or in chronic stress conditions.
Decision-making is a multi-dimensional process including timing, inhibition, attentional set-shifting and risk assessment, thus involving a complex network. Frontostriatal nodes are known to be of the uttermost importance in these processes as revealed by many clinical and preclinical studies in both normal and disease conditions. Notably, the medial prefrontal (mPFC)and orbitofrontal cortices (OFC), dorsal striatum (Str) and nucleus accumbens (NAcc) have wellstablished roles in inhibition, outcome value updating, goal-direct to habit-based shifts and motivation, respectively. However, it remains a gap in our knowledge how these areas interact (i) what is the hierarchical relation between them, if any (ii), how does the activity of these areas evolve within the time window preceding the decision (iii), what are the differences in their activity leading to different behavioral outcomes (iv) and which

nodes/processes are affected in conditions of defective decision-making (v).
Recently, we observed that before decision-making, the activity of the mPFC, OFC, Str and NAcc was markedly different if the outcome, 3 seconds later, was a timed or an impulsive decision in the variable delay-to-signal task (VDS). Interestingly, as time elapsed and decision approached, most of these differences in activity disappear and synchrony between the mPFC, more specifically the prelimbic (Prl) region in both hemispheres and OFC and NAcc emerged differentiating timed and impulsive decision-making. With this set of data we proved that local field potentials (LFPs) can be obtained from a large number of areas (8 vs 1-2 in the majority of the studies) in a complex operant task where the animal is free to make decisions. More importantly, we demonstrated thatthe decision was encoded in the network seconds before the behavioral outcome.
In this project we will depart from this set of data aiming to attend to the following questions:
i. how comparable is frontostriatal network activity in different decision-making domains, specifically VDS (impulsivity) and attentional set-shifting task (ASST; stimulus selection and cognitive flexibility)?
ii. what is the role of each node during the time window of decision i.e. how do the nodes sequentially interact until the behavioral outcome?
iii. what is the impact of a targeted shutdown of one of the network's node/area in behavior
iv. and how does the network compensate?
In order to accomplish these objectives the project is organized in 3 main tasks. In the first task we will measure LFPs in the areas mentioned above – Prl, OFC, Str and NAcc in both hemispheres – during the execution of the VDS and attentional set-shifting (ASST) tasks. In the former, rats are presented with variable delays to a cue (light) and premature responses, i.e. during the delay, are used as a proxy of impulsive behavior. In the second task – ASST –, rats are presented with multiple stimuli (odors, images, etc) and have to discriminate relevant from irrelevant stimuli in order to obtain a reward (the ASST is an analogous to the human Wisconsin card sorting task). The set of rules determining relevant and irrelevant dimensions is periodically updated allowing to test for behavioral flexibility. In this task we will learn how the activity in the network – power in each node and coherence between areas – evolve in the seconds preceding the behavioral output; in addition, by using different paradigms, we will identify functional signatures specific of different decision domains. In task 2, we will use a chemogenetic approach to silence the activity of specific nodes of the network and therefore to validate results found in task 1; based on our preliminary VDS data described above, the Prl is an obvious target but others might also be considered. Furthermore, LFPs will also be recorded both off task and during the execution of the VDS and ASST allowing us to study the impact of the functional ablation of one node in the entire network as well as in decision-making. Finally, in task 3 we will use optogenetics to interfere (inhibit or excite) in precise timeframes of the decision-making enabling us to dissect with precision the evolution of the entire process. The position of the animals in relation to the decision magazine will be monitored in real time ensuring, via a closed-loop system, a temporally precise manipulation.
In conclusion, we will characterize a frontostriatal network in 2 decision-making paradigms.Pharmaco- and optogenetic tool will then be used to assess the relevance of key nodes and to precisely define the time window of decision processing.