

Network Dynamics of Basal Forebrain and Parietal Cortex Neurons

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Abstract

The current study examined the firing properties of basal forebrain and parietal cortex neurons across multiple phases of a visuo-spatial selective attention task. A wide variety of work in the parietal cortex has shown the parietal cortex to be important for spatial attention and route centered firing activity [14,18]. Anatomical studies of the basal forebrain have shown it is capable of selectively modulating various cortical structures dynamically [3,5,15]. At issue was the question of whether the anatomical and cell-type complexity of basal forebrain projections to cortex is paralleled by a complexity in the firing patterns of its neurons or whether basal forebrain neurons exhibit more generic responses primarily to relevant stimuli and rewards [4,10,17]. A second major question was whether recipients of basal forebrain output such as the parietal cortex, a structure important for spatial attention and spatial mapping, carry related firing pattern responses as found with basal forebrain neurons. Using a variety of clustering techniques we categorized responses of basal forebrain and parietal cortex neurons across task phases, which revealed a wide variety of highly distinct firing patterns in both brain regions. Our data suggests basal forebrain neurons can have much more complicated temporal dynamics than has been previously shown, and that such activity may impact or run parallel to processes in cortical targets.

Introduction

Previous studies of the basal forebrain (BF) indicate that this brain region is composed of a variety of cell types, responsive to different neurotransmitters [3]. Further investigation has suggested that cholinergic neurons in this area receive prefrontal glutamatergic input and that GABAergic, glutamatergic, and cholinergic neurons project to various cortical targets [3,4,6]. Lesion studies also suggest that the BF is important for incrementing attention [2]. Considering these projection patterns and the different neurons that make up structures of the BF, it has been suggested that there may be “several functionally segregated cortico-prefronto-basal forebrain-cortical circuits” [5]. Additionally the posterior parietal cortex (PPC) has been implicated as a component in one of these neural circuits, and has been shown to be important for changes in spatial attention [1,7,8]. The PPC is influenced by neurons of the BF, which itself receives input from the prefrontal cortex [6, 8, 9].

Cholinergic, GABAergic, and glutamatergic neurons of the basal forebrain (BF) are anatomically positioned to affect a wide array of cognitive operations via their cortical projections. Accordingly, BF lesions clearly impact learning and regulation of attention. While anatomical studies have begun to describe the complex structure of these neural circuits, little is known about the firing dynamics in relation to behavior. We have found that the network dynamics of the basal forebrain are closely related to specific phases of a selective attention task. Across different phases of such tasks, activity of most or all BF neurons is specific to transient periods of time through out the sequence of actions that make up this task. Alternatively, periods of activation and inhibition of different neurons are distributed across all phases of a task involving cue detection, response, and reinforcement. This complex response would suggest that the BF neurons can provide a temporal framework against which the activities of multiple cortical regions can be coordinated. It would also distinguish this cortically-projecting system from others, such as the noradrenergic and dopaminergic systems where neurons tend to exhibit brief phasic bursts timed to a specific stimulus and have more global projection patterns. Finally, in addition to signaling salience of cues and/or reinforcers, BF neurons provide information

concerning the level of task proficiency.

To address whether BF activity provides a temporal framework, multiple neurons in the BF were simultaneously recorded in freely-behaving rats during a selective attention task. Task conditions demanded accurate detection of a light flash position at the perimeter of an arena, traversal to that position where an identifying nosepoke was made, and return to the arena center for receipt of reward (or lack thereof if the light origin was misidentified). Results from eight animals show that BF neurons mapped all task phases. The presence or absence of reward impacted the activity of most neurons upon the animal's return to the center. More surprisingly, the firing profiles of a smaller but significant number of neurons predicted task accuracy, exhibiting firing rate differences between success and failure trials over the time period prior to cue delivery and up to the time of reward delivery.

Methods

Task

Animals perform a probabilistic uncertainty task in a circular arena with 4 foot diameter. The circumference of the arena contains 36 paired light-ports, located every 10 degrees. After stimulus presentation, the animal must nose-poke the port in which the light previously flashed, then return to the plate for reward. Rodents will perform 100 trials in a single session. This task requires the animal to attend to a specific spatial probability distribution of light stimuli. Neurons in multiple animals have been recorded in all three of the light flash distributions. In the following analyses we begin to address neuronal dynamics between different distributions. See Figure 1.

Surgery

After behavioral training, rodents are implanted with a total of 24 stereotrode recording wires with approximate targeting in the substantia inominata subregion. Sets of stereotrodes are independently moveable along the dorsal-ventral axis. For further surgery details see Wilent et al. 2007 [8].

Electrophysiology

Stereotrodes are formed by twisting 2 separate 17 micrometer diameter tungsten wires (California Fine Wire, Grover Beach, CA) together and fixing together with light heat. Wires are gold plated to decrease impedance. Microdrives created utilizing screws, steel tubing, and fun plastic. Stereotrodes are lowered approximately 1/3 micrometers per day until characteristic waveform properties of the region of interest are observed.

A video camera and tracking system (CinePlex) is positioned above the arena and temporally synced with the electrophysiological data. Position information was captured in pixels at a sampling rate of 60 Hz. Commercial software (Plexon) will be used to discriminate single-units based on tetraode specific waveform parameters. See Nitz et al. 2004 for a description of single-unit isolation using this technique.

Data Processing

Mean firing rate vectors are calculated for each cell on each recording day. This is accomplished by time normalizing every trial to a total of 69 time bins. The first 22 bins occur over a period of 2 seconds before the stimulus is flashed and the animal leaves the center pedestal. Bins 23-28 are normalized over the period of time it takes for the animal to move from the center to the moment he pokes his nose. Bins 29-46 are normalized across the amount of time it takes the animal to move from

nose poke to crossing the boundary of the center pedestal. Bins 46-69 occur over a period of 2 seconds after the animal has crossed back to the center boundary and is engaged in either reward consumption or preparation for next trial. After the trial has been normalized, the mean firing rate is calculated by summing the number of spikes in each bin and dividing by the total amount of time in which the bin was ‘occupied.’ A total of 1,221 basal forebrain neurons and 137 parietal cortex neurons were recorded from seven rats are included in this analysis.

Basal Forebrain

Categories

Using several unsupervised clustering algorithms, similarities between neuronal firing patterns can be observed. Using a Gaussian Mixture Model and a variant of Multi-view spectral clustering these neurons were categorized based on their average firing rate throughout the task [19]. K-means, hierarchical linkage, and spectral clustering were also used and showed similar category separation. For all algorithms a number of “categories” was selected, ranging from 5 to 50. As the number of categories increases, the variance within categories goes down. This relationship also means there may be no “correct answer” for how many categories there should be only different levels of separation proportional to the number of categories. See Figure 2.

Success or Failure is predicted by neuronal firing

Basal forebrain neurons also predict task performance. On successful trials any given neuron may have a distinct mean firing pattern. However if we compare successful and failure trials we see these patterns break down or change in specific ways. Some neurons completely change their firing pattern(fig1 diffs), some change at only one phase of the trials(2), and others may seem to have the same firing pattern regardless of success or failure(3). See Figure 3.

Parietal Cortex

Categories

Using the same algorithms as with basal forebrain neurons, similarities and differences were observed in the population of parietal cortex neurons recorded when compared with basal forebrain neurons. See Figures 4 & 5.

Firing activity prior to stimulus

A feature of many parietal cortex neurons that differs from the basal forbrain is their firing activity prior to the stimulus onset. Many cells either have a steady increase or decrease in overall firing rate during the 2 seconds prior to light flash and start of a trial. See Figure 6.

Interactions between BF and PC

Many analyses have yet to be done that will examine both brain regions simultaneously. Figure 7 depicts a specific group of parietal cortex neurons being compared with the entire population of basal forebrain neurons.

Distribution of stimuli

Basal forebrain neurons were recorded on three separate distributions; narrow, medium, and broad [Figure 1]. Of these we were interested in any neuronal differences in relation to the task. To accomplish this, linear discriminant analysis (LDA) was run on the average firing rate of all recorded neurons, where they are labeled based on which distribution the rat was on while recorded. The training set consisted of ~80 percent of all neurons, and the test set consisted of the remaining ~20 percent. The training and test sets were randomly assigned for 1000 iterations of LDA. Performance, for each iteration, was gauged as a percent correct on the test data set in determining which distribution the rat was on when the neuron was recorded. Figure 5 depicts the mean percent correct of LDA on individual distributions. To determine chance performance, distribution labels were randomly mixed on 1000 iterations. When this is done, LDA percent correct values drop to ~33 percent as expected. LDA determines which distribution a neuron is from significantly more than would be expected by chance. Figure 8

Discussion

These neuronal firing patterns relative to the described task ultimately show several things. First, the function of the basal forebrain may be as complex as its anatomy suggests. It is certainly doing more than responding to relevant stimuli and rewards. Second, the parietal cortex may have some similar processes running in parallel to the basal forebrain while having some different spatial processes as well. The last important feature this data points out is that both of these regions have to anatomical and functional capabilities to be important regions for shifting attention in the manner that our selective attention task demands.

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Figure 1

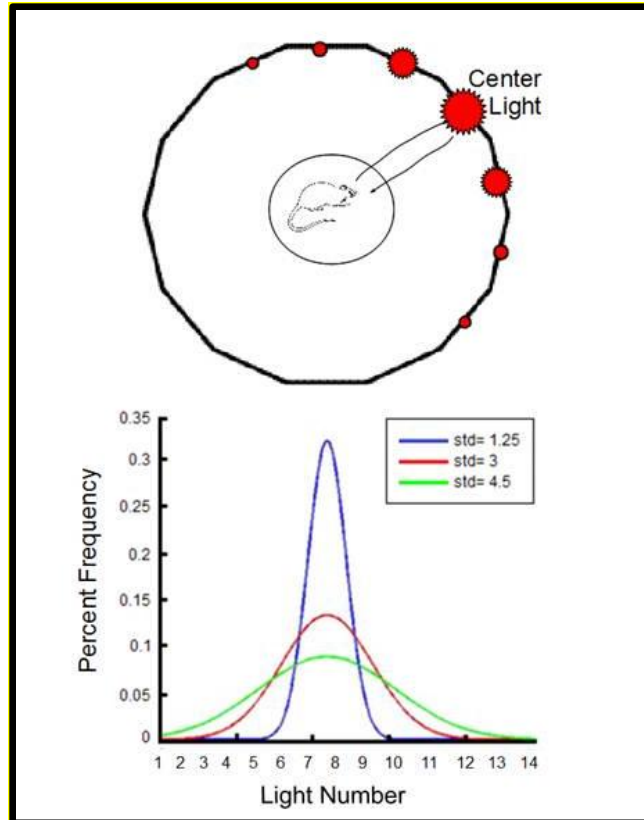


Figure 2

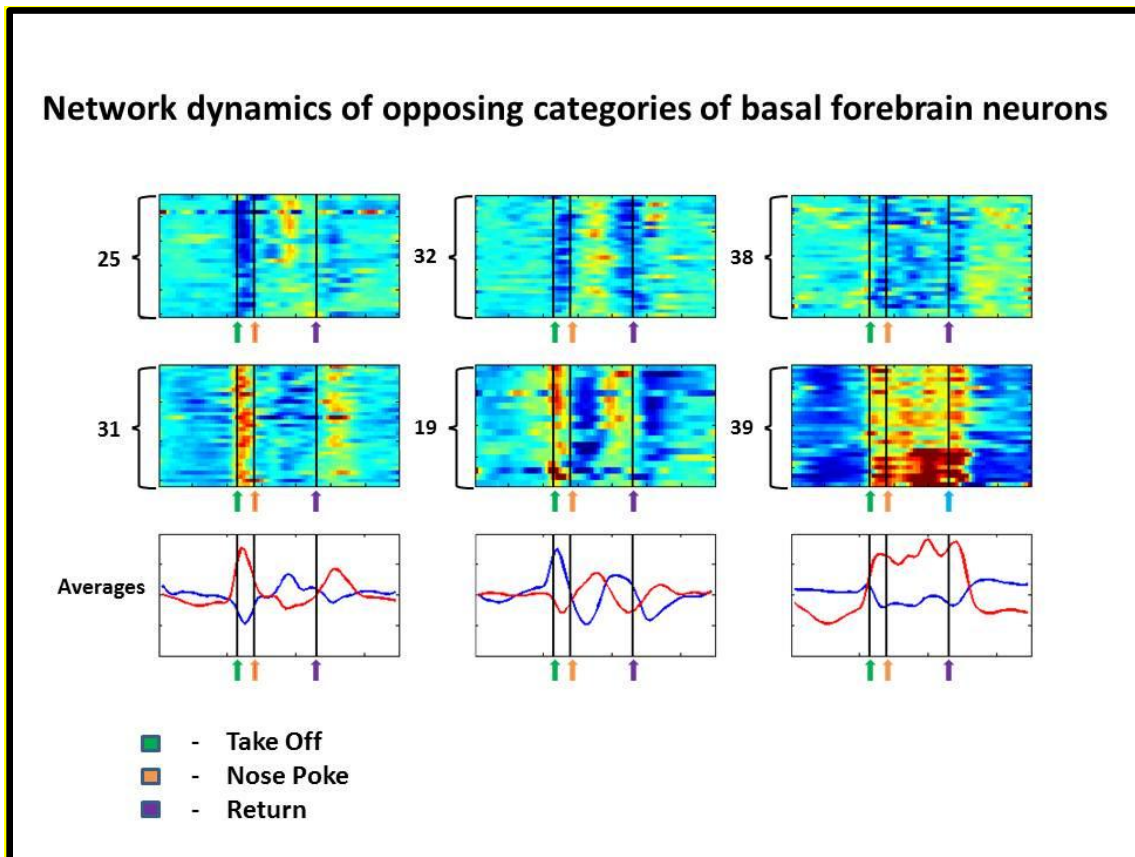


Figure 3

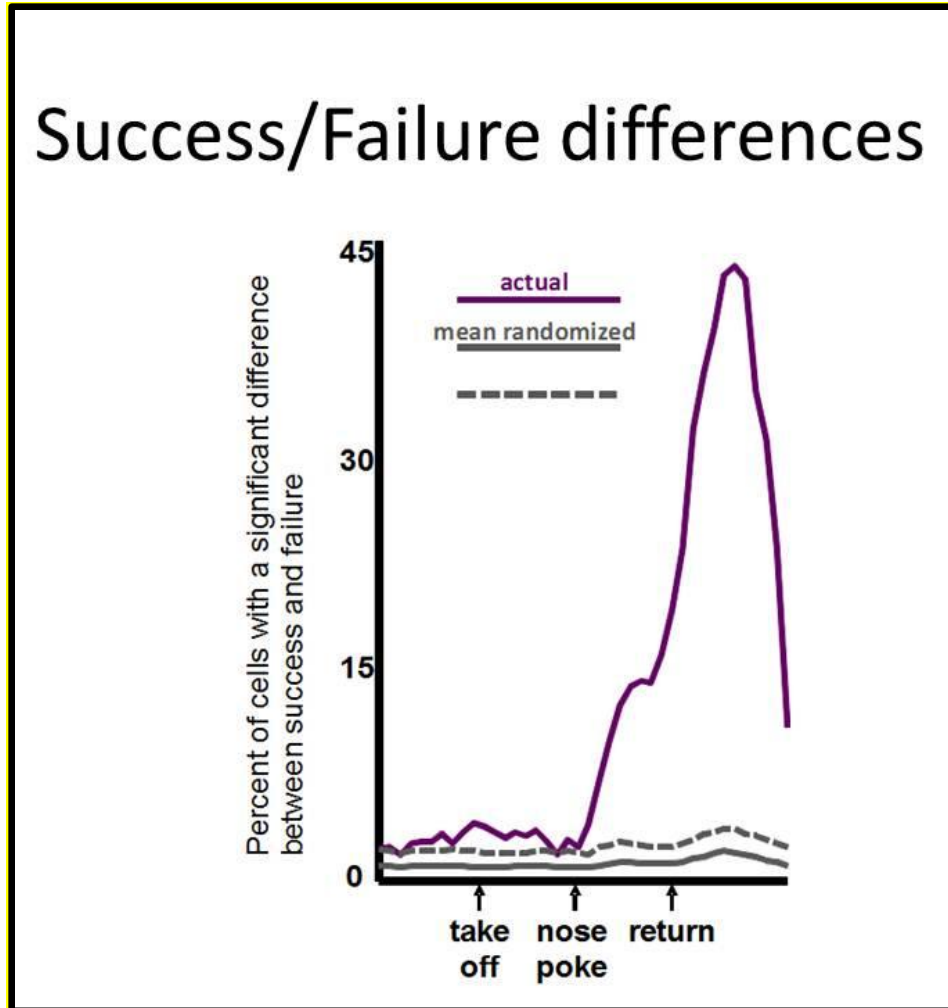


Figure 4

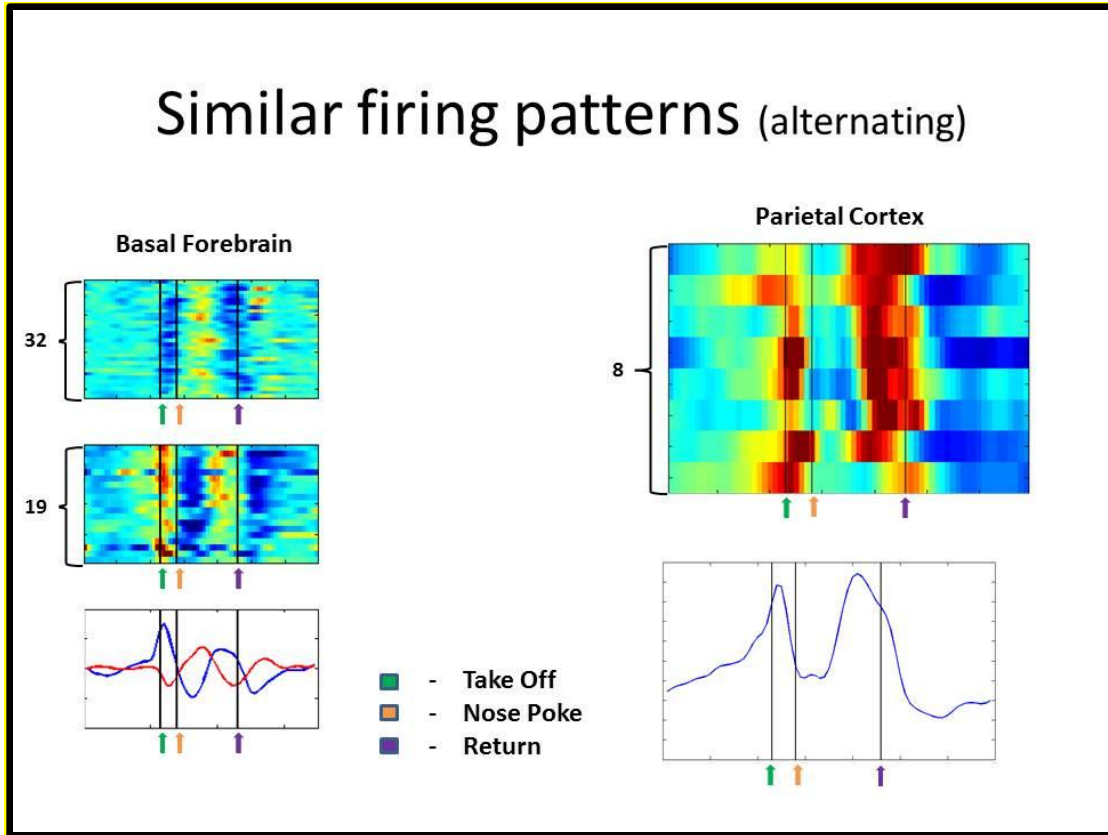


Figure 5

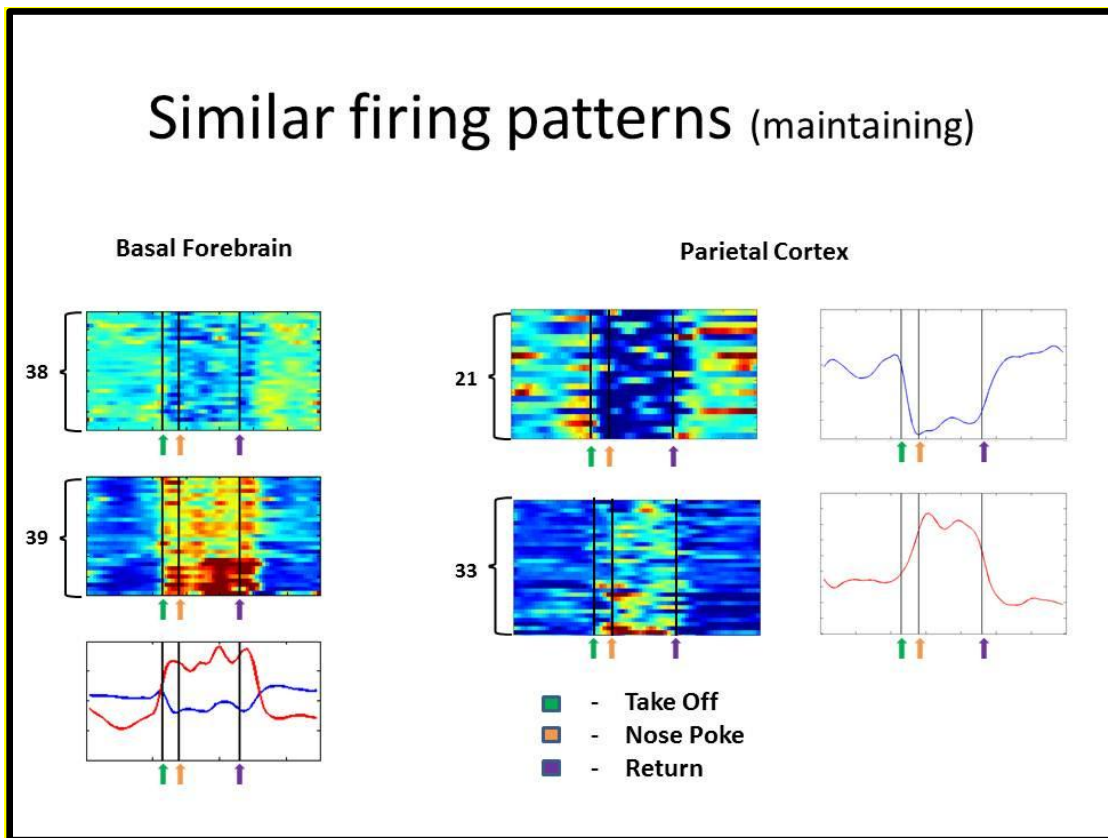


Figure 6

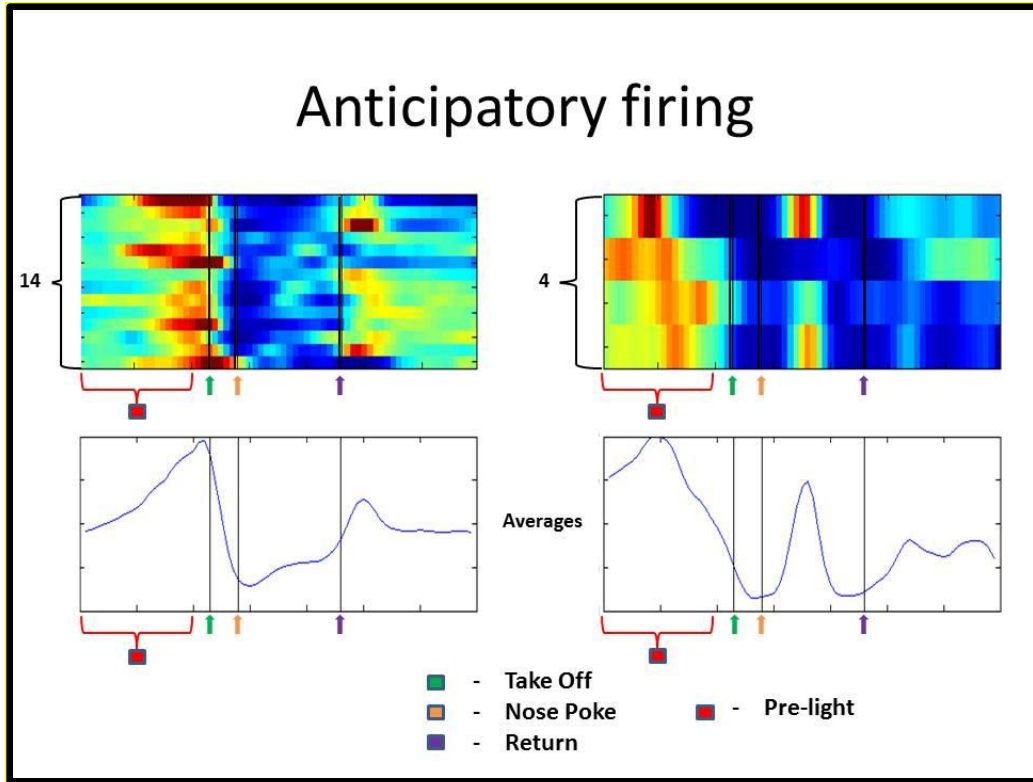


Figure 7

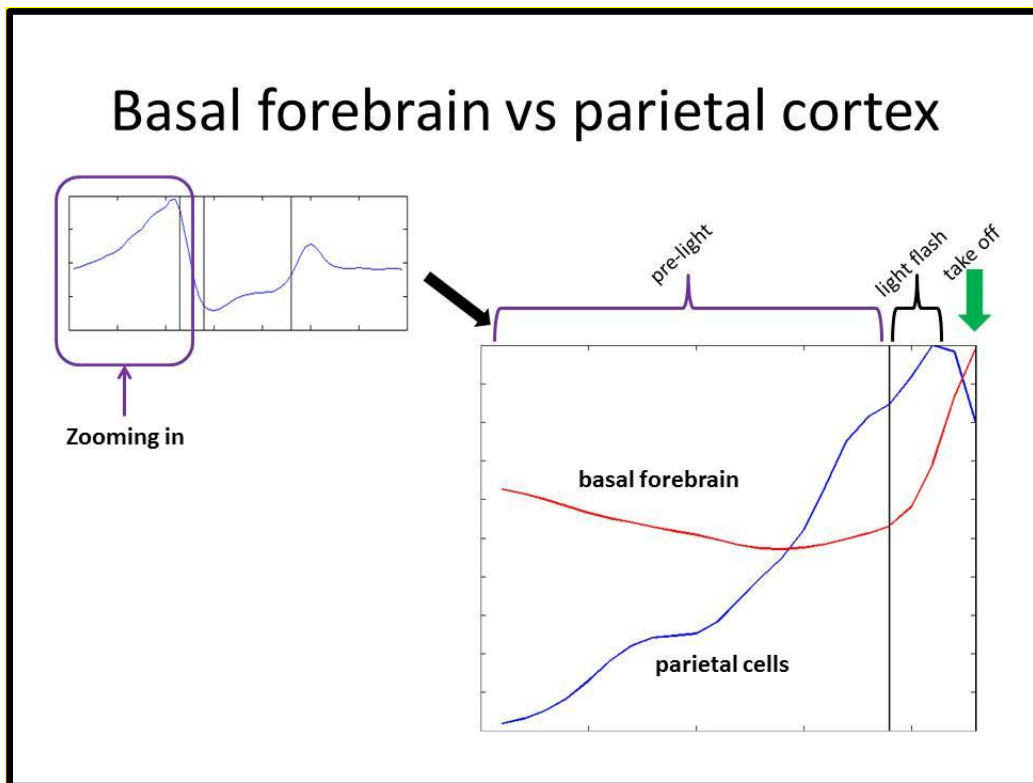


Figure 8

