

Diverse and precise tuning of neuronal activity in serotonergic brainstem nuclei

Sachin Ranade^{1,2}, and Zachary Mainen¹

¹Cold Spring Harbor Laboratory, ²Stony Brook University

Serotonin is an important neuromodulator implicated in diverse range of physiological functions as well as psychiatric disorders. It is released in the forebrain by neurons in a set of brainstem nuclei called the raphe nuclei. Dorsal raphe (DR) and median raphe (MR) nuclei send divergent ascending projections in the forebrain. Our current understanding of serotonin function is mostly gained from pharmacology and lesion studies. Neuronal recordings in animals performing specific behavioral tasks have greatly increased our knowledge of other neuromodulatory systems e.g. dopamine. There has been no report of recordings in raphe neurons during behavioral tasks. We believe such study will give us novel insights about raphe function at fast time scales.

In this study, we recorded from DR in rats performing a two-alternative choice odor discrimination task. Rats were trained to associate single odors to availability of water at one of two choice ports. Rats sampled odor by poking into the center port and responded with a poke into a choice port. Correct responses were rewarded probabilistically after a variable delay. Well-trained rats performed at more than 80% in 100 - 300 trials per session. This paradigm allowed us to study sensory, motor and reward related responses with high temporal precision. After training, rats were chronically implanted with a 6-tetrode recording drive targeted to the DR using a guide cannula. 54 neurons were recorded in 7 rats over an average of 4-8 sessions per rat. Recording locations were verified histologically. Raphe neurons showed diverse firing properties with respect to waveform characteristics, firing rate, sleep state modulation. By conventional criteria, 10% of neurons were putative serotonin neurons.

Neuronal responses were analyzed with respect to four behavioral epochs: odor sampling, movement, reward anticipation and reward consumption. Firing rates of >70% neurons were specifically modulated during at least one epoch, many tuned to multiple epochs. Many neurons responded to behavioral events within 100 ms. A subpopulation of neurons were even more precisely time locked (~ 20 ms), with a very strong (> 40 sp/s) phasic response, apparently to the water valve click. During odor sampling, approximately one third of units showed decrease in firing rate while a subset also showed odor-induced activation, in rare cases, stimulus selective. During movement, equal proportion of neurons showed enhancement and suppression of firing. A large proportion of neurons (~ 40%) were inhibited during reward anticipation while a subset (10%) showed changes in firing rate around time of expected reward. Putative serotonin neurons showed no obvious association with a specific response profile.

These recordings demonstrate that, like neurons in other neuromodulatory nuclei, raphe neurons are rapidly and precisely modulated by various behavioral events. The functional diversity of raphe responses likely reflects in part diversity of intrinsic properties and synaptic connectivity of neurons and is consistent with the possibility that significant information processing may occur within the raphe. This study highlights the need for methods to relate firing patterns to precise identification of neuronal cell types.

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