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A comparison of rule, decision, reward, and feedback-related activity in different frontal cortical and limbic structures in primates

200.11

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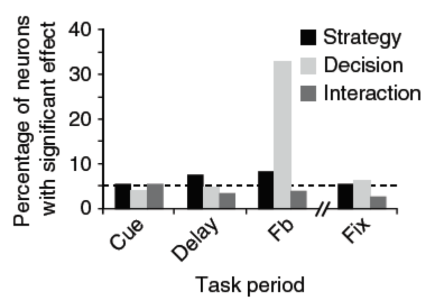
Introduction

- ❖ For complex, rule-guided decision making, multiple cognitive processes are required, including rule selection and switching, working memory, and outcome monitoring and adjustment[1]
- ❖ Most studies have focused on just one of these core processes, and just one brain region in isolation; and thus it is unclear exactly how widely distributed the networks are that underlie these processes
- ❖ Recently, Tsujimoto and colleagues[2] conducted a single-unit recording study in frontal pole cortex as rhesus monkeys performed an abstract strategy task (switch vs. stay) for fluid reward. They discovered that frontal pole cortex neurons were significantly modulated for saccade decision (left or right) only in the feedback (Fb) epoch of each trial and not significantly modulated for strategy or interaction (see *Figure 1*). This result was independent of the appetitive nature of the feedback and the motor saccade itself
- ❖ To further explore how rules, decisions, rewards, and feedback are encoded in different areas of the brain, we recorded from multiple prefrontal and limbic regions as two rhesus monkeys performed a two-alternative *rule*-based choice task similar to Tsujimoto and colleagues[2]

Figure 1:



Methods

- ❖ Subjects were two male rhesus macaques (*Macaca mulatta*), denoted as monkeys A & W. Each monkey sat comfortably in a custom-made primate chair with his head fixed, left arm comfortably restrained, and his right arm free to reach.
- ❖ The monkeys were trained on two rules using a custom-made pellet dispenser system:
  - ❖ **1.** The reverse-reward contingency task—called reversed contingency for short **(RC)** (see *Figure 2A*) :
  - ❖ **2.** The prepotent-response task **(PP)** (see *Figure 2B*) :

Figure 2:

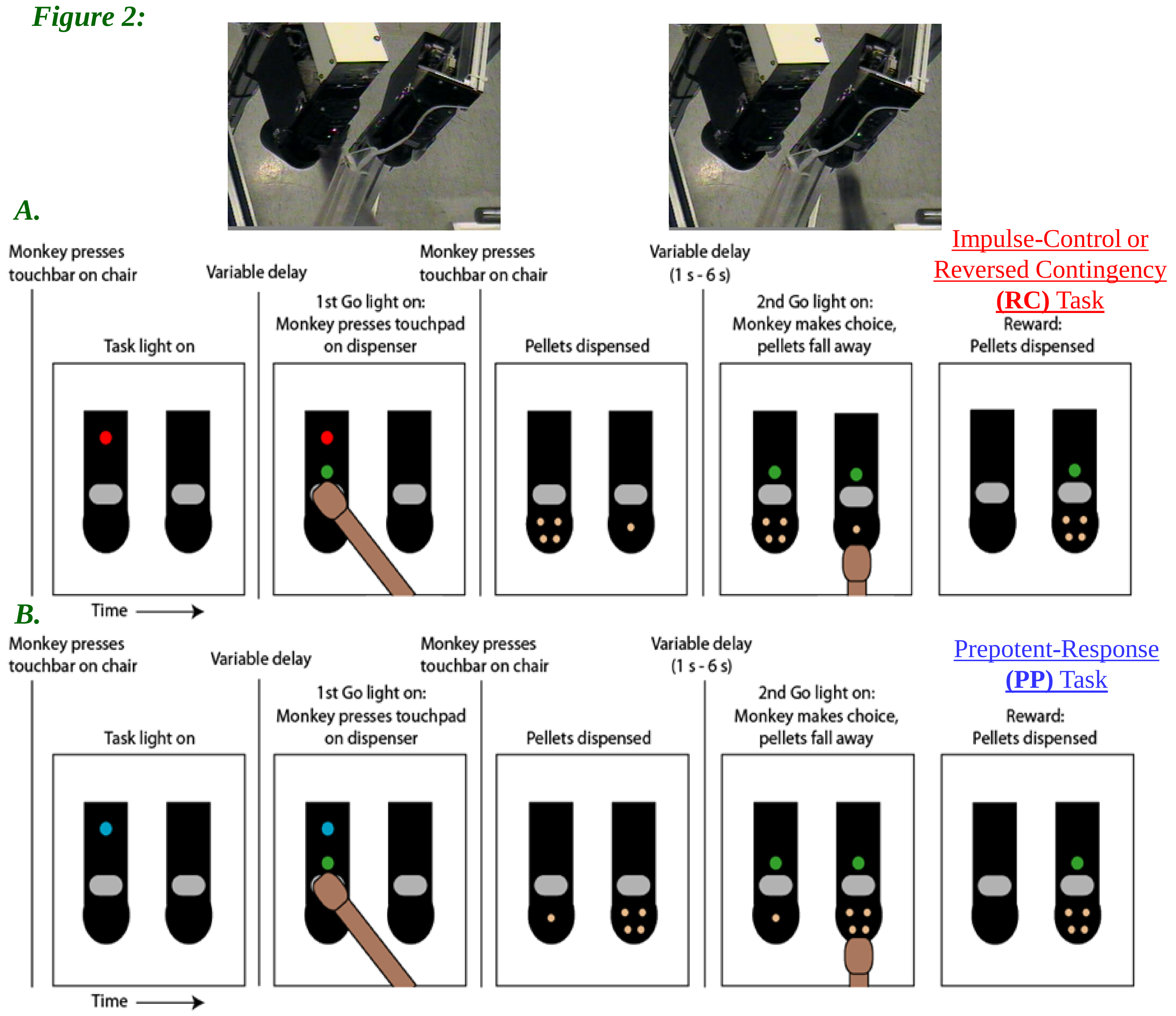
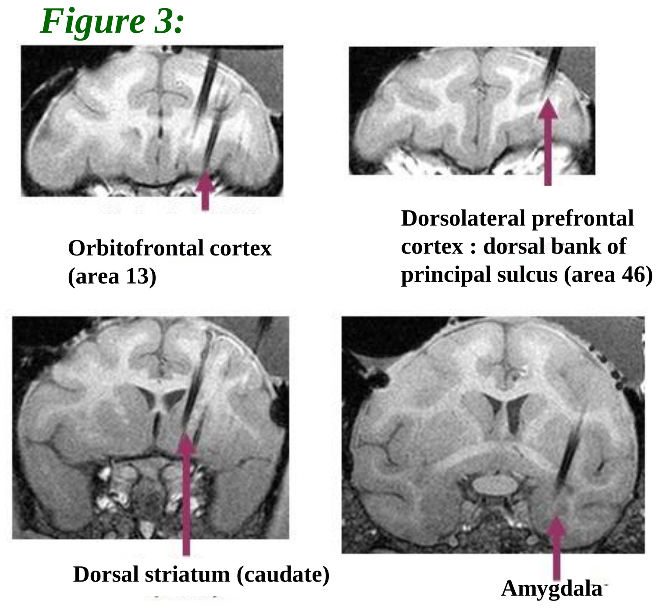


Figure 3:



❖Following Tsujimoto and colleagues[2], decision was denoted as the monkey's reaching direction (left or right dispenser) after the 2nd go light turned on

❖While the two monkeys performed the choice task, we used a multi-electrode system *(Plexon, Inc., Dallas, TX)* to record single neurons from the left and/or right hemisphere in different frontal cortical and limbic structures

❖We used magnetic resonance imaging (MRI) to verify that the electrodes were reaching the targeted sites for both monkeys. *Figure 3* shows four coronal slices of one monkey's brain, with arrows pointing to electrode tips

Results

Table 1:

Area	Monkey	Total neurons	Task/window modulated	Percentage (%)
LPFC	A	125	80	64
	W	212	141	67
OMPFC (includes ACC)	A	110	65	59
	W	196	108	55
ACC	A	68	43	68
	W	160	89	56
Insula	A	64	39	61
	W	39	23	59
Premotor & FEF	A	64	48	75
	W	241	168	66
Striatum	A	88	56	64
	W	66	36	55
Amygdala	A	60	38	63
	W	13	8	62
Mediodorsal Thalamus	A	51	31	61
	W	5	4	80
ALL	A & W	1334	837	63

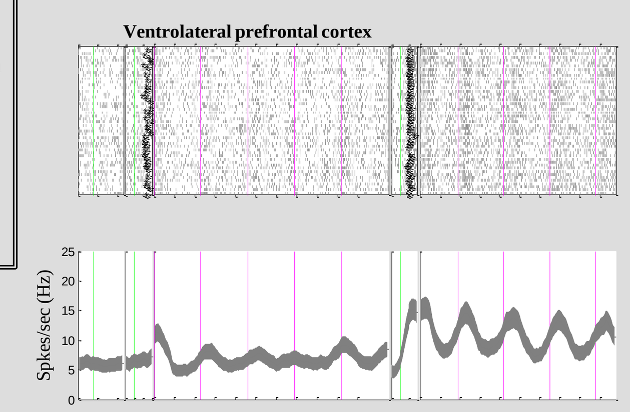
Table 1: LPFC is lateral prefrontal cortex, and includes neurons in the dorsolateral prefrontal cortex (Walker's area 46), dorsal prefrontal (area 9), and Ventrolateral prefrontal cortex (12, 44, & 45). OMPFC is orbitomedial prefrontal cortex, which includes dorsal and ventral anterior cingulate cortex (32 & 24), orbitofrontal cortex (11 & 13), and infralimbic cortex (25). Insula is agranular insula. FEF is frontal eye fields (8). Striatum includes dorsal and ventral striatum.

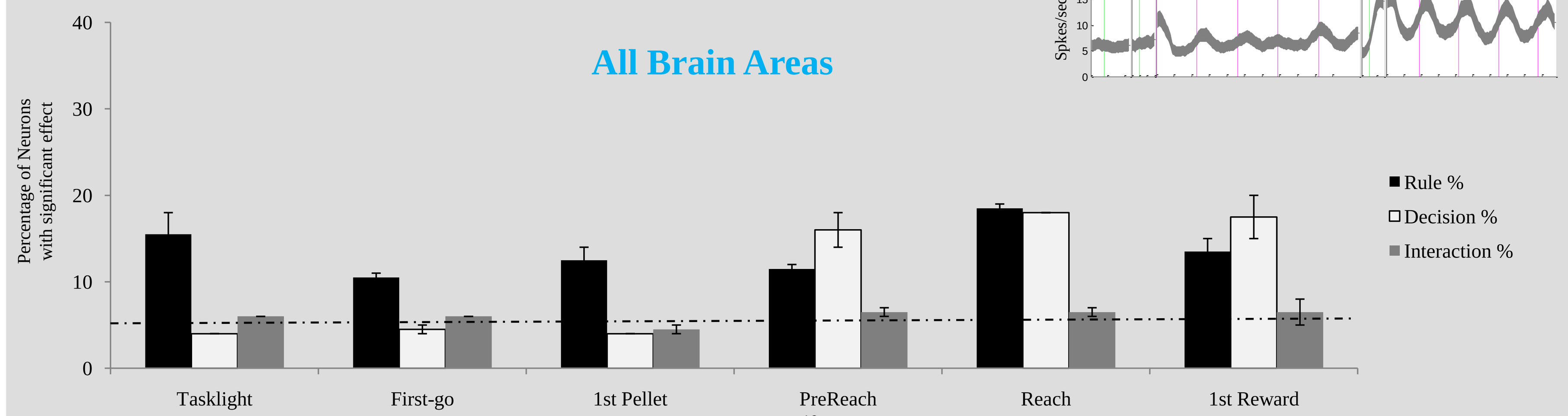
❖The first three columns of Table 1 show the recorded brain areas and number of neurons for each monkey

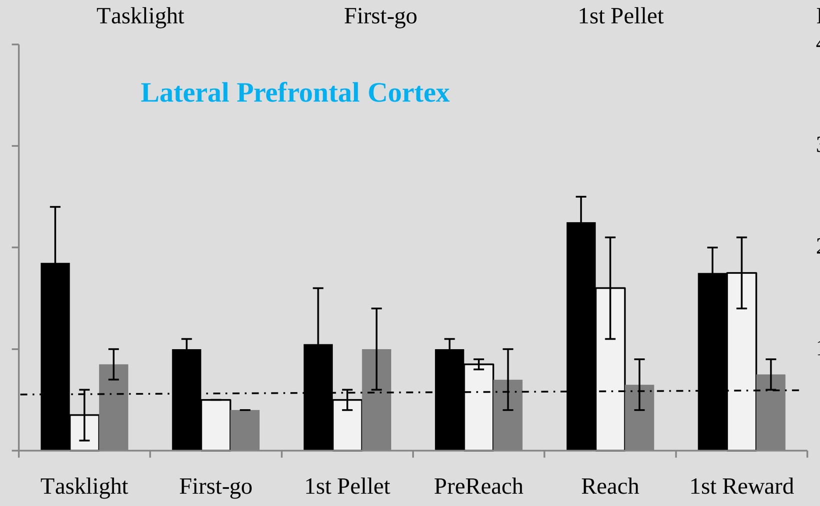
❖Column four shows the number of cells that showed significant task/window modulation (ANOVA, $p \leq 0.05$) in the task light, 1st presentation pellet, pre-reach, reach, and1st reward epochs. Only these cells were used for further analysis

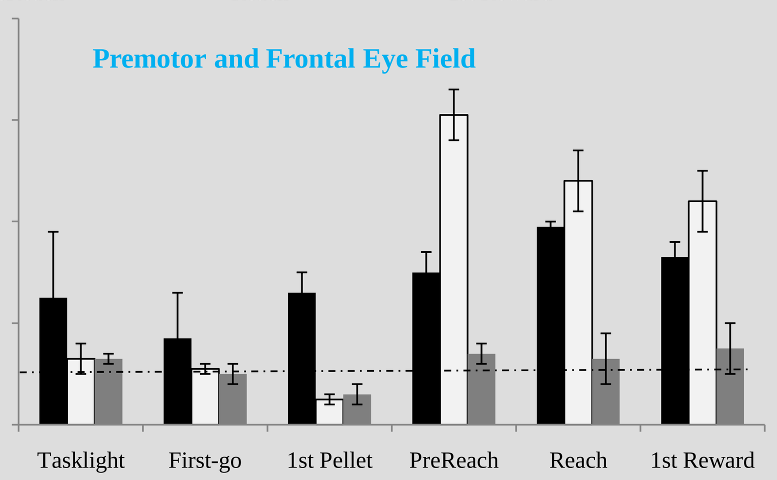
❖Column five shows the percentages of task/window modulated neurons

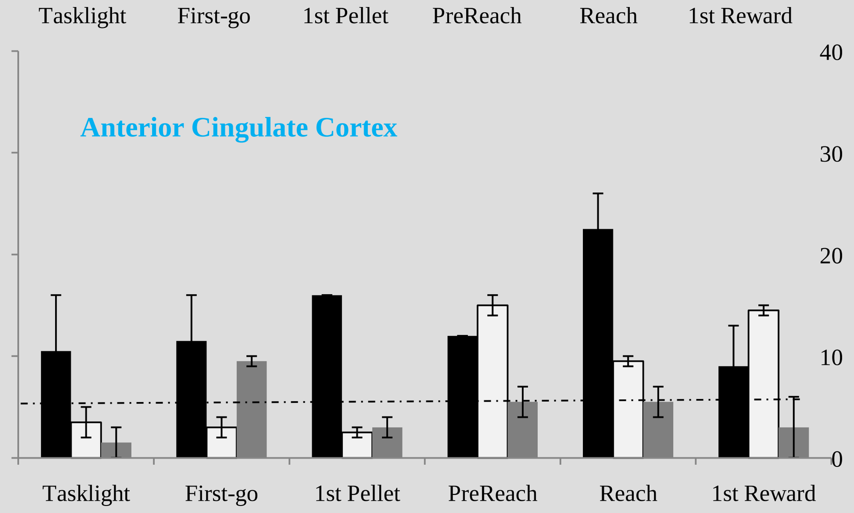
Task/Window modulated neuron

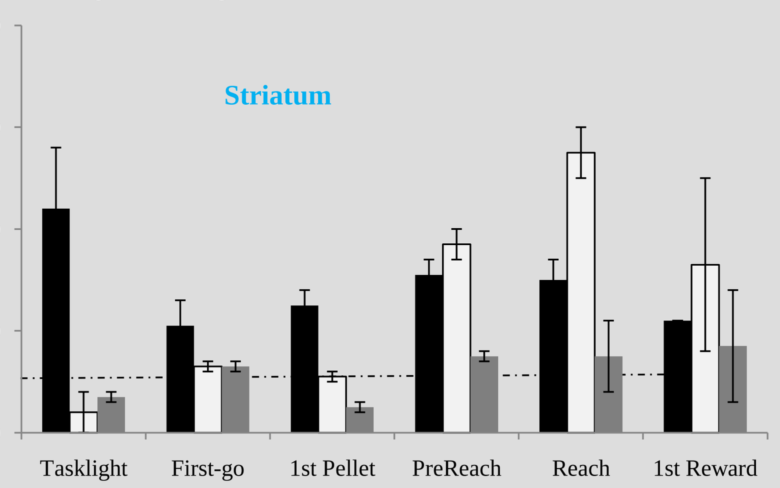


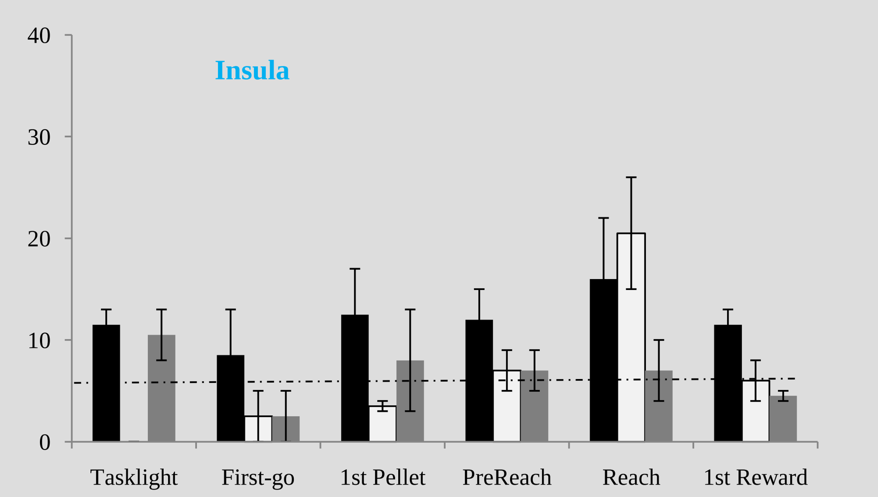












❖Rule, decision, and rule by decision interaction selectivity plots were generated using a 2-way ANOVA for each epoch (*Tasklight, First-go, 1st Pellet, PreReach, Reach, 1st Reward)*. The dependent variable was firing rate within the epoch and the two independent two-level factors were rule (RC vs. PP) and decision (left vs. right choice).

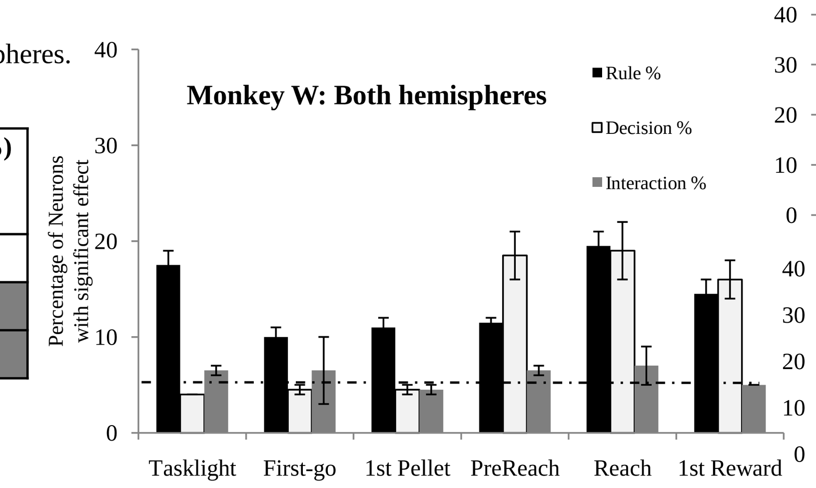
❖In all neurons and brain areas combined, note the general pattern of rule tuning early, followed by an increase in decision tuning later in the trial. This pattern was found in all recorded brain areas

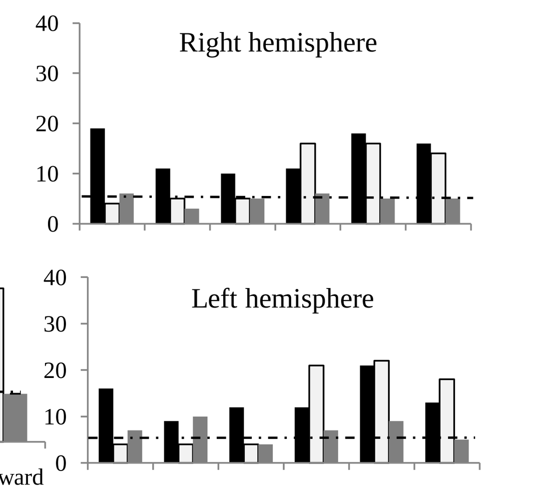
❖Also note the differences in brain areas, such as relatively more rule tuning in prefrontal areas versus more decision tuning in premotor cortex and striatum

❖Bilateral recordings were made in monkey W but not monkey A. Rule and decision selectivity analysis across epochs did not reveal significant differences between hemispheres.

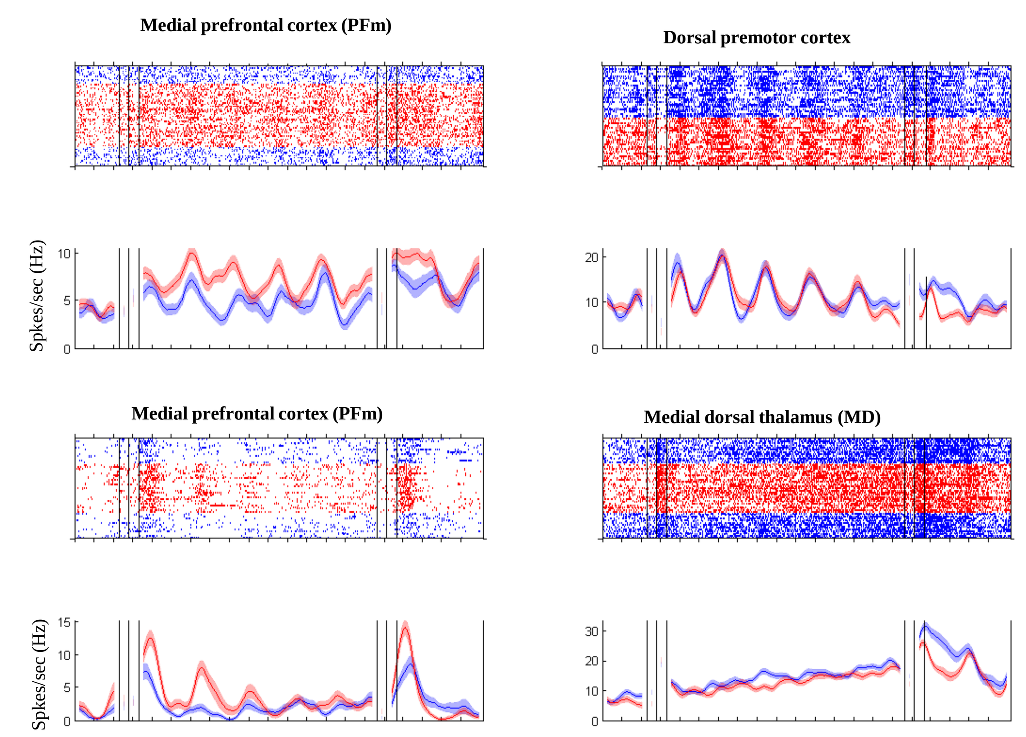
Table 2:

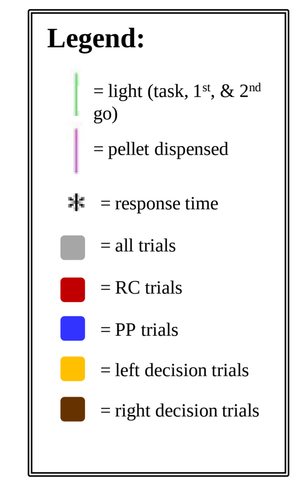
Monkey	Hemisphere	Total neurons	Task/window modulated	Percentage (%)
A	Left	562	357	**64**
W	Left	502	316	**63**
	Right	270	164	**61**

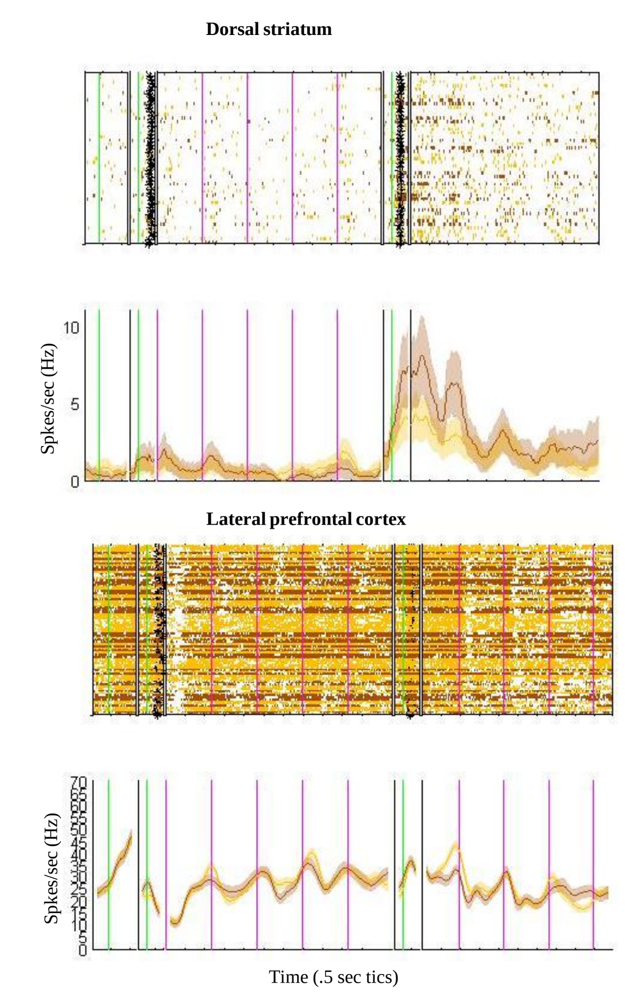




More Example Neurons



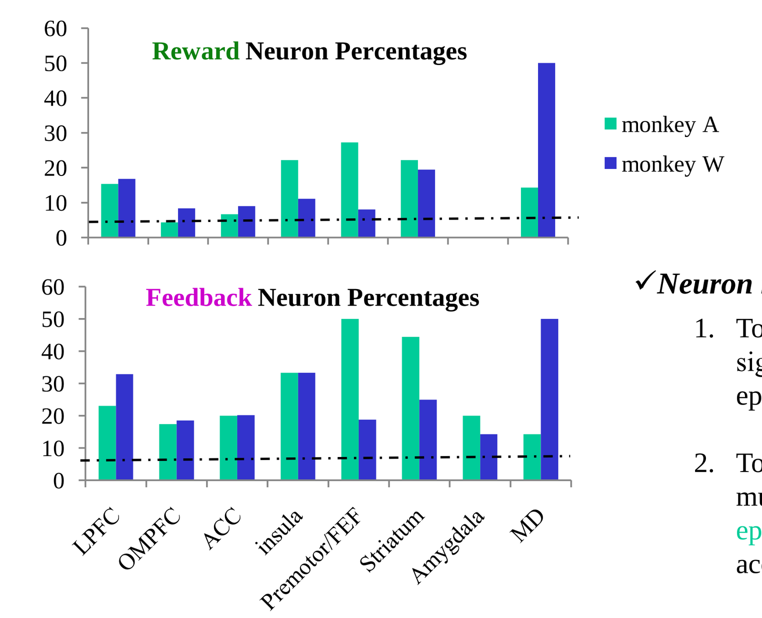




Reward/Feedback related activity

✓***Neuron must pass all the <u>three</u> criteria below to be considered a reward neuron.***

1. To control for acoustic and visual effects of pellets, neuron must be significantly ($p \leq 0.05$) more active during the first two reward epochs compared to the first two pellet-presentation epochs
2. To control for reaching, the neuron must be significantly more active when reaching for the reward (after 2nd go light) compared to reaching to the switch (after 1st go light)
3. To control for eating, the neuron must **not** be significantly more active at the 3rd reward epoch (when the monkeys were eating) compared to the 1st reward epoch.



✓***Neuron must pass both criteria below to be considered a feedback neuron***

1. To control for acoustic and visual effects of pellets, neuron must be significantly ($p \leq 0.05$) more active during the first two reward epochs compared to the first two pellet-presentation epochs
2. To find neurons related to feedback versus reward *per se*, the neuron must be significantly more active during the 1st and 2nd reward epochs (where the monkeys were initially receiving feedback and accuracy information) compared to the 3rd and 4th reward epochs.

Conclusions and future directions

❖In all brain areas tested, and for both monkeys, we found an overall tuning modulation pattern in which rule tuning began with the instruction cue, generally persisted throughout pellet presentation, and then increased again during reach. In contrast, direction tuning increased later in the trial.

This overall tuning pattern across the trial suggests a widely distributed network involved in rule-based decision making[3]

❖Differences can also be seen across areas, such as prefrontal regions showing more relative task tuning, and premotor and striatum showing more relative decision tuning. These differences will be characterized in more detail in future work

❖Reward-related activity was mixed, with only LPFC and striatum showing a consistent percentage across monkeys. This may be due to the strict criteria used to identify reward-related neurons

❖A consistent finding was that the firing rate was higher for the first two reward epochs than the second two. This difference does not appear to be due to visual stimuli, reaching or eating, and suggests that neurons in most brain areas are responding differently to the first two and last two reward pellets. The first two pellets provide information regarding subsequent reward.

References

1. S. P. Wise, *Trends Neurosci* 31, 599 (Dec, 2008)
2. S. Tsujimoto, A. Genovesio, S. P. Wise, *Nat Neurosci* 13, 120 (Jan, 2010)
3. S.L. Bressler, V. Menon, *Trends Cogn Sci* 14:277-290

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