Reaching for the larger or smaller of two rewards: How prefrontal cortex and limbic structures underlie conventional and unconventional task performance

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Introduction

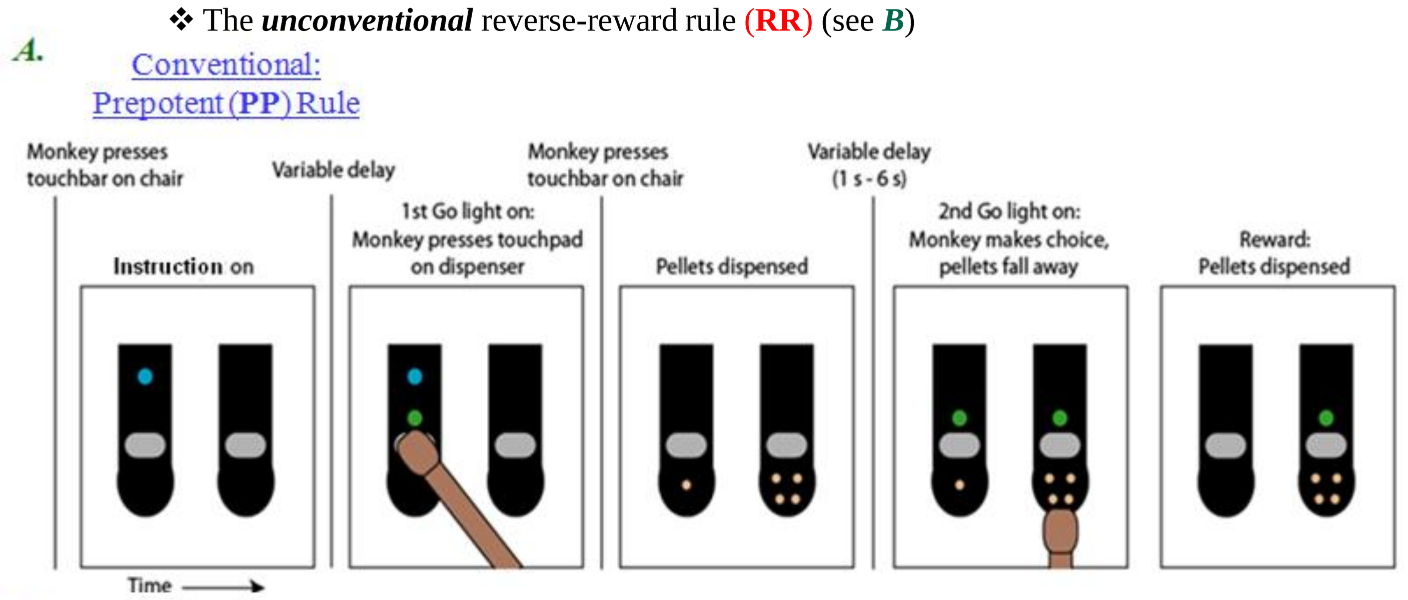
- ❖Rules allow us to generalize beyond stimulus-response associations, and they enhance cognitive flexibility, creativity, learning, and survival.
- ❖Abstract rules may also enable some animals to suppress conventional responses in favor of less conventional ones.[1,2]
- ❖Previous studies have looked at neural encoding of abstract rules such as match/non-match,[3,4] but few studies have looked at rules in which one behavior is significantly harder and more unconventional than the other.[5-7]
- ❖To characterize how conventional and unconventional rules are encoded in the brain, we recorded from multiple prefrontal and limbic regions as rhesus monkeys performed a two-alternative *rule-based* choice task, with one rule being conventional and the other unconventional.

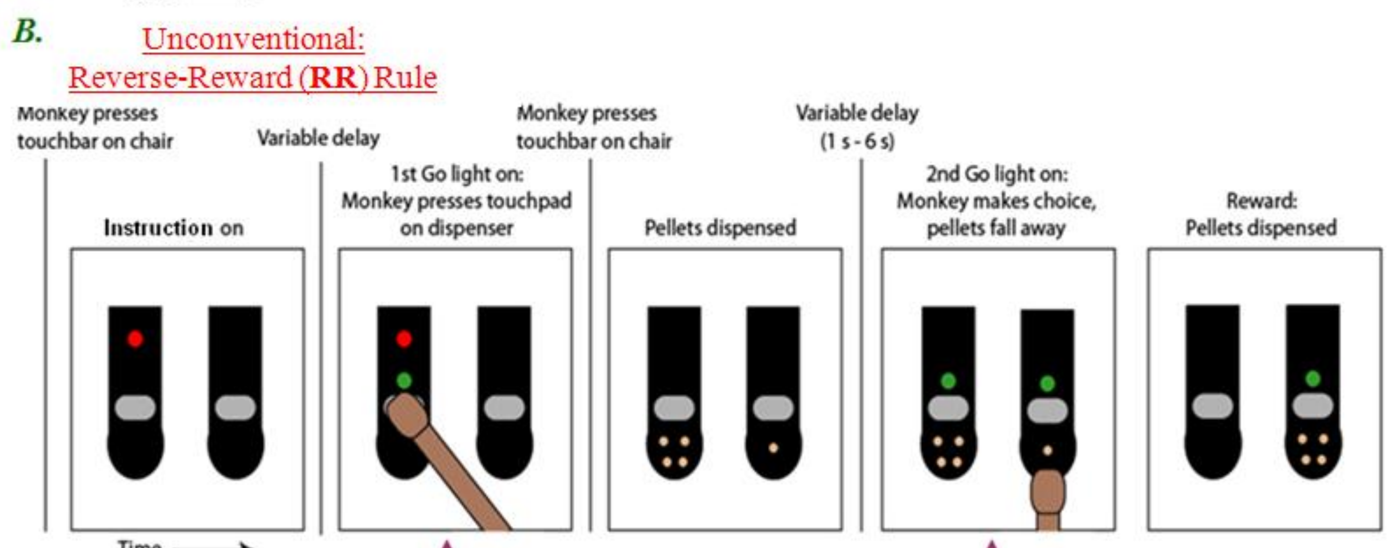
Methods

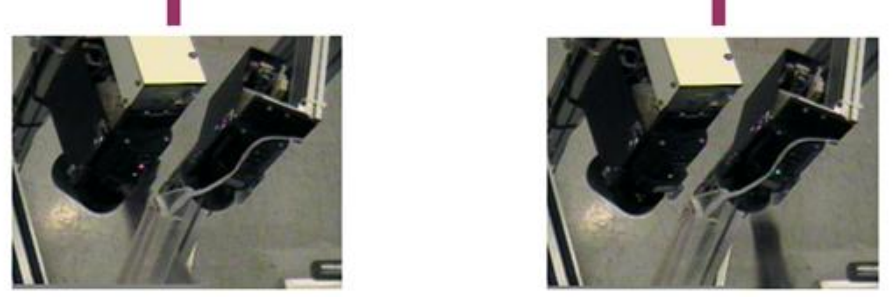
❖ We tested two male rhesus monkeys (*Macaca mulatta*), denoted as monkeys A & W. Each monkey sat in a custom-made primate chair with his head fixed, his left arm comfortably restrained, and his right arm free to reach.

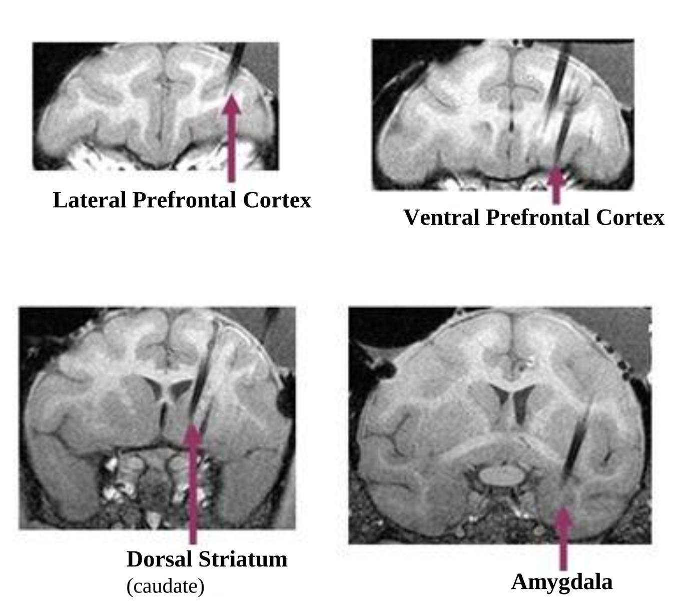
❖ The monkeys were trained on two rules using a custom-made pellet dispenser system:

- ❖ The ***conventional*** prepotent rule (**PP**) (see *A*)
- ❖ The ***unconventional*** reverse-reward rule (**RR**) (see *B*)









❖We conducted the test sessions in both *block* and *mix* conditions. In *block*, there were 12 prepotent rule trials, then 24 reverse-reward trials, then 12 prepotent trials. In *mix*, both rules were pseudo-randomly interleaved. In our analyses, the block and mix conditions are combined.

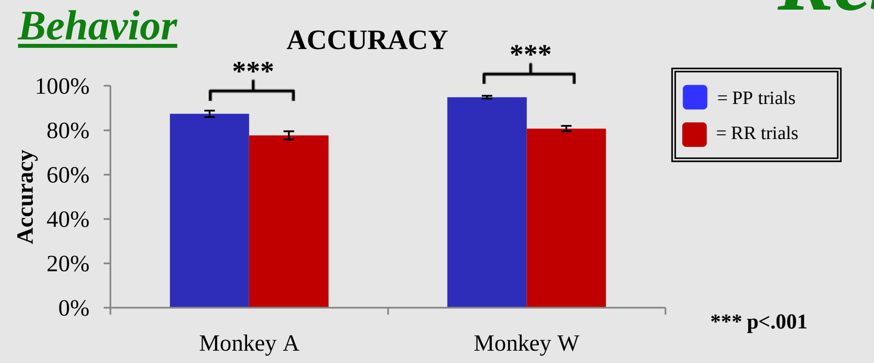
❖Along with the two rules, we also denoted two spatial goals, based on the monkey's reaching direction (left or right dispenser) after the 2nd go light turned on.[8]

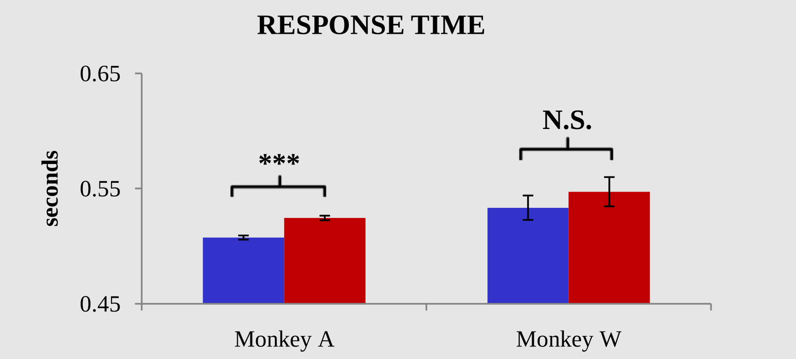
❖While the two monkeys performed the choice task, we used a multi-electrode system *(Plexon, Inc., Dallas, TX*) to record single neurons from different frontal cortical and limbic structures.

❖We used magnetic resonance imaging (MRI) to verify that the electrodes reached the targeted sites for both monkeys. The figures to the left show four coronal slices of one subject's brain, with arrows indicating electrode tips.

Results

Behavior





❖Both monkeys were significantly less accurate performing the reverse-reward rule compared to the prepotent rule, which shows that the RR rule was more challenging than the PP rule.

❖In addition, Monkey A was significantly slower performing the RR rule compared to the PP rule.

Neurophysiology

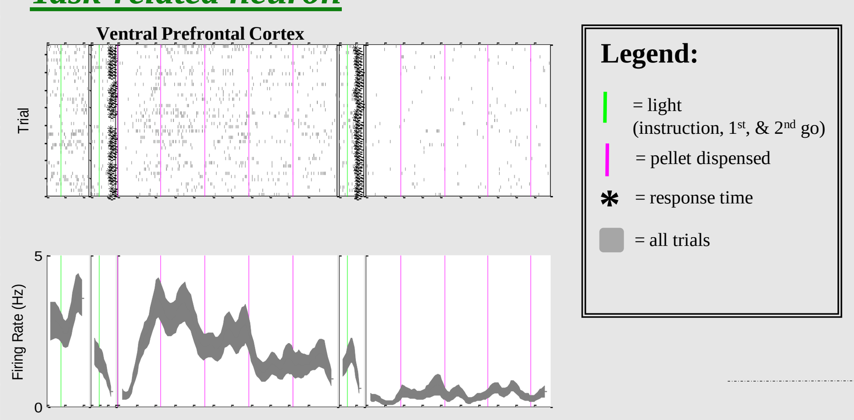
Area	Monkey	Total neurons	Task related	Percentage (%)
Lateral Prefrontal Cortex	A	118	102	86
	W	158	120	76
Medial Prefrontal Cortex	A	101	80	79
	W	173	117	68
Ventral Prefrontal Cortex	A	136	105	77
	W	128	79	62
Premotor Cortex	A	104	92	88
	W	276	197	71
Dorsal/Medial Striatum	A	68	56	82
	W	28	16	57
Ventral Striatum	A	84	56	67
	W	76	47	62
Mediodorsal Thalamus	A	94	80	85
	W	9	8	89
Amygdala	A	120	88	73
	W	16	11	69
Insula	A	97	73	75
	W	39	21	54
ALL	A & W	1755	1292	74

❖The first three columns of the table to the left show the recorded brain areas and number of neurons for each monkey.

❖The *Task-related* column shows the number of cells with significant firing rate modulation (ANOVA, p≤0.05) between the (1) instruction light, (2) 1st pellet presentation, (3) pre-reach, (4) reach, and (5) post-reach periods. Only these cells were used for further analysis.

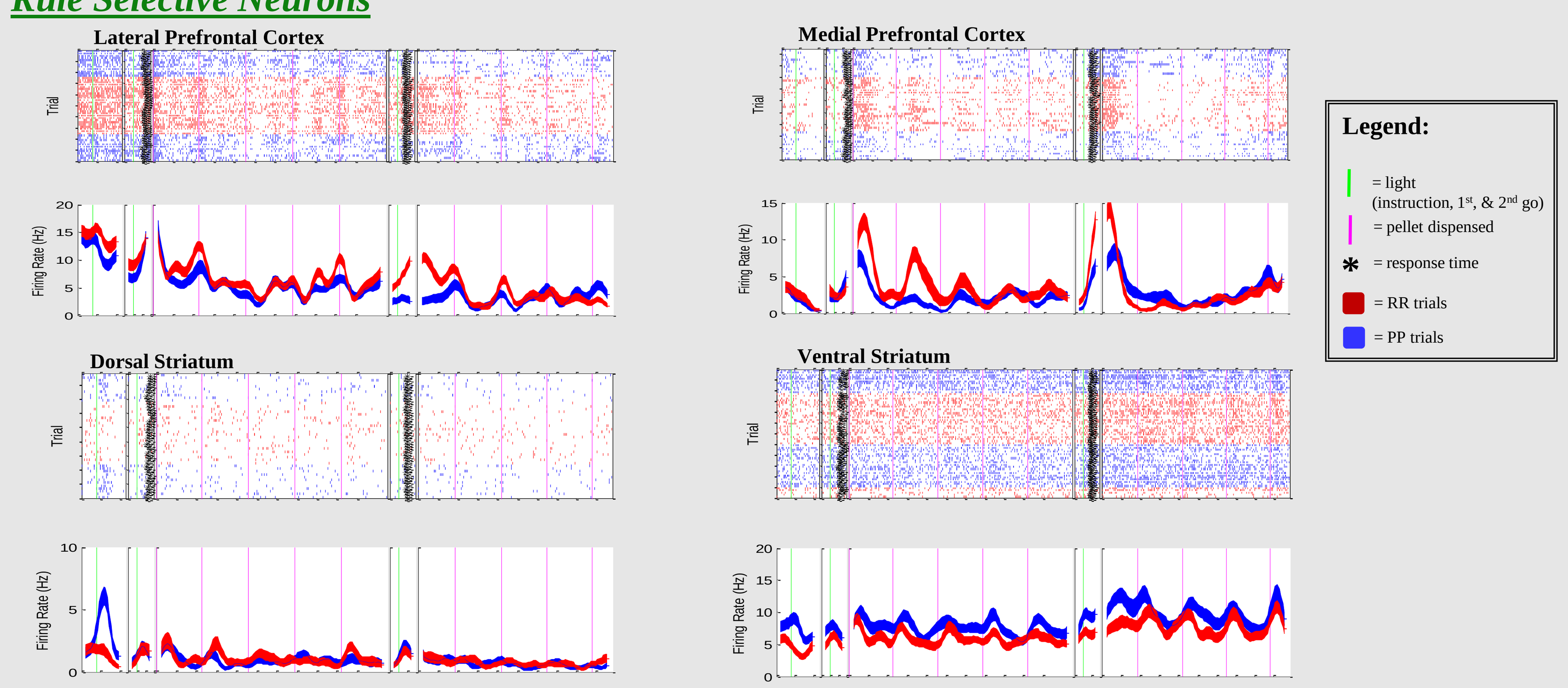
❖The last column shows the percentages of task-modulated neurons.

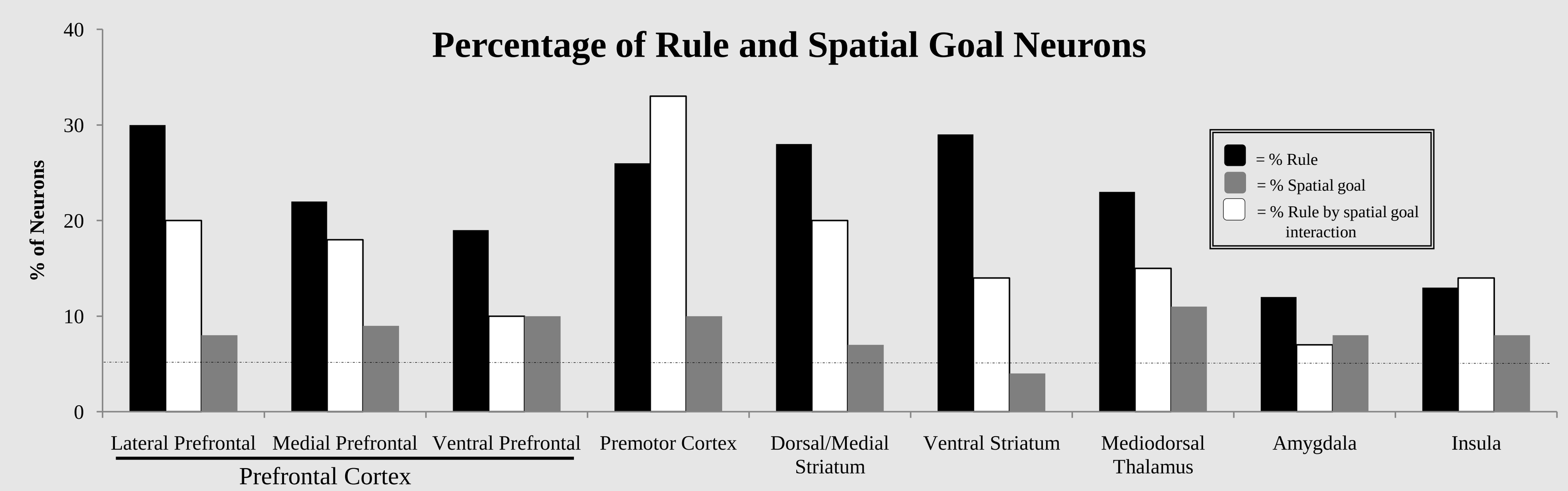
Task-related neuron



❖The firing rate of this neuron significantly increased during the instruction period and significantly decreased during the 1st pellet, reach, and post-reach periods.

Rule Selective Neurons



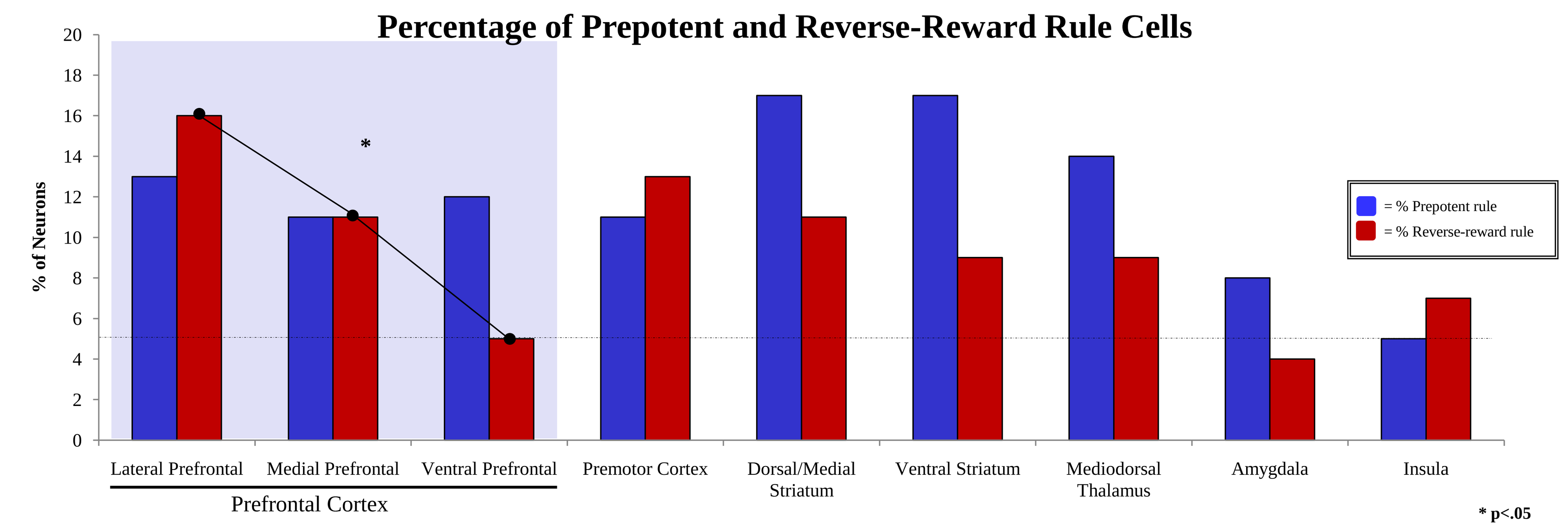


❖We analyzed rule and spatial goal selectivity using a 2-way ANOVA (p≤.01) for each period (*Instruction, Pellet, PreReach, Reach, Post-Reward).*[4,8] The dependent variable was firing rate within the period and the two independent two-level factors were rule (PP vs. RR) and spatial goal (left vs. right choice).

❖There was a significant difference across brain areas for the percentage of neurons showing selectivity for rule (X^2(8)= 19.94, p<.01) and spatial goal (X^2(8)= 31.91, p<.01) but not rule by spatial goal interaction. There was also a significant difference (X^2(1)=6.67, p<.01) between the percentage of rule- and spatial goal-selective neurons in the ventral striatum.

❖The highest percentages of rule selective neurons were found in lateral prefrontal and striatum and the lowest percentages were found in the amygdala and insula.

❖The highest percentage of spatial goal selective neurons was found in premotor cortex and the lowest percentages were found in ventral prefrontal, amygdala, and insula.

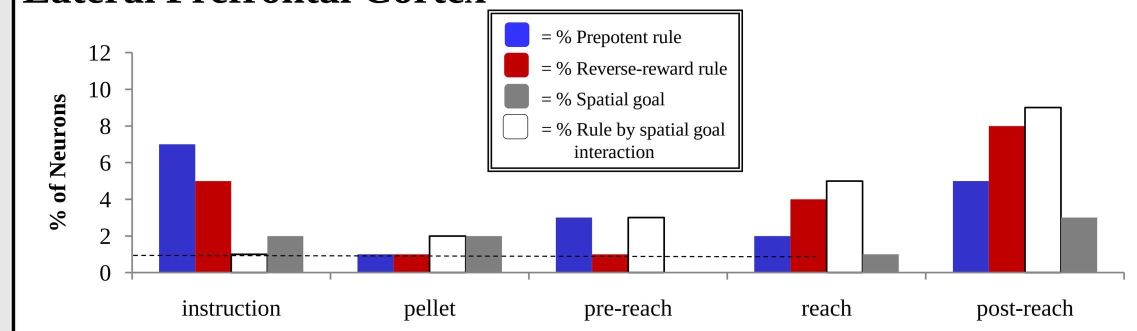


❖X^2 did not reveal a significant difference in the percentage of PP and RR cells across all brain areas.

❖Within prefrontal cortex, we found a significant difference (X^2(2)= 6.37, p<.05) in the percentage of RR neurons, with the highest in lateral prefrontal, fewer in medial prefrontal, and the lowest in ventral prefrontal cortex.

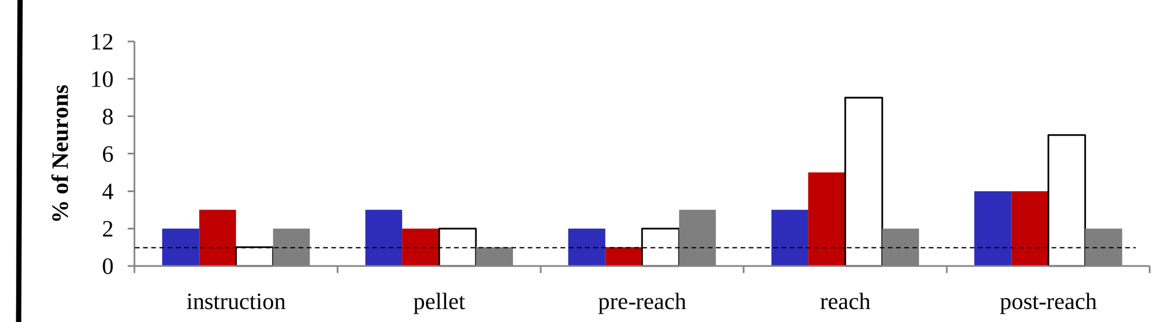
❖The percentage of PP selective neurons was highest in striatum while the percentage of RR selective neurons was highest in lateral prefrontal and premotor cortices.

Lateral Prefrontal Cortex



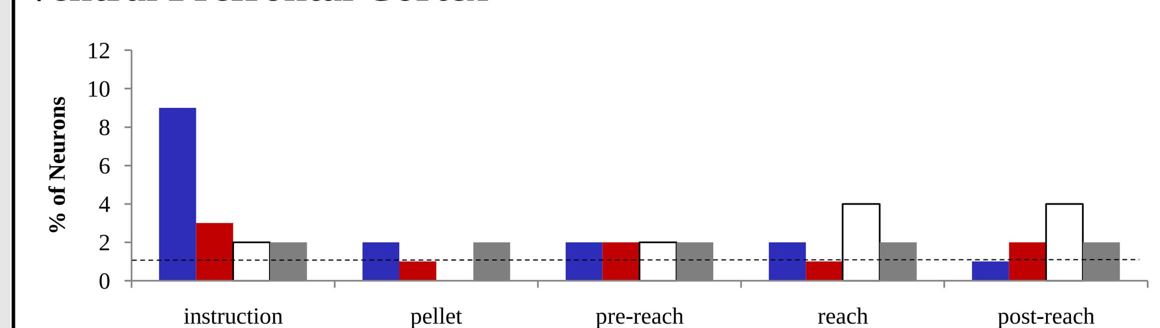
❖There was more rule selectivity during the instruction, reach and post-reach periods. There also was significant spatial goal selectivity during the reach and post-reach periods.

Medial Prefrontal Cortex



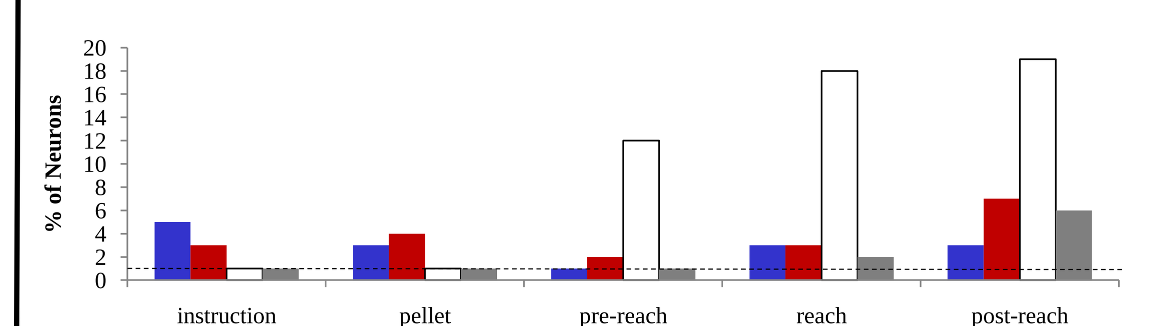
❖More rule and spatial goal selectivity during the reach and post-reach periods

Ventral Prefrontal Cortex



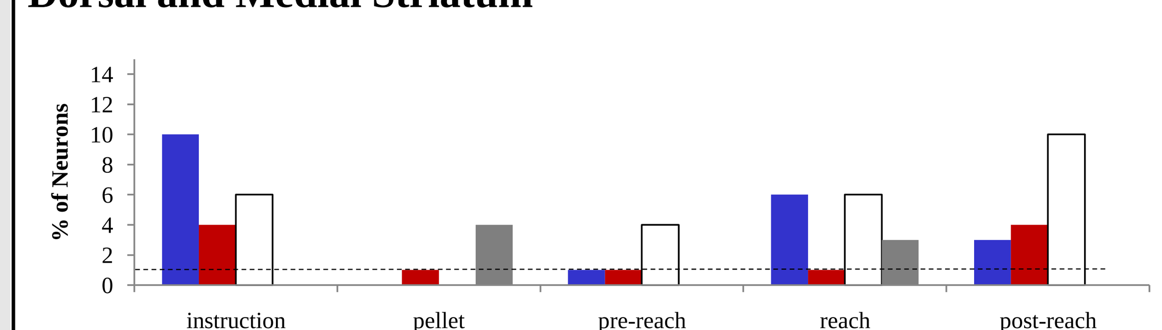
❖More PP rule selectivity in the instruction period, and some spatial goal selectivity during the reach and post-reach periods

Premotor Cortex



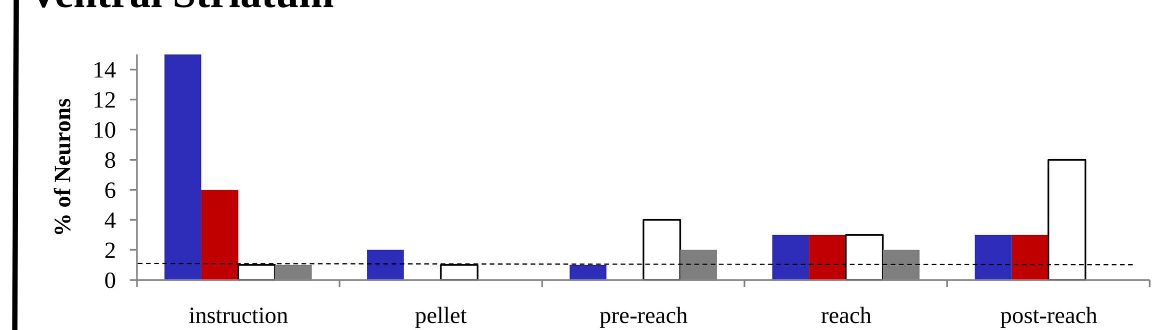
❖More spatial goal selectivity during and after pre-reach and more RR selectivity during the post-reach period

Dorsal and Medial Striatum



❖More PP rule selectivity during the instruction and reach periods and more spatial goal selectivity in the instruction, pre-reach, reach, and post-reach periods.

Ventral Striatum



❖More PP rule selectivity in the instruction period and more spatial goal selectivity during the post-reach period.

Conclusions and future directions

❖Both monkeys were significantly less accurate using the reverse-reward (RR) rule compared to the prepotent (PP) rule, suggesting that these rules did not become equally 'automatic' and that we were tapping into conventional versus unconventional behavior.

❖Across brain areas, we found the highest percentage of rule selective neurons in the lateral prefrontal cortex and striatum and the highest percentage of spatial goal selective neurons in the premotor cortex.

❖For rule selective neurons, the highest percentage of PP rule neurons were found in the striatum, while the highest percentage of RR neurons were found in lateral prefrontal cortex.

❖We found a significant difference in the percentage of RR neurons within prefrontal cortex, with the highest in lateral prefrontal, fewer in medial prefrontal, and the lowest in ventral prefrontal cortex.

❖Across trial periods, the lateral prefrontal cortex showed RR selectivity during the instruction, reach and post-reach periods; medial prefrontal showed the same for the reach and post-reach periods; premotor cortex showed RR selectivity mostly during the post-reach period. Whereas ventral prefrontal cortex and striatum showed more PP rule selectivity, especially during the instruction period.

❖Because the lateral prefrontal cortex is more active during abstract rule,[3,4] anti-pointing,[6,7] anti-saccade,[6,7] and self-control tasks,[5] our results are consistent with the literature that this area may be involved in the promotion of challenging, unconventional behavior, which may explain its great expansion during primate and human evolution.[1,2]

References

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