Prefrontal cortex ensemble activity during associative visuomotor rule learning in primates

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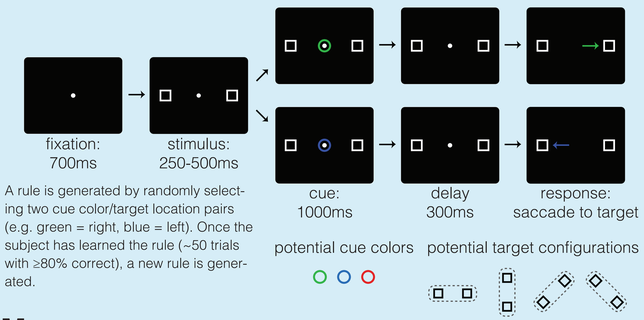
Introduction

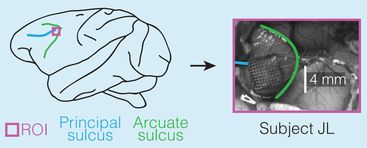
The lateral prefrontal cortex (LPFC) is necessary for learning associations between arbitrary pairs of stimuli and responses. Lesions to LPFC area 8a severely impair the ability of macaques to learn associations between more than one stimulus-response pair simultaneously (Petrides, 1987). Saccade direction selectivity in single LPFC neurons has also been shown to emerge earlier in a trial as macaques learn the associations between objects and saccade directions (Asaad et al.,1998). However, the ensemble-level mechanisms of conditional associative learning (CAL) in LPFC are poorly understood. The need to average neuronal activity across multiple instances of learning in single neuron recordings can maskunderlying dynamics in the neural activity, obscuring the relationship between neuronal activity and behavior. We predict that trial-to-trial variability in the learning curve will be reflected in the ensemble state.

Conditional associative learning (CAL) task



A rule is generated by randomly selecting two cue color/target location pairs (e.g. green = right, blue = left). Once the subject has learned the rule (~50 trials with ≥80% correct), a new rule is generated.

Multielectrode array recording



Two *Macaca fascicularis* were implantated with 96-electrode microarrays (Blackrock Microsystems, Utah) in LPFC area 8a. We recorded neuronal ensemble activity across dozens of recording sessions. Ensemble sizes ranged from 40-70 units. The data presented here are from a single recording session of 69 units.

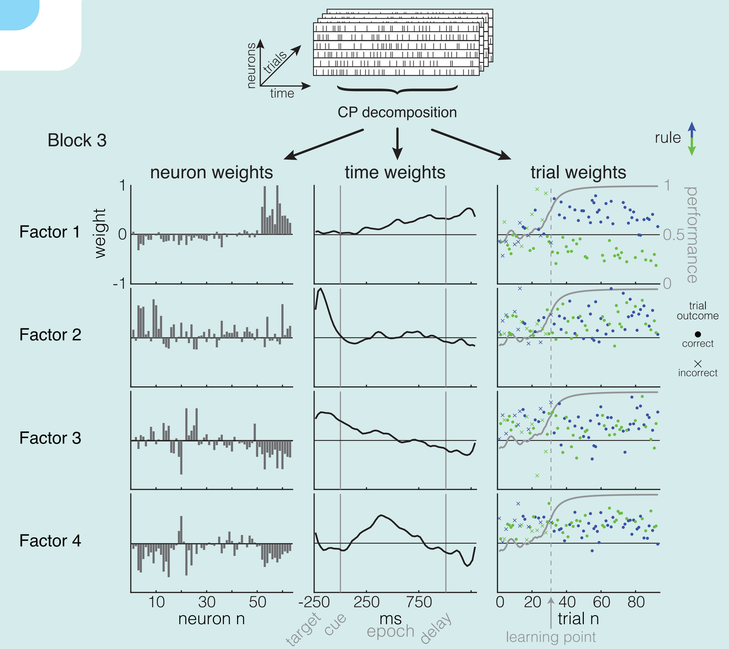
TCA for exploratory data analysis

We applied tensor components analysis (TCA; courtesy of the Ganguli Lab), an extension of PCA to higher-order matrices, to our neural data. TCA separates within-trial time variability and across-trial variability. Isolating the trial-related variability can reveal learning-related changes in the neuronal ensemble activity.

The results of four factor TCA applied to an example rule block (block 3 in **Quantifying Performance and Behavior**) are plotted here. The time weights (2nd column) show how the neuron weights (1st column) vary across time within a trial. The trial weights (3rd column) show how the neuron weights vary across trials.

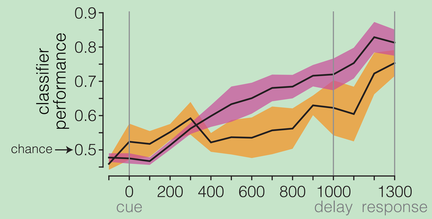
Note how the separation between trial weights for for opposing saccades in Factor 1 (top right) correlates with the animal's performance. TCA has identified a neuronal subpopulation strongly modulated by saccade direction in a learning-dependent manner as a major latent feature of the ensemble.

For more information on TCA see:
biorxiv.org/content/early/2017/10/30/211128



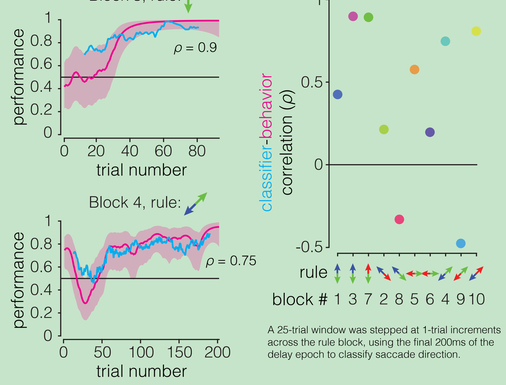
Saccade choice representation changes with learning

Decoding saccade direction before vs. after learning



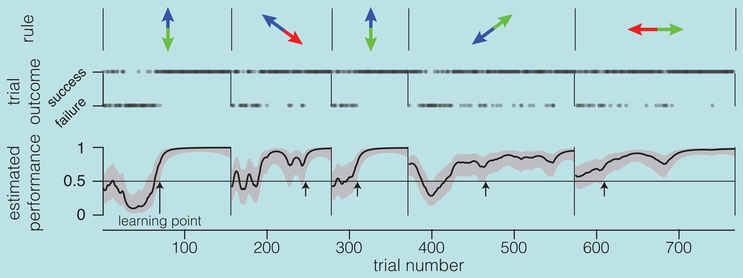
200ms window, 100ms steps
shaded region = s.e.m. for n = 5 blocks
only correct trials were analyzed.

Correlating decoding & behavioral performance



A 25-trial window was stepped at 1-trial increments across the rule block, using the final 200ms of the delay epoch to classify saccade direction.

Quantifying performance and behavior

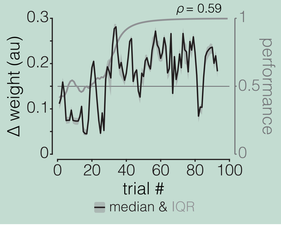


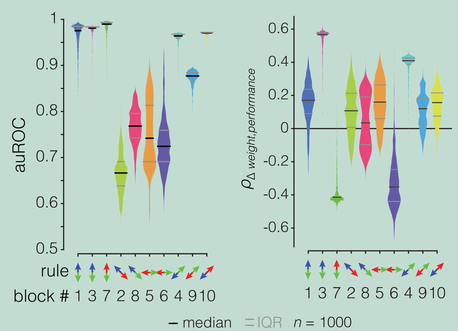
Here we show the subject's performance for five example rule blocks from a single session. The rule is displayed in the top row (e.g. blue = top, green = bottom). Trial outcomes are displayed in the middle row. The bottom row shows a continuous estimate of the animal's performance (i.e. learning curve), estimated as in Smith et al. (2004) *J. Nsci.* The 95% confidence interval (shaded grey region) can be used to determine the first trial in which the animal's performance was significantly above chance.

Unsupervised discovery of performance-related latent factors

We applied TCA to the ensemble firing rates for each rule block and computed the auROC for saccade direction using the weights of each trial factor. The distributions of auROC values for the best of the four factors in each block are shown in the center plot. Interestingly, rule blocks with identical saccade directions did not necessarily contain similar amounts of saccade-related information.

If the saccade-related factor in each block is modulated by changes in performance, the difference between weights for opposite saccade directions should be greater during periods of high performance than during periods of poor performance. The lower left plot displays the weight differences between adjacent trials with opposing saccades and the performance curve for the same example block as in **TCA for Exploratory Data Analysis**. The correlation between weight differences and performance for each block is shown on the rightmost plot.





Conclusions

Unsupervised dimensionality reduction reveals neuronal sub-population in prefrontal area 8a whose saccade selectivity is modulated in a learning-dependent manner.

Saccade choice representation in prefrontal neuronal ensembles during a rule-learning task is more robust after the rule is learned.

Short-timescale fluctuations in behavioral performance correlate with the strength of choice representation.

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