Analyzing the Effect of Timing on Spatiotemporal Sequence Learning in Mouse Primary Visual Cortex

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Abstract

Recognizing and predicting spatiotemporal sequences is a fundamental component of neural function. We studied this ability in the mouse primary visual cortex (V1), where studies have shown that visual experiences drive plasticity using the same mechanisms involved in learning. We assayed plasticity using electrodes implanted in V1 to record visually evoked potentials (VEPs). Previous studies show that VEPs increase in magnitude following repeated exposure to a fixed 4 element long sequence of sinusoidal gradients with differing orientations, labeled ABCD. This increased response is not seen when the same visual elements are presented with an unexpected order, DCBA. In our experiment, we tested how the timing of the visual presentation elements affect V1's ability to learn the sequence. Specifically, we used a training time of 300 ms, which is twice the duration used in previous experiments. We found that the magnitude of VEP responses to temporally and ordinally novel sequences appeared smaller than those of VEPs in response to familiar sequences. However, the difference between those magnitudes was not as large as that seen in previous experiments. These results are highly unexpected, and more research and statistical tests should be done to confirm these results.

Introduction

The primary visual cortex (V1) is the simplest and earliest cortical visual area, receiving information directly from the lateral geniculate nucleus (LGN) **(Fig. 1)**, and is the first cortical stage of visual processing. Mouse V1 is a well studied region that has been used in past experiments to analyze experience-dependent plasticity, with documented responses to stimulus orientation, size, motion, and serial order.

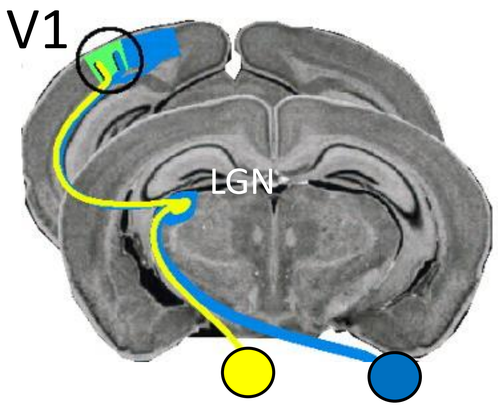

Figure 1 | Mouse Visual Pathway

Previous studies found that repeated exposure to sequential visual stimuli over multiple days was sufficient to encode predictive representations in V1 of both ordinal and temporal components of stimulus patterns. These stimulus patterns consisted of fixed four element long sequences of sinusoidal gradients of differing orientations, labeled $ABCD_{150}$, where the subscript indicates the duration of each sequence element in milliseconds. However, the effects of individual sequence element durations on learning to recognize and predict such sequences is unclear. Thus, this experiment's goal is to determine whether the learning mechanisms seen in previous studies at element durations of 150 ms applies to other durations too, specifically 300 ms, by using electrophysiology to measure visually evoked potentials (VEPs) in response to familiar and novel visual stimuli.

Methods

Four male mice were obtained and housed together. Two electrodes were implanted, one in each primary visual cortex (V1) of the two hemispheres. A ground electrode was implanted in the frontal region of the cortex.

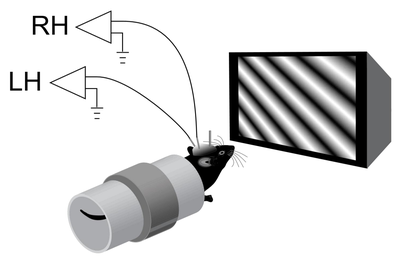

Figure 2 | Fixed-head Presentation Apparatus

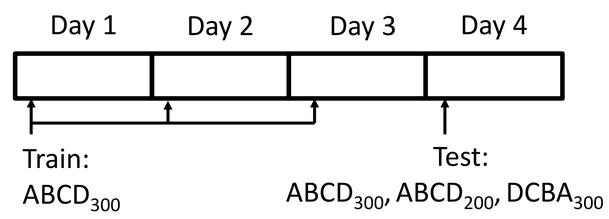

Figure 3 | Experimental Outline

The day after the implant surgery, each mouse was habituated in the head-fixed recording apparatus **(Fig. 2)** by exposing them to a gray screen for 30 minutes. Each mouse was then trained for 3 days by exposing them to 200 presentations of a fixed 4 element long sinusoidal gradient sequence, labeled $ABCD_{300}$, in four groups of 50 presentations each separated by 30 s **(Fig. 3)**.

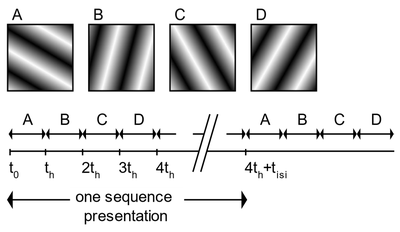

Figure 4 | Training Stimulus Presentation

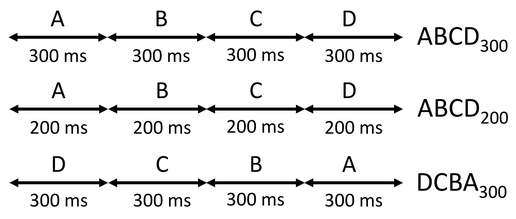

Figure 5 | Sequence Presentations

On the fourth day of the experiment, each mouse was exposed to the familiar $ABCD_{300}$ sequence, a temporally novel $ABCD_{200}$ sequence, and an ordinally novel $DCBA_{300}$ sequence **(Fig. 5)**.

Results

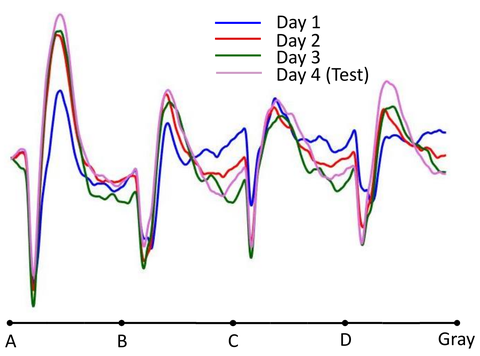

Figure 6 | Potentiation Over Days

VEPs in V1 right and left hemisphere potentiate following repeating exposure to $ABCD_{300}$

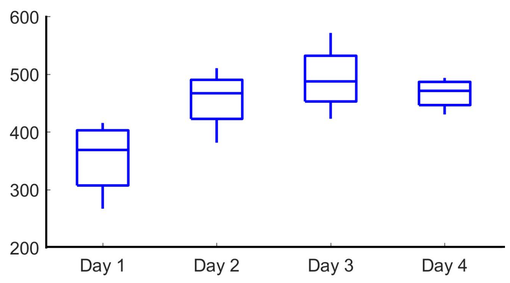

Figure 7 | Box Plot of Potentiation

Box plot interpretation of magnitudes of VEPs in **Fig. 6**

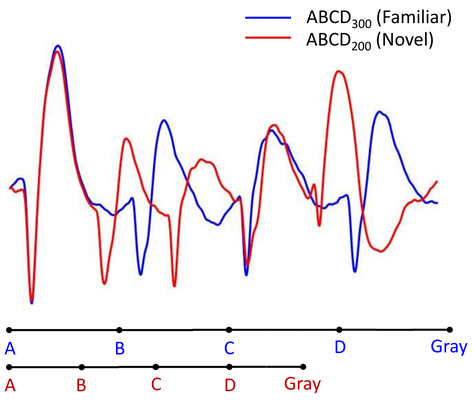

Figure 8 | Familiar vs. Novel Time

Magnitudes of VEPs **(Fig. 10)** in familiar $ABCD_{300}$ sequence appear similar to those of VEPs in novel $ABCD_{200}$ stimuli.

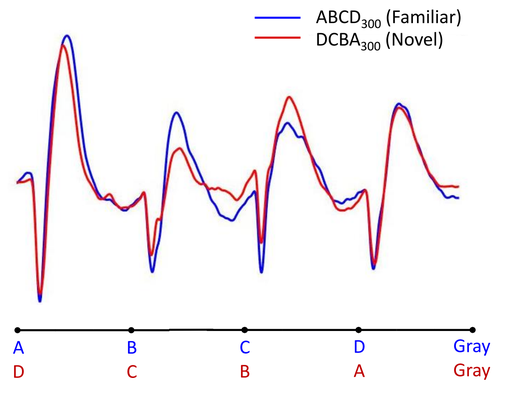

Figure 9 | Familiar vs. Novel Order

Magnitudes of VEPs **(Fig. 11)** in familiar $ABCD_{300}$ sequence appear similar to those of VEPs in the novel $DCBA_{300}$ stimuli, except element B.

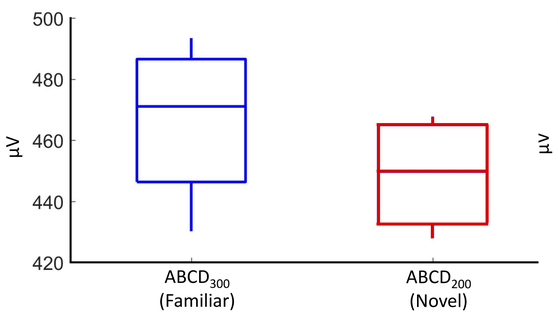

Figure 10 | Box Plot of Familiar vs. Novel Time

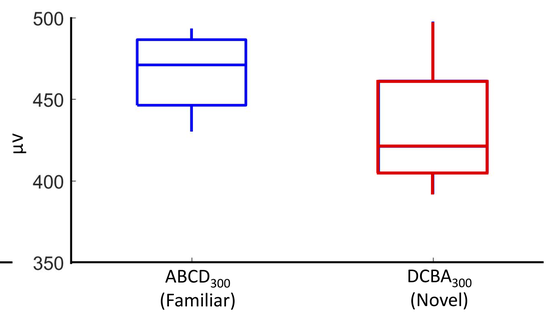

Figure 11 | Box Plot of Familiar vs. Novel Order

Discussion

The results **(Fig. 6,7)**, show that potentiation occurred in response to $ABCD_{300}$ over the 3 day training period. Day 1 to 2 showed more potentiation than that which occurred from day 2 to 3. There did not appear to be any potentiation from day 3 to the familiar $ABCD_{300}$ on the test day (day 4). The total magnitude of potentiation in this experiment was generally smaller than that of potentiation to 150 ms in previous studies.

There does not appear to be a major difference in the magnitudes of VEPs in response to familiar $ABCD_{300}$ and temporally novel $ABCD_{200}$ **(Fig. 8,10)**. Training mice to a time of 300 ms results in responses of similar magnitudes between familiar and shorter times, specifically 200 ms. Past experiments have shown the opposite to be false, where training mice to 200 ms resulted in smaller magnitudes of VEPs in response to a novel 300 ms timing than to a familiar 200 ms timing.

There also did not appear to be a large difference in the magnitudes of VEPs in response to familiar $ABCD_{300}$ and ordinally novel $DCBA_{300}$ **(Fig. 9,11)**. This is unexpected as V1 has documented plasticity to serial order, yet when exposed to a novel order, the response magnitude is similar to that of a familiar order. This applies to elements A,C,D, but not B **(Fig. 12).**

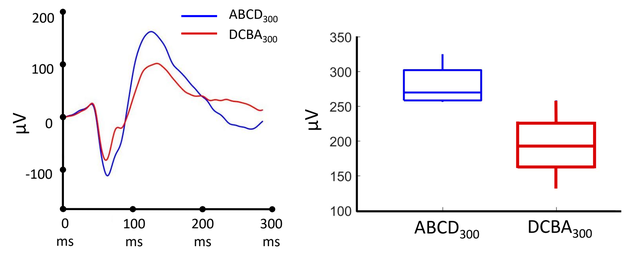

Figure 12 | Element B: Familiar vs. Novel Order

While the differences in VEP responses between familiar and novel sequences do not appear significant, the general trend of smaller responses to novel stimuli are still apparent **(Fig. 10,11)**. More research and statistical tests need to be done to draw further conclusions.

Conclusions

- Potentiation occurred over the course of the experiment, but plateaued after day 2
- No notable difference in magnitude of VEP responses between familiar $ABCD_{300}$ and novel timing $ABCD_{200}$
  - Potentiation to longer duration sequences still evokes VEPs to shorter duration sequences
- No notable difference in magnitudes of VEP responses between familiar $ABCD_{300}$ and novel order $DCBA_{300}$, except in element B
  - Possibly due to error, more tests should be done with varying sequence element durations
- General trend of decreased responses to novel sequences is still apparent

References

Gavornik, Jeffrey P, and Mark F Bear. "Learned Spatiotemporal Sequence Recognition and Prediction in Primary Visual Cortex." Nature Neuroscience, vol. 17, no. 5, 2014, pp. 732–737., doi:10.1038/nn.3683.ss

Acknowledgements

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