Comparison of Three Mouse Strains in Discrimination and Reversal Learning of the Conditioned Eyeblink Response

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Background

Eyeblink conditioning is a powerful experimental paradigm for studying the neural basis of learning during development and aging in humans (Woodruff-Pak&Steinmetz,2000a) and laboratory animals (Woodruff-Pak&Steinmetz,2000b). Studies of eyeblink conditioning in the mouse are expanding rapidly because they provide an opportunity to use gene-targeting techniques to examine the molecular and cellular mechanisms of neural plasticity and behavioral change. Examining the interactions of forebrain regions with this circuitry (e.g. Kishimoto, 1998) and interactions of forebrain regions with this circuitry (e.g. Kishimoto, 2006). Most of this work has involved single-condition (delay or trace) in C57/6 mice. The present study examines discrimination learning because this procedure offers a nonassociative control condition and a probe of cerebellar (acquisition) versus forebrain (reversal) substrates of learning (Berger&Orr, 1983) all within the same subjects. Subjects are important in behavioral genetics (Holmes, et al., 2002) and have been examined to some extent in single-conditioning (Bos,Chen,&Thompson,1998). The present study examines discriminative eyeblink conditioning and reversal learning in C57/6, 129/SvlmJ, and a first-generation hybrid cross of these two strains (F1 Hybrid).

Methods

- Mice (C57/B6 n=13, 129/svlmJ n=7), and a hybrid of these two strains (F1, n=19) were implanted with bipolar stimulating electrodes caudal to the left eye and EMG recording electrodes into the eyelid muscle and were given one week to recover (Stanton & Freeman, 1994;2000).
- Mice were allowed to habituate to the testing environment and recording cable for 45 minutes one day before training began and for 10 min prior to each training session.
- Mice were trained to discriminate CS+ and CS- by receiving 50CS+(a) and 50CS(b) trials per day for 4 days - Trials were presented every 18-42s (mean=30sec) in pseudorandom order with no more than three consecutive trials being identical; 10 CS+ trials were CS- alone test trials (details see Paczkowski, et al., 1999).
- Reversal sessions were identical to acquisition sessions except CS- and CS+ contingencies were switched

Table 1. Mean (±SEM) UR maximum amplitudes (UMA) and startle maximum amplitudes (SMA) for each strain. There were strain differences only in UMA measures due to lower URS in C57 mice.

<table>
<thead>
<tr>
<th>Strain</th>
<th>UMA</th>
<th>SMA</th>
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<tbody>
<tr>
<td>C57/6</td>
<td>335.86±38.22</td>
<td>618.94±86.27</td>
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<tr>
<td>129/SvlmJ</td>
<td>618.94±86.27</td>
<td>507.55±66.51</td>
</tr>
<tr>
<td>F1 Hybrid</td>
<td>618.94±86.27</td>
<td>8.76±32.37</td>
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Figure 2. Mean (±SEM) percentage CRs (upper panels) and CR maximum amplitude (bottom panels) in Light+/Tone- and Tone+/Light- subgroups in each strain. All strains acquired differential responding to CS+ vs. CS- across acquisition sessions. There was an enhancement of the CS effect in the light+/tone- subgroup and an attenuation of the CS effect in the Tone+/Light- subgroup; this effect was particularly prominent in C57 mice in third and fourth acquisition sessions. All strains showed discrimination reversal such that by the end of 8 sessions of reversal training CRs to the new CS- (former CS+) were higher than to the new CS+ (former CS-). In all strains; however, there was a large effect of modality on discrimination learning in the 129 mice. During reversal, these mice showed a strong carryover of conditioning from acquisition when the light was the CS- (former CS+). These mice also showed a weak conditioning to the tone CS+ during reversal. Consequently, reversal is enhanced in the tone+/light- subgroup but absent in the light+/tone- subgroup. This effect did not occur in the C57 and F1 strains.

Summary

- C57/6, 129/SvlmJ, and F1 Hybrid mice did learn to discriminate CS+ than CS- and did exhibit reversal learning when the contingencies were switched, particularly in the CMA measure.
- These data, taken with the emergence of these particular strains as common backgrounds for gene-targeting manipulations, establish discriminative eyeblink conditioning as a useful behavioral preparation for examining molecular mechanisms of neural plasticity and behavioral change.
- 129/SvlmJ mice showed a modality-specific pattern of responding during reversal. We are currently exploring variations in stimulus salience that may correct this problem. These mice are known to have motivational impairments that hinder other behavioral testing (Holmes, et al., 2005) making their performance on the reversal learning component of this task potentially valuable.
- Ongoing research continues to examine the performance of these strains on other eyelid tasks including trace conditioning and latent inhibition to further equip behavioral phenotyping studies.

References

Support: NIH grant R01 76168