Examining the Effects of Context and Time on Contextual Generalization in a Rodent Model of PTSD

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PTSD and Contextual Generalization

Post-traumatic stress disorder (PTSD) is defined as the psychological response exhibited in an individual after they are exposed to a trauma or life-threatening experience.

PTSD patients may experience intrusive symptoms (flashbacks and hallucinations) even if they are not in a context that directly reminds them of their trauma. This is referred to as contextual generalization and can be studied using animal models of PTSD, such as contextual fear conditioning (CFC).

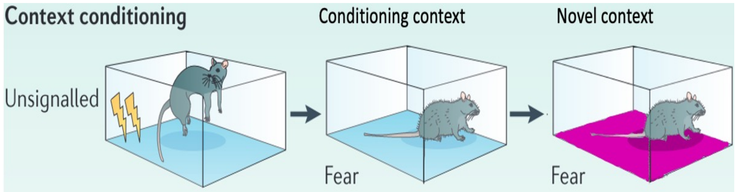

Figure 1. Depiction of contextual generalization. Fear is generalized from the conditioning context in which the fear is gained, to a safe novel context. Fear is still expressed in the safe context in the case of generalization. Adapted from Maren et al. (2013).

Aim

Investigate how the generalization of fear across two contexts with different tactile, spatial, and visual features is affected by the amount of time that has passed in fear conditioned C57BL/6J mice.

Methods

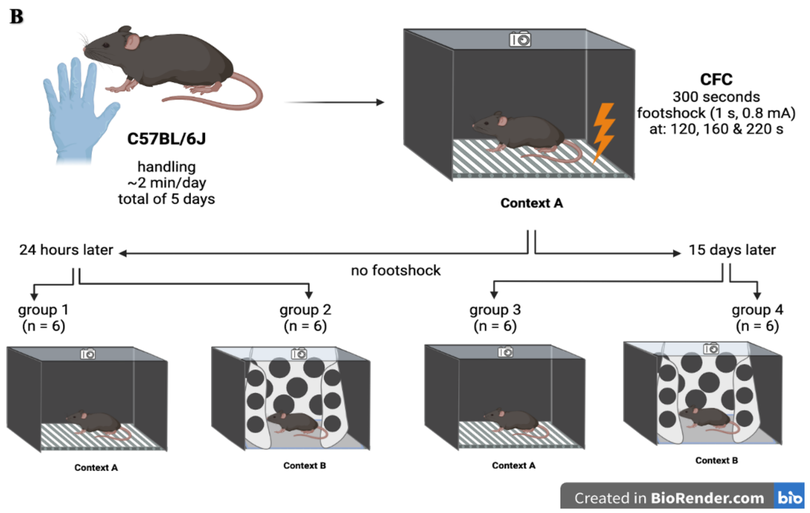

Figure 2. Fear conditioning and testing paradigm. Mice were handled for five days, then conditioned in context A using a footshock (1s, 0.8 mA) at 120, 160, and 220 seconds. Testing for contextual generalization was done after 24 hours in context A (n=6) or context B (n=6), or 15 days in context A (n=6) or context B (n=6).

1. Contextual fear conditioning on male and female mice (n=24).
2. Testing for contextual generalization in familiar and novel contexts, as well as at early and remote time points.
3. Score videos to quantify amount of time spent freezing. More freezing indicates greater fear of the context.

Conclusions

- An effect of context on memory was found. Mice tested in the conditioning context exhibited overall higher levels of freezing than mice tested in the novel context.
- An effect of time on memory was found. Mice tested at the near time point exhibited less freezing than mice tested at the remote time point.
- Results showed no sex differences between mice across groups, which allowed for the collapsing of data across sexes. More power is needed to look at sex differences.
- There was no interaction between the test context and test time, indicating that contextual generalization did not increase with the passage of time.
- Instead, incubation of fear was observed.

Future Directions

- Look at differential activation of the ventral hippocampus using immunohistochemistry to determine c-Fos levels.
- Change contextual features individually or create a third context with the same elements but changed to different parameters.
- Extend the remote time point further to check for contextual generalization.

Results

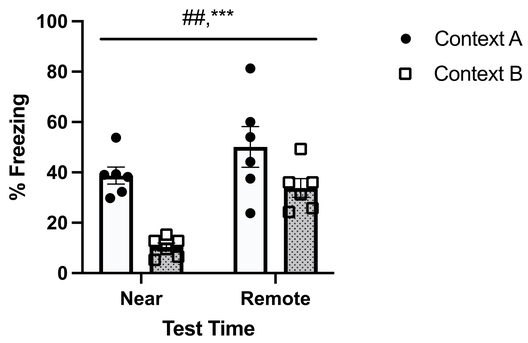

Figure 3. Contextual fear memory measured in four groups of conditioned mice (n=6), at a near and remote time point, in two different contexts. Mean percentage of time spent freezing is shown. Mice tested in the familiar context (context A) or the novel context (context B), at a near time point (24 hours), exhibited significantly lower levels of freezing compared to mice tested in the familiar or novel context at the remote time point (15 days) (Main effect of time, ##$p < 0.01$). Mice tested in context A exhibited significantly higher levels of freezing at both time points when compared to mice tested in context B, showing an effect of context on contextual generalization (Main effect of context, ***$p < 0.001$). Error bars represent ± SEM.

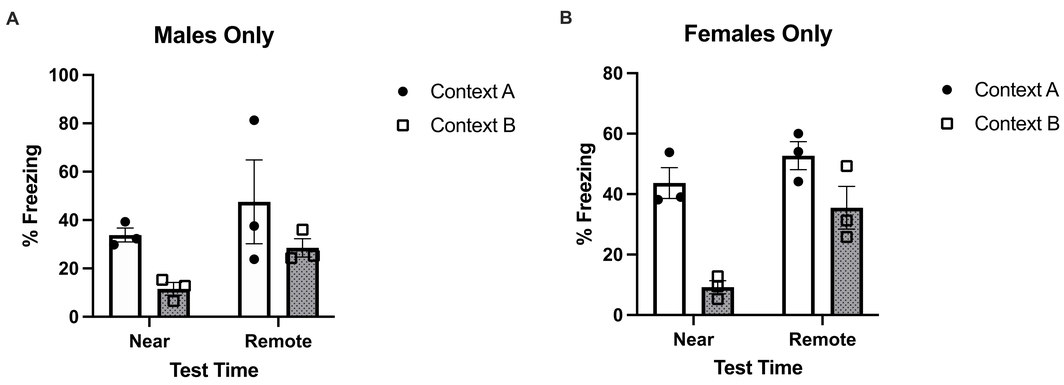

Figure 4. Contextual fear memory measured in four groups of conditioned mice, separated by sex. (A) Mean percentage of time spent freezing in males only is shown. No significant effects of sex were observed on fear memory of context (context A, context B) or time (near, remote). **(B)** Mean percentage of time spent freezing in females only is shown. No significant effects of sex were observed on fear memory of context (context A, context B) or time (near, remote).

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