FROM NEURONS TO NETWORKS: MACHINE LEARNING-BASED ANALYSIS OF FEAR CIRCUITS

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ABSTRACT

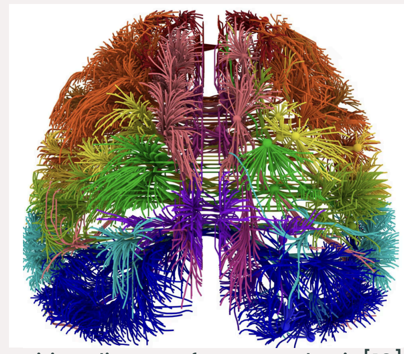
While fear-related disorders affect millions globally, our understanding of fear patterns in the brain remains limited [8]. This study develops a novel computational approach combining whole-brain imaging and machine learning to investigate neural mechanisms of fear generalization in mice. The research aims to understand fear pattern emergence during generalization and learning, with potential applications in treating anxiety disorders and PTSD and developing broader frameworks for analyzing complex neural circuits [9].

LITERATURE REVIEW

Technological advances in neuroscience have transformed our understanding of brain activity. Immediate early genes (IEGs) serve as key markers of neural plasticity and learning [5][6]. The combination of tissue clearing techniques, light sheet microscopy, and automated detection enables whole-brain mapping of IEG expression, complemented by genetic tools like TRAP2 for tracking activated neurons [3][4]. Recent research has demonstrated how machine learning can classify different psychoactive compounds based on brain-wide c-Fos expression patterns, providing a novel approach for drug screening and validation [3]. This computational approach has been particularly valuable in studying fear generalization and associated prefrontal functioning in trauma-related disorders, where understanding pre-existing cognitive traits and their relationship to post-trauma outcomes is crucial.

INTRODUCTION

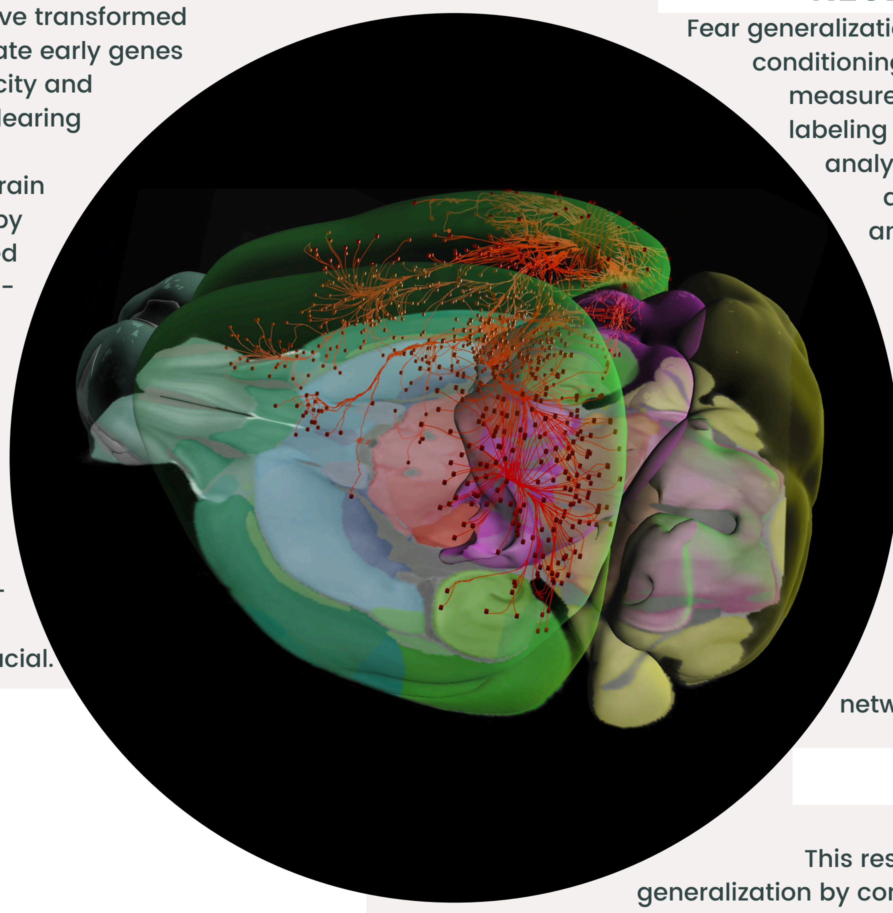
Fear generalization, where learned fear responses extend beyond the original threat, is crucial for survival but can become maladaptive in anxiety disorders. While key brain regions involved in fear learning are known, the neural mechanisms underlying fear generalization across brain-wide networks remain poorly understood. This research combines behavioral measurements with whole-brain neural activation patterns and machine learning algorithms to identify neural signatures that differentiate between adaptive and maladaptive fear generalization responses, advancing our understanding of fear-related neural circuits and their therapeutic implications. [1].

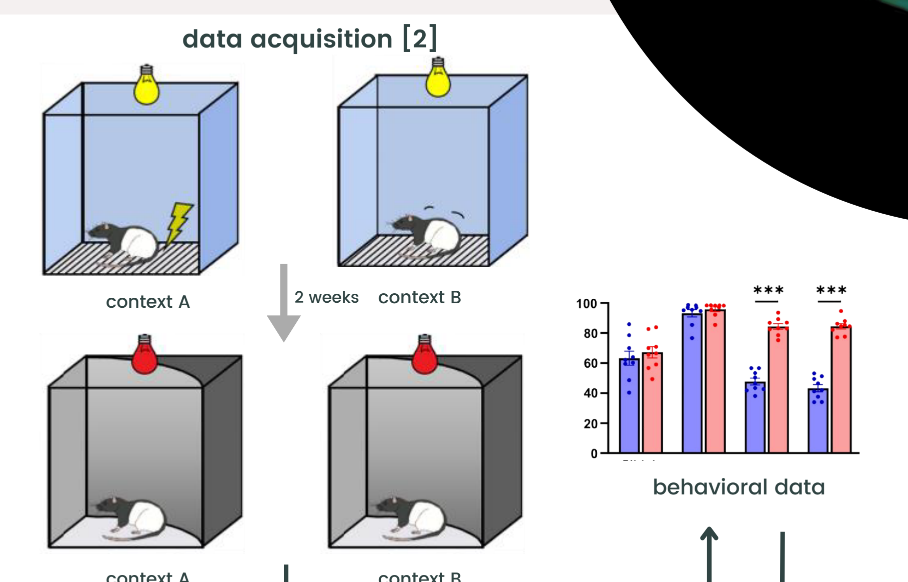


wiring diagram for mouse brain[10]

RESEARCH METHODOLOGY

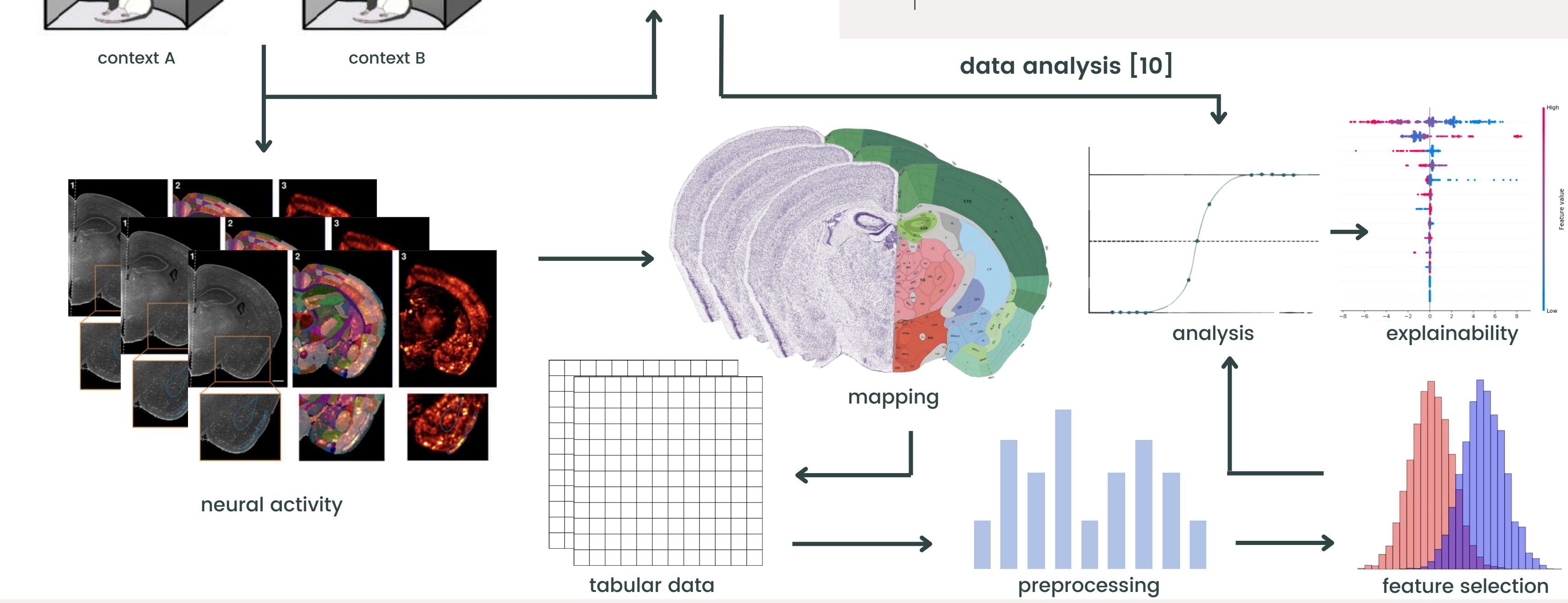
Fear generalization is studied using a two-context fear conditioning paradigm in mice, combining behavioral measurements with neural activation data from TRAP labeling and c-Fos immunostaining. Brain samples are analyzed using light-sheet fluorescence microscopy and mapped to the Allen Brain Atlas. The core analysis implements a machine learning pipeline to analyze patterns of neural activation and their network properties, beginning with data normalization and feature selection to identify relevant brain regions. The analysis examines how these regions form functional networks through their connections and co activation patterns, with machine learning models trained to predict behavioral outcomes. This network analysis enables tracking of changes in circuit organization between contexts and timepoints, providing insights into how fear memories are encoded and retrieved across interconnected brain networks.





CONCLUSION

This research advances the understanding of fear generalization by combining neural imaging with machine learnin analysis to identify specific neural signatures of adaptive and maladaptive fear responses. The proposed computational approach to analyzing complex fear circuits has significant implications for clinical applications, particularly in treating anxiety disorders and PTSD. Beyond immediate applications in fear-related conditions, the developed machine learning pipeline could serve as a framework for analyzing other complex neural circuits, potentially advancing therapeutic strategies across various neurological and psychiatric disorders.



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