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"Using machine learning to analyze individual differences in stress coping in C57BL/6J Mice"

BACKGROUND: Repeated exposure to social stress increases the risk for neuropsychiatric conditions such as depression, anxiety-like, and substance use disorders (SUDs). The neural mechanisms by which individual differences in stress responsivity that shape resilience or susceptibility to stress remain poorly understood. Ethology—the study of animal behavior—is a vital tool for the understanding of neuropsychiatric conditions. For decades, it had been common practice to analyze and score animal posture and behavior manually, which is a tedious and subjective process. However, recent advances in machine learning have enabled automated, high-resolution behavioral tracking. One such program, DeepLabCut (DLC), provides accurate pose estimation with minimal manual input, making it a powerful method for quantifying behavior.

OBJECTIVE: This study combines DLC with a repeated SDS model—a robust and ethologically relevant model of stress in male and female C57BL/6J mice—to investigate the development of resilient and susceptible phenotypes. The primary goal is to determine whether DLC-generated pose estimation data from video recordings of social stress can be used to identify behavioral signs of stress resilience and susceptibility. The secondary goal is to use pose estimation data to determine whether male and female mice employ unique stress coping strategies.

METHODS: A cohort of eight male and eight female C57BL/6J mice were individually housed and assigned to either a control group or an SDS group based on body weight, with the lightest 4 mice deemed the SDS mice (n = 4 per sex group). SDS mice were subjected to 10 consecutive days of social defeat using a resident-intruder protocol. Each SDS session consisted of (1) a **pre-defeat threat phase**, (2) a **post-defeat threat phase**, during which the resident (an aggressive Cartworth Farms White [CFW] mouse) and the intruder were separated by a perforated barrier to allow sensory but not physical contact, and (3) a **defeat phase**, during which the barrier was removed, and the intruder received 20 attacks (females) or 30 attacks (males) from the resident. Defeats were conducted in a custom 3D-printed enclosure equipped with a top-mounted Raspberry Pi camera for video recording. Each session was analyzed using DLC. Following the 10-day SDS protocol, mice were evaluated in a series of behavioral tests that included the dyadic social interaction test, the modified open field interaction test, and the Elevated Plus Maze (EPM) to assess social and anxiety-like behaviors.

RESULTS: Male SDS mice showed an increase in anxiety-like behaviors on the EPM as shown by decreased open arm time and percent of open arm entries. Additionally, the male SDS group greater individual variability suggesting the presence of resilient and susceptible mice. Female SDS mice had no significant differences in anxiety-like behaviors at the population level; however, a mixed population of susceptible and resilient mice were seen when analyzing percent open arm entries. Analysis of the open field experiment reveals a trend toward decreased social interaction by evaluating time spent in the corners of the field versus time spent in the SI Zone, with indications of wider phenotypic spreads of social behaviors. DLC will be used to correlate these results with pose estimation data to determine how susceptible and resilient behaviors and coping mechanisms emerge within the population.