

Social Defeat Stress Induces Depression-like Behaviors in Adolescent C57BL/6 Mice

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Abstract

Exposure to stress is highly correlated with the emergence of mood-related psychopathologies, such as general anxiety and major depressive disorder. Because the first episode of major depression often emerges in adolescence, we investigated the effects of chronic social defeat stress on responses to emotion-eliciting stimuli in juvenile mice. Specifically, postnatal day (PD) 35 male C57BL/6 mice were exposed to 10-minute episodes of social defeat stress for 10 consecutive days (PD35-44), while control mice were handled daily. Twenty-four hours after the last episode of stress (PD45), separate groups of mice were tested on a battery of emotion-eliciting tests, including the social interaction-, forced swim-, and sucrose preference- test. Defeated adolescent mice exhibited a depression-like phenotype as inferred from increased avoidance behavior in the social interaction test, increased time spent immobile in the forced swim test, and a lower preference for a sucrose solution (a measure of anhedonia), when compared to non-defeated controls. In general, we show that exposure to social defeat stress during adolescence induces a depression-like behavioral phenotype in C57BL/6 mice. Thus, our findings suggest that the social defeat paradigm may be used as a model to examine the emergence of stress-induced mood-related disorders during the adolescent stage of development.

Social Interaction

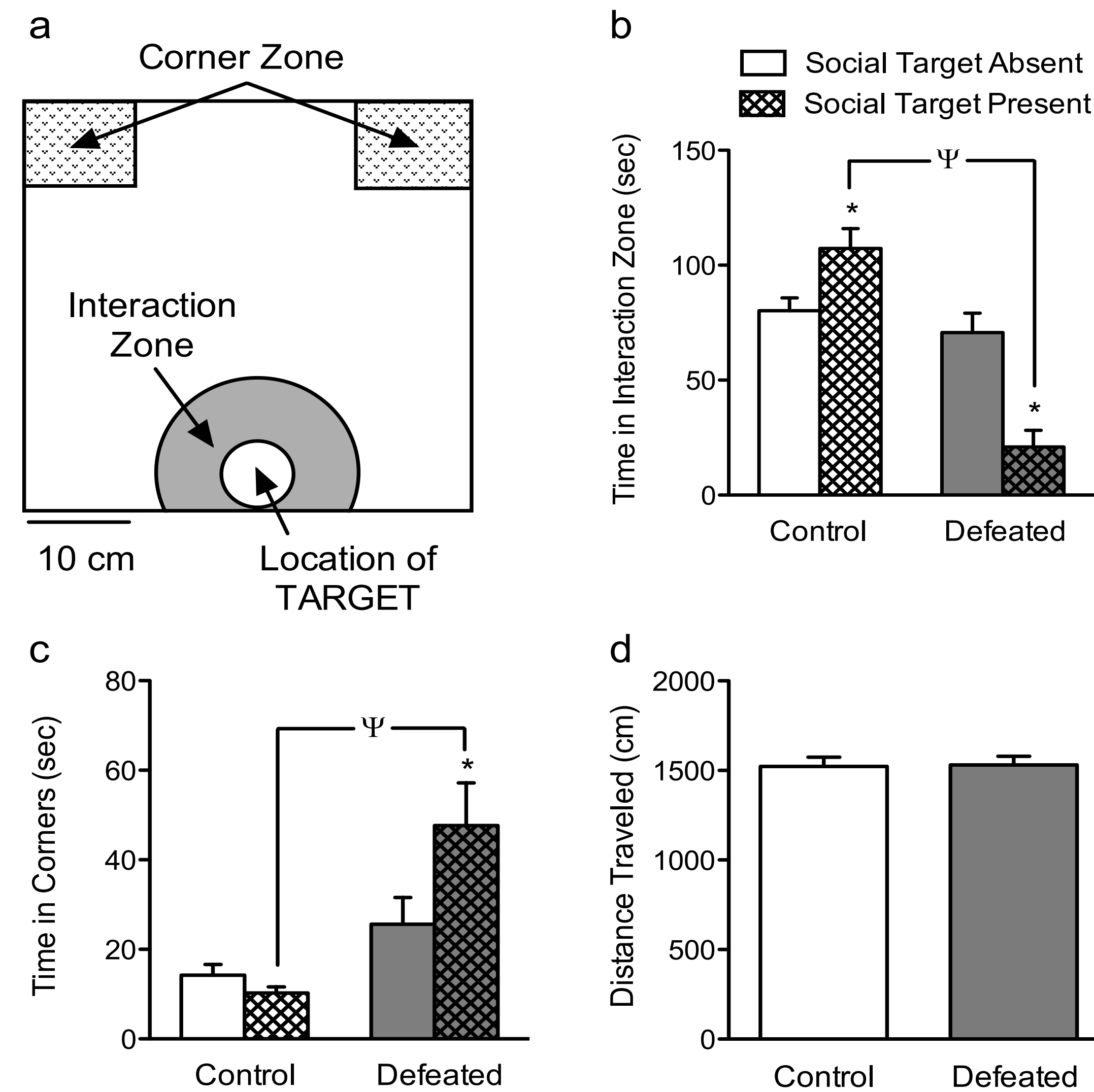


Figure 2. Ten days of social defeat stress induces avoidance behaviors in adolescent C57BL/6 male mice. (a) Schematic of the social interaction/avoidance arena. (b) Control (non-stressed; n=10) mice showed significantly higher levels of interaction time ($p < 0.05$), whereas socially defeated mice (n=10) spent significantly less time interacting ($p < 0.05$), in the presence of a social target. (c) This avoidance behavior as a result of social defeat was also evident when assessing time in the corner zones, in which defeated (stressed) mice spent significantly more time in the corner zones in the presence of the social target ($p < 0.05$). (d) No differences in locomotor activity (distance traveled in cm) during the first 2.5 min trial of the social interaction test was observed between the groups ($p > 0.05$). * $p < 0.05$, within group comparison; presence vs absence of social target. $\Psi p < 0.05$, between group comparison. Data are presented as mean time (sec) and distance traveled (cm) + SEM.

Forced Swim Test

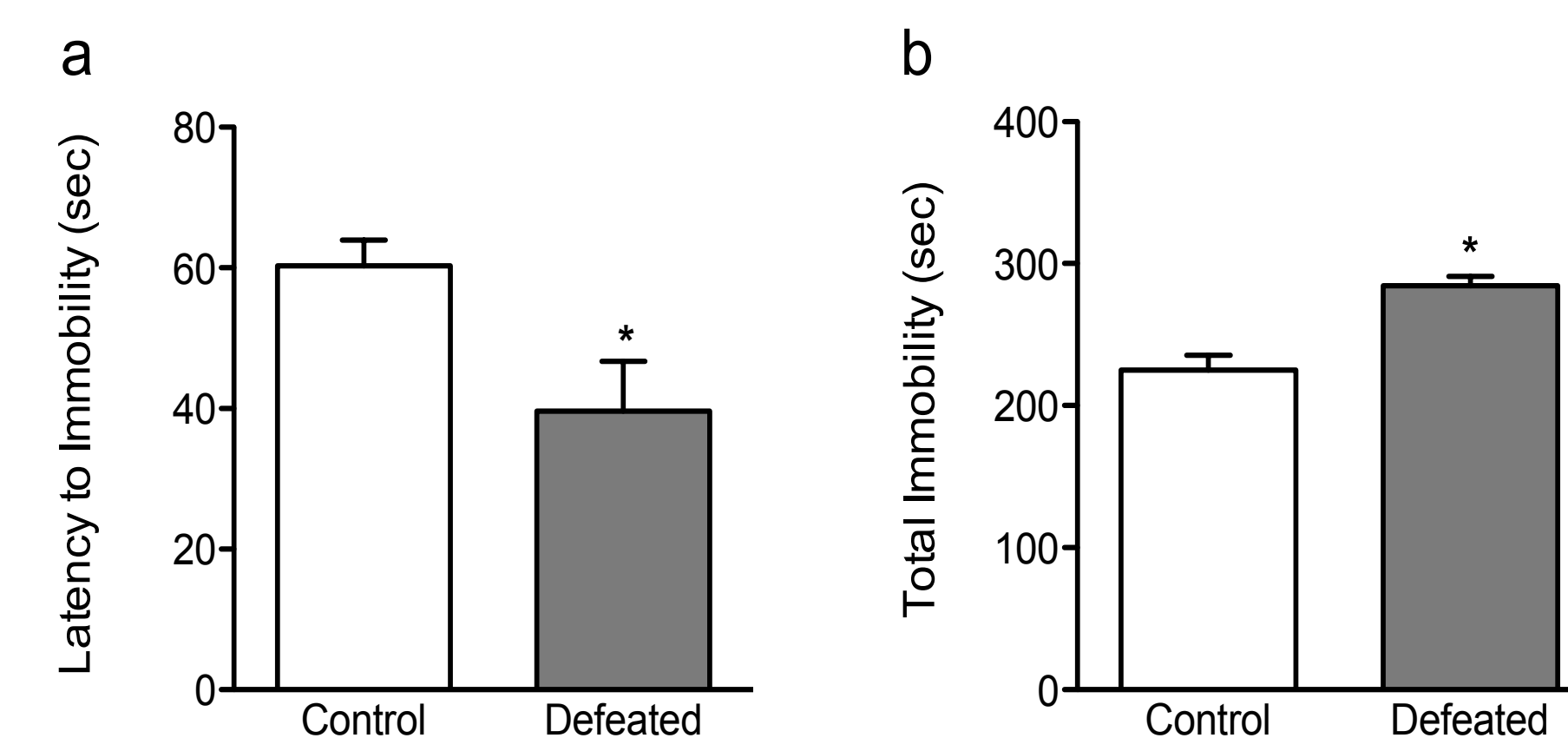


Figure 3. Effects of 10 days of social defeat stress on forced swimming behavior, 24 hr after the last social defeat episode. Defeated (stressed; n=10) adolescent mice exhibited a depressive-like behavior as inferred by (a) lower time to adopt an initial posture of immobility and conversely (b) spending significantly more time in the immobile position, when compared to control (non-stressed; n=8) mice. *Significantly different from controls ($p < 0.05$). Data are presented as mean time (sec) + SEM.

Sucrose Preference

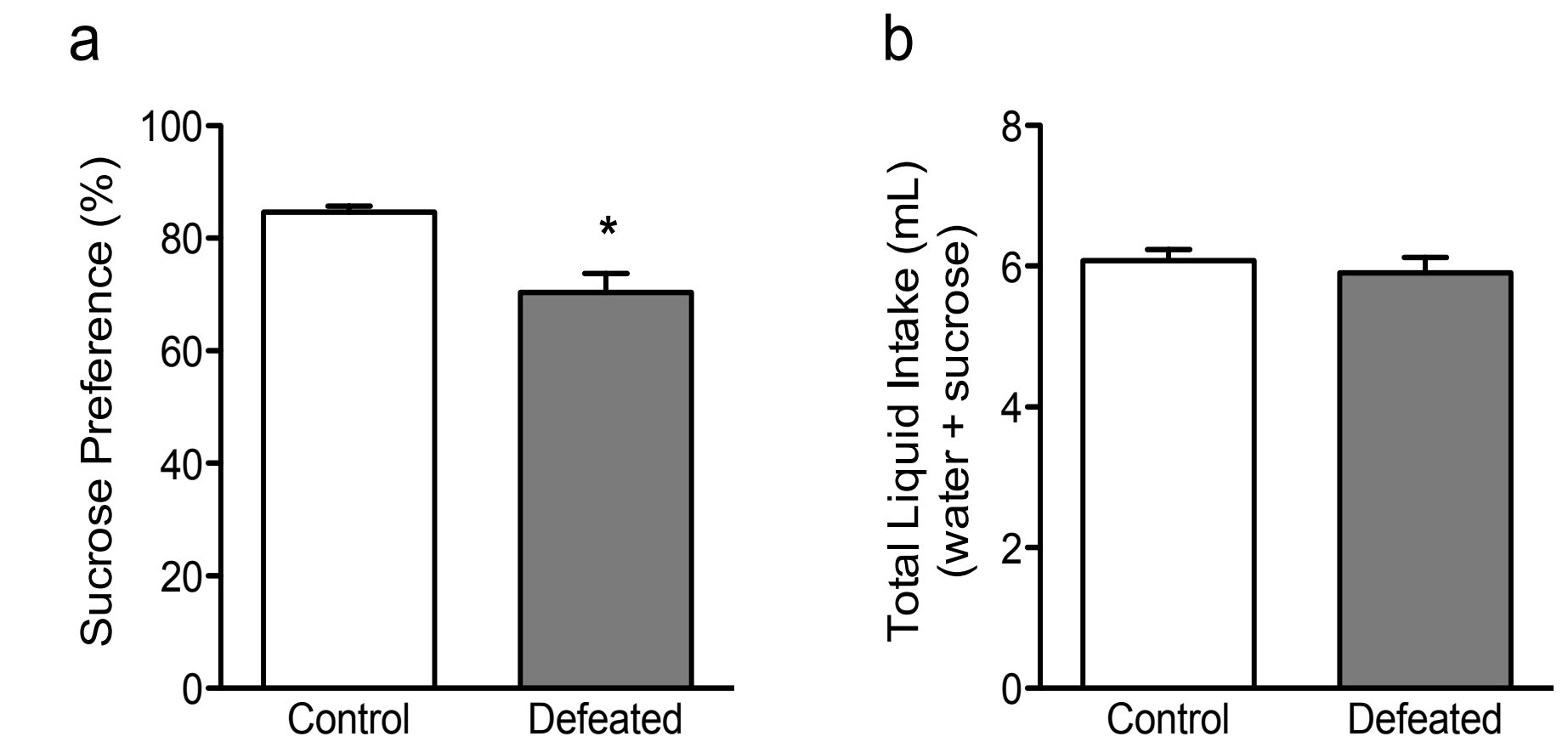


Figure 4. Effects 10 days of social defeat stress on sucrose preference in adolescent male C57BL/6 mice. (a) Twenty-four hr after social defeat (postnatal day 45), stressed (defeated; n=12) adolescent mice showed a decrease in the preference for a 1% sucrose solution, when compared to control (non-stressed; n=10) mice. (b) No differences in total fluid intake (sucrose + water) were detected between the groups. Data are presented as percentage or total mL consumed (mean + SEM).

Elevated Plus-maze

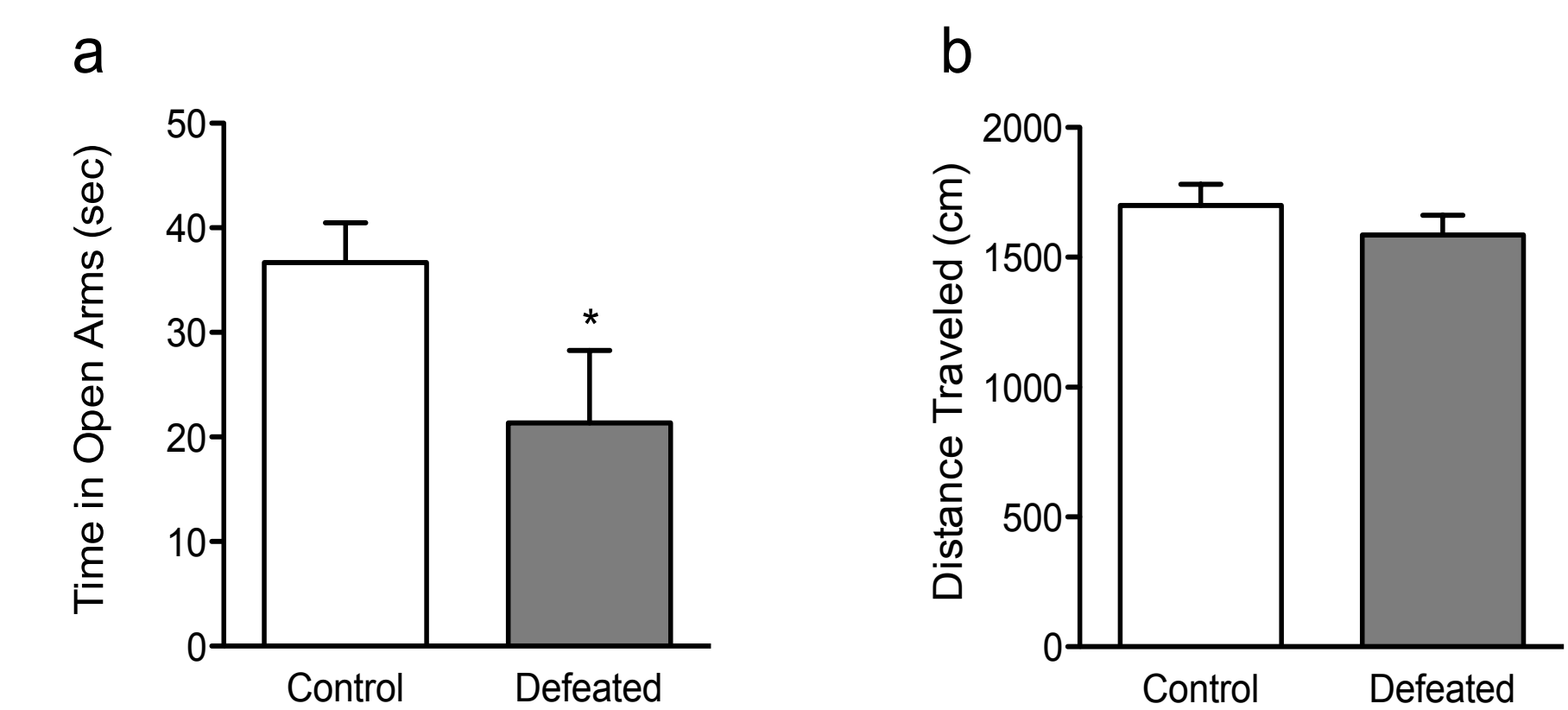


Figure 5. Effects of 10 days of adolescent social defeat stress on anxiety-like behavior in the elevated plus maze. (a) Twenty-four hr after the last social defeat episode (n=7 per group) the adolescent stressed (defeated) mice spent significantly less time in the open arms of the maze, when compared to control (non-stressed) mice. (b) No differences in the total distance (cm) traveled within the 5 min test was observed between the groups. *Significantly different from controls ($p < 0.05$). Data are presented as mean time (sec) and distance traveled (cm) + SEM.

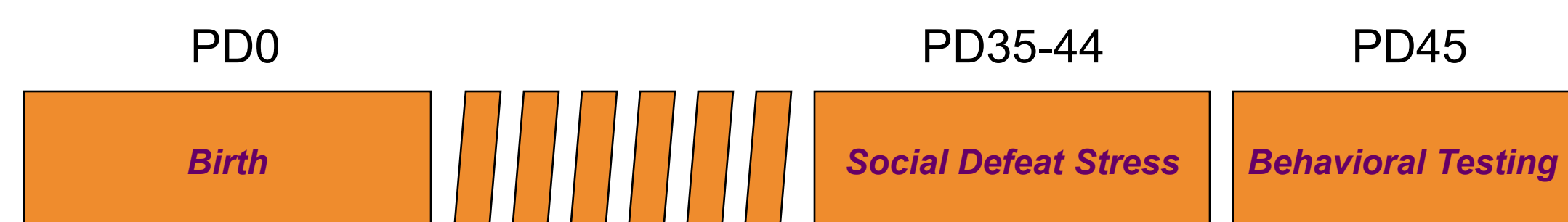
Conclusion

- These results demonstrate that exposure to social defeat stress during adolescence results in a depression-like phenotype, as inferred from:
 - ✓ Increased avoidance behavior.
 - ✓ Higher sensitivity to behavioral despair measures (helplessness).
 - ✓ Decreased preference for sucrose (anhedonia).
 - ✓ Higher sensitivity to anxiety-inducing situations.
- The neurobiological mechanism underlying this behavioral phenotype is currently not known.

Acknowledgements

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Strategy



Animals

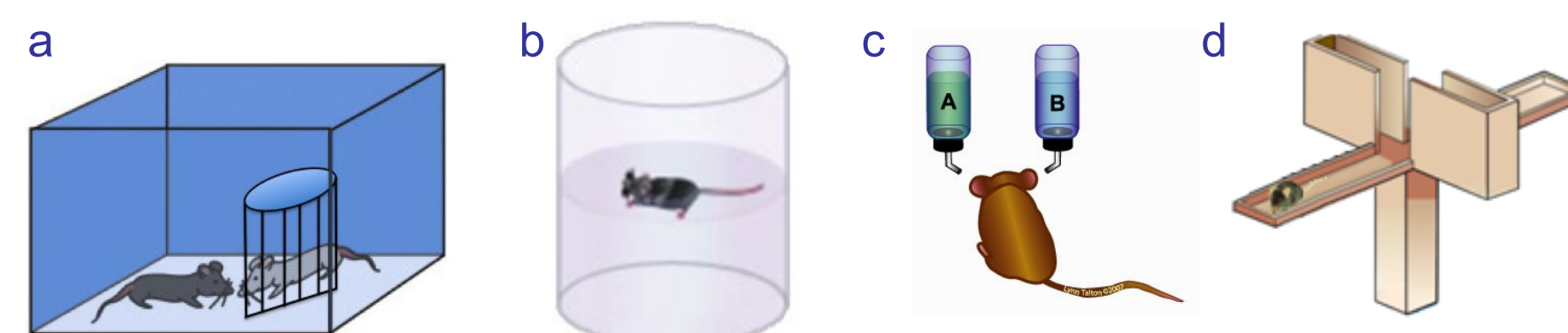
- C57BL/6 male mice
- CD1 retired male breeders

Social Defeat Procedure

- 10 min encounter with CD1 mouse
- 10 days (PD35-44)

Behavioral Testing

- Social interaction
- Forced swim test
- Sucrose preference
- Elevated plus-maze



Body Weight

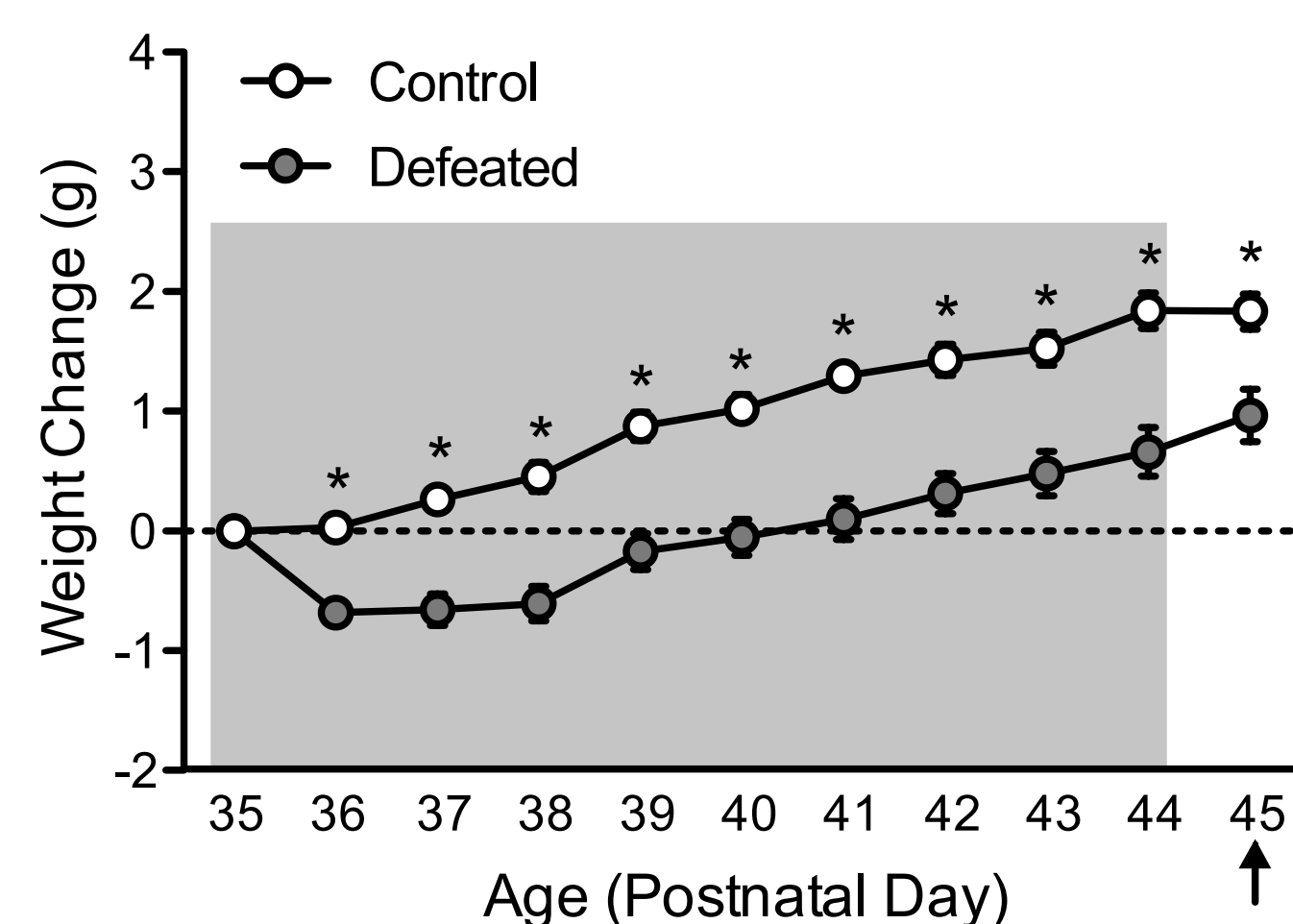


Figure 1. Effects of 10 days of social defeat stress on body weight change in adolescent male C57BL/6 mice. Defeat stress resulted in significantly lower body weight-gain as of the 2nd day of stress exposure, when compared to non-stressed (control) mice. Weight remained lower 24 hr after the last day of defeat (arrow). *Significantly different when compared to controls ($p < 0.05$). Data are presented as weight change in grams (mean + SEM).