Differences in threat and reward processing between adult and adolescent mice

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Introduction

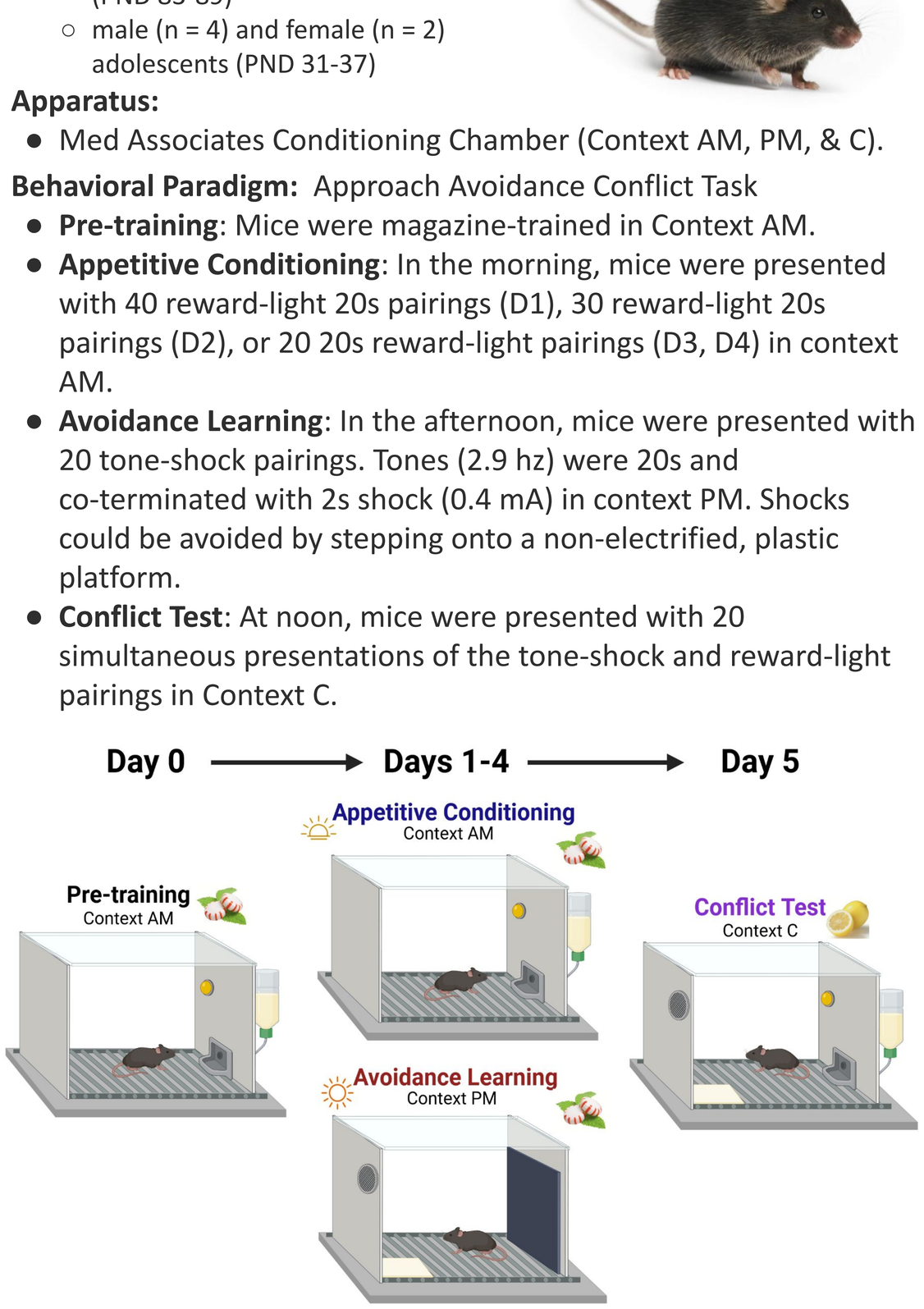
- Depression and anxiety are highly comorbid emotional regulation disorders that disrupt threat and reward processing in adults. However, these disorders have differing impacts - depression and anhedonia are correlated with reduced responsivity to rewarding stimuli and decreased reward seeking, while anxiety disorders prevent risk-taking behavior in accordance to reward processing and are associated with excessive, maladaptive avoidance.
- Depression and anxiety are the biggest mental health challenges adolescent face, yet we do not fully understand how reward and threat processing occur during this age period, and how they might relate to the development of these disorders.
- To explore this question, we created a modified version of the platform-mediated avoidance task[1] that allows us to assess how threat and reward learning occur during adolescence, and how that prior learning then translates to how adolescents navigate states of conflict where both appetitive and aversive stimuli are present.

Methods

Subjects: C57 BL/6J in-house mice
- male (n = 4) and female (n = 3) adults (PND 83-89)
- male (n = 4) and female (n = 2) adolescents (PND 31-37)

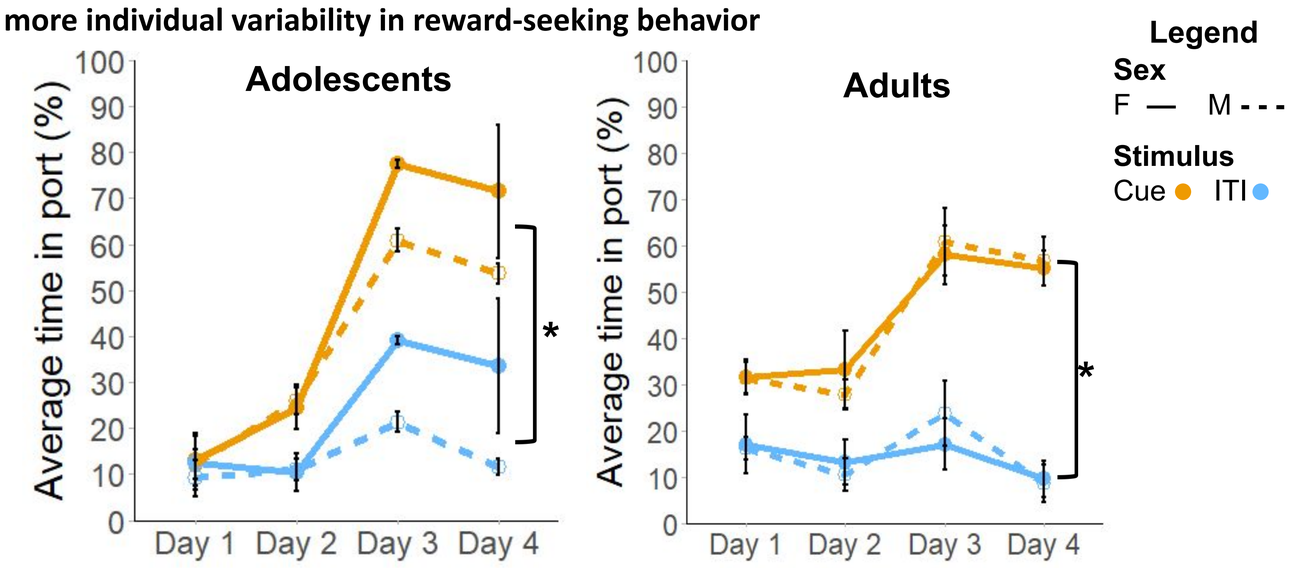
Apparatus:
- Med Associates Conditioning Chamber (Context AM, PM, & C).

Behavioral Paradigm: Approach Avoidance Conflict Task
- **Pre-training**: Mice were magazine-trained in Context AM.
- **Appetitive Conditioning**: In the morning, mice were presented with 40 reward-light 20s pairings (D1), 30 reward-light 20s pairings (D2), or 20 20s reward-light pairings (D3, D4) in context AM.
- **Avoidance Learning**: In the afternoon, mice were presented with 20 tone-shock pairings. Tones (2.9 hz) were 20s and co-terminated with 2s shock (0.4 mA) in context PM. Shocks could be avoided by stepping onto a non-electrified, plastic platform.
- **Conflict Test**: At noon, mice were presented with 20 simultaneous presentations of the tone-shock and reward-light pairings in Context C.



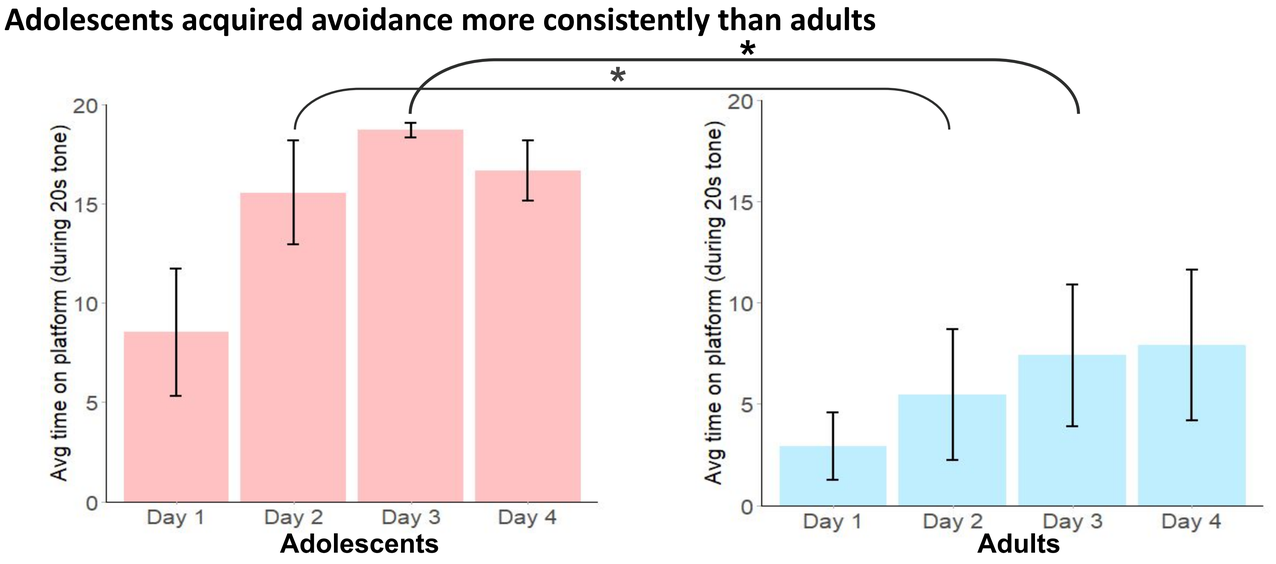
Results

Adults and adolescents learn appetitive conditioning at similar rates - but adolescents show more individual variability in reward-seeking behavior



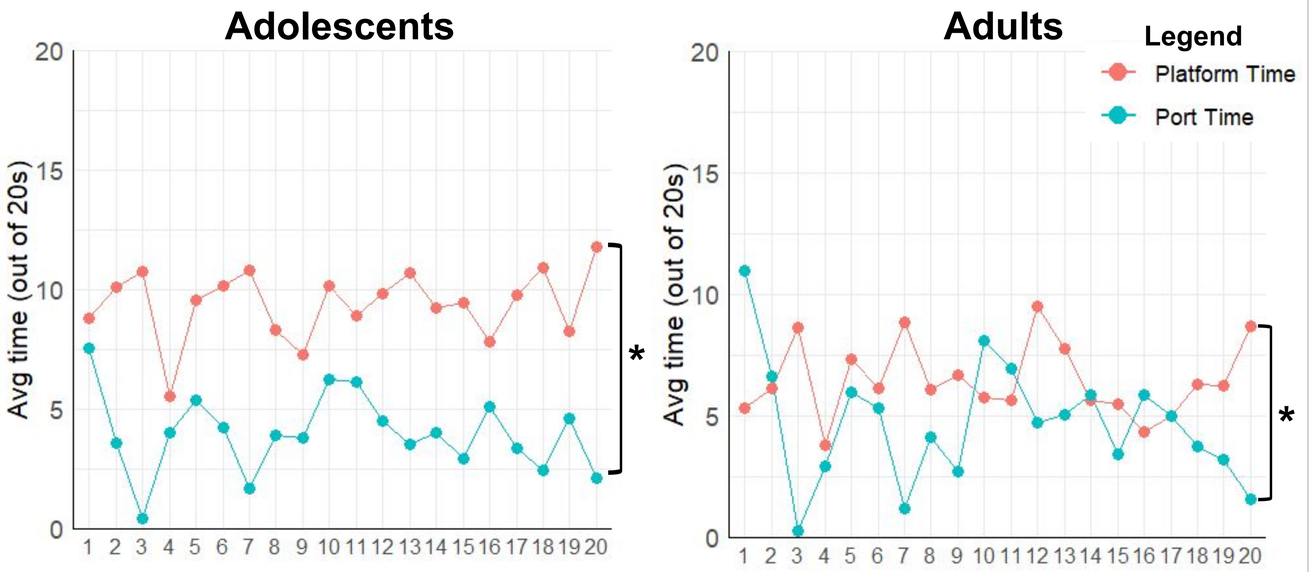
Adolescents have more individual variability in how much time they spend in the port compared to adults. A marginal sex difference was observed in adolescents, with females spending more time in the port than males.

Adolescents acquired avoidance more consistently than adults



Adolescents spent significantly more time on the platform than adults on days 2 (p = 0.04) and 3 (p = 0.03).
All adolescents (n = 6) learned avoidance, while only a subset of adult mice successfully learned avoidance (n = 3).

Adults adaptively split time between the port and platform more than adolescents



Both adolescents (p < 0.01) and adults (p = 0.03) spent significantly more time on the platform than in the port.
Adolescents spent significantly more time on the platform than adults (p < 0.01).

Discussion

- Adolescents had more individual variability than adults in appetitive conditioning, and all adolescent mice successfully learned avoidance.
- Adolescents spent more time on the platform than adults - adolescents learned avoidance more successfully.
- During the conflict phase, both adolescents and adults spent more time on the platform. However, adults seem to be more efficient at splitting their time between the port and the platform throughout the test session.

Challenges/limitation:
- Uneven distribution of the sexes made it difficult to assess for sex differences in appetitive and avoidance learning within both age groups.
- There were 4 non-learners in the adult group. Our task is also more prone to developing passive avoiders than active avoiders since the platform is present throughout the entire training session.

Future Directions: Characterize individual variations in avoidance learning (passive v. active disorders)

References & Acknowledgements

1. Bravo-Rivera C, Roman-Ortiz C, Brignoni-Perez E, Sotres-Bayon F, Quirk GJ. Neural structures mediating expression and extinction of platform-mediated avoidance. J Neurosci. 2014 Jul 16;34(29):9736-42. doi: 10.1523/JNEUROSCI.0191-14.2014.

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