**Effects of Maternal Separation on Punishment-driven Risky Decision Making Across the Lifespan**

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**Abstract**

Early life adversity (ELA) is associated with a multitude of enduring neural and behavioral aberrations. To develop treatments to mitigate the effects of ELA, it is critical to determine which aspects of cognition are affected and when these disturbances manifest across the lifespan. Here, we tested the effects of maternal separation, an established rodent model of ELA, on punishment-driven risky decision-making longitudinally in both adolescence (25-55 days old) and adulthood (80-100 days old). Risk-taking was assessed with the Risky Decision-making Task, wherein rats choose between a small, safe reward and a large reward accompanied by an escalating risk of punishment (foot shock). We observed that rats exposed to maternal separation were more prone to risk-taking than controls during adolescence, and demonstrated reduced latency to make both risky and safe decisions. Interestingly, this augmented risk-taking was no longer evident in adulthood. Males and females displayed comparable levels of risk-taking during adolescence then diverged in adulthood, with adult males displaying a sharp increase in risk-taking. Finally, we observed that risk-taking changed across the lifespan in rats exposed to maternal separation, but not in control rats. Collectively, these data reveal that ELA engenders risk-taking in adolescence but not adulthood, and that sex differences in risky decision-making are not evident until adulthood. This has important implications for the development of both behavioral and biological treatments to improve decision-making during the vulnerable adolescent period.

## Introduction

Early life adversity (ELA) is associated with a multitude of enduring neural and cognitive aberrations. A common form of ELA is sustained parental neglect, which predicts health problems, psychopathology, and social/financial hardship later in life (Chen et al., 2021; Matthews et al., 2022; Bowirrat et al., 2023). However, because incidence of childhood neglect is increased in marginalized individuals and those with low socioeconomic status (Reiss et al., 2019; Smith and Pollak, 2020; Howell et al., 2021), it is difficult to disentangle effects of childhood neglect from co-occurring sources of trauma. Problems with causality can be addressed using rodent models such as the maternal separation protocol (MSEP), wherein rat pups are separated from dams during early development (Ader et al., 1960). While rodent models have revealed that MSEP has enduring and often sex-specific effects on brain function and behavior (Andersen, 2015; Ellis and Honeycutt, 2021; Rincón-Cortés, 2023), many of the aspects of cognition altered by MSEP remain unclear.

Risky decision-making, or risk-taking, is defined as willingness to pursue rewards associated with adverse outcomes (Orsini et al., 2015b). While a moderate amount of risk-taking can be beneficial, excessive risk-taking can engender a range of deleterious physical, financial, and social consequences. ELA has been associated several disorders characterized by risk-taking, such as substance use disorder and gambling disorder (Lotzin et al., 2018; Loo et al., 2019; Bristow et al., 2022; al'Absi et al., 2023). Furthermore, MSEP in rodents has been shown to affect general motivation (Waters and Gould, 2022), the mesolimbic dopamine system (Jahng et al., 2010; González-Pardo et al., 2020; Hamdan et al., 2022; Rincón-Cortés, 2023), and prefrontal cortical areas/higher cognitive processes (Brenhouse et al., 2013; Boutros et al., 2017; Honeycutt et al., 2020), all factors involved with ability to assess and respond to risk and reward. In addition, ELA increases vulnerability to substance use in rodent models (Levis et al., 2022), which is associated with risk-taking (Mitchell et al., 2013; Gabriel et al., 2019; Orsini et al., 2020). Despite correlational evidence and overlapping neuronal substrates, the causal relationship between MSEP and punishment-driven risky decision-making has yet to be investigated.

Here, we tested the effects of MSEP on punishment-driven risky decision-making at different developmental stages in male and female rats. Rats were exposed to MSEP or control conditions from PD11-21, then tested in the risky decision-making task (RDT). This task measures preference between small rewards and larger rewards associated with an escalating risk of footshock punishment (Simon et al., 2009a; Simon and Setlow, 2012). Critically, preference for risky options in RDT is associated with a variety of addiction-relevant phenotypes, including impulsivity (Gabriel et al., 2019, 2023), cocaine and nicotine sensitivity (Mitchell et al., 2014; Gabriel et al., 2019; Orsini et al., 2020), cue salience (Olshavsky et al., 2014), and dopaminergic alterations in both dorsal and ventral striatum (Simon et al., 2011; Mitchell et al., 2014; Freels et al., 2020), suggesting that this form of risk-taking contributes to addiction vulnerability. Moreover, males are more risk-prone than females in

RDT (Orsini et al., 2016, 2021; Gabriel et al., 2023), making this task a valuable tool for studying sex differences in decision-making.

We first tested rats in RDT during late adolescence (pd 25-60) in male and female rats exposed to MSEP or standard conditions. Then, we re-trained and tested animals at pd 70-85 to determine if effects persisted into adulthood. Finally, to confirm that any effects (or lack-thereof) of MSEP in adulthood were not limited to RDT with a specific punishment intensity, we tested rats on RDT with an increased shock amplitude (.2mA to.3mA).

**Materials and Methods**

*Subjects:*

Male and female Long-Evans rat breeders were obtained from Charles River Laboratories. Four litters were bred in house, with one pup from each litter switched with a sex matched pup from another to mitigate litter bias. Litters were then subjected to either maternal separation (n=18; 10F/8M) or standard care (n=16; 8F/8M) from PD11-PD20. At PD21, rats were weaned and individually housed throughout the duration of the experiments. All rats were maintained on a reversed 12-hour light/dark cycle with testing conducted during dark hours to ensure maximum activity. During testing, rats were maintained at 90% of their free-feeding weight and ad libitum access to water. During adolescence, this was based on Long-Evans adolescent growth curves for males and females obtained from Charles River. Animal procedures were approved by the University of Memphis Institutional Animal Care and Use Committee.

*Materials:*

Clear plastic cages with wire top grates, bedding material, and kimwipes for enrichment were used to house all rats. For the maternal separation procedure, additional cages were be used to house pups while separated from the dam for each maternal separation session. After completion of MSEP, animals were pair housed with a littermate. Standard operant chambers (MedAssociates) were used to measure risky decision-making. Each chamber contained 2 retractable levers, an illuminable food trough, a nose-poke apparatus, a pellet dispenser, and a shock grate. Standard dustless sucrose pellets (Bio-serv) were be used as behavioral reinforcers.

*Overall Experimental Procedure:*

Rats were exposed to either maternal separation or control conditions from PD11-21, then were weaned and pair-housed. Food restriction began on PD22. Rats began shaping procedures for RDT on PD25, then began RDT between PD30 and 40. Rats ran RDT for a minimum of 20 sessions, culminating on PD60. Rats were given a 10 day rest with free access to food, then were restricted to

90% weight and retrained on RDT in adulthood (PD70-85). Then, rats again performed RDT with the shock intensity increased from .2 to .3mA. from PD86-93. See Figure 1 for full visual timeline.

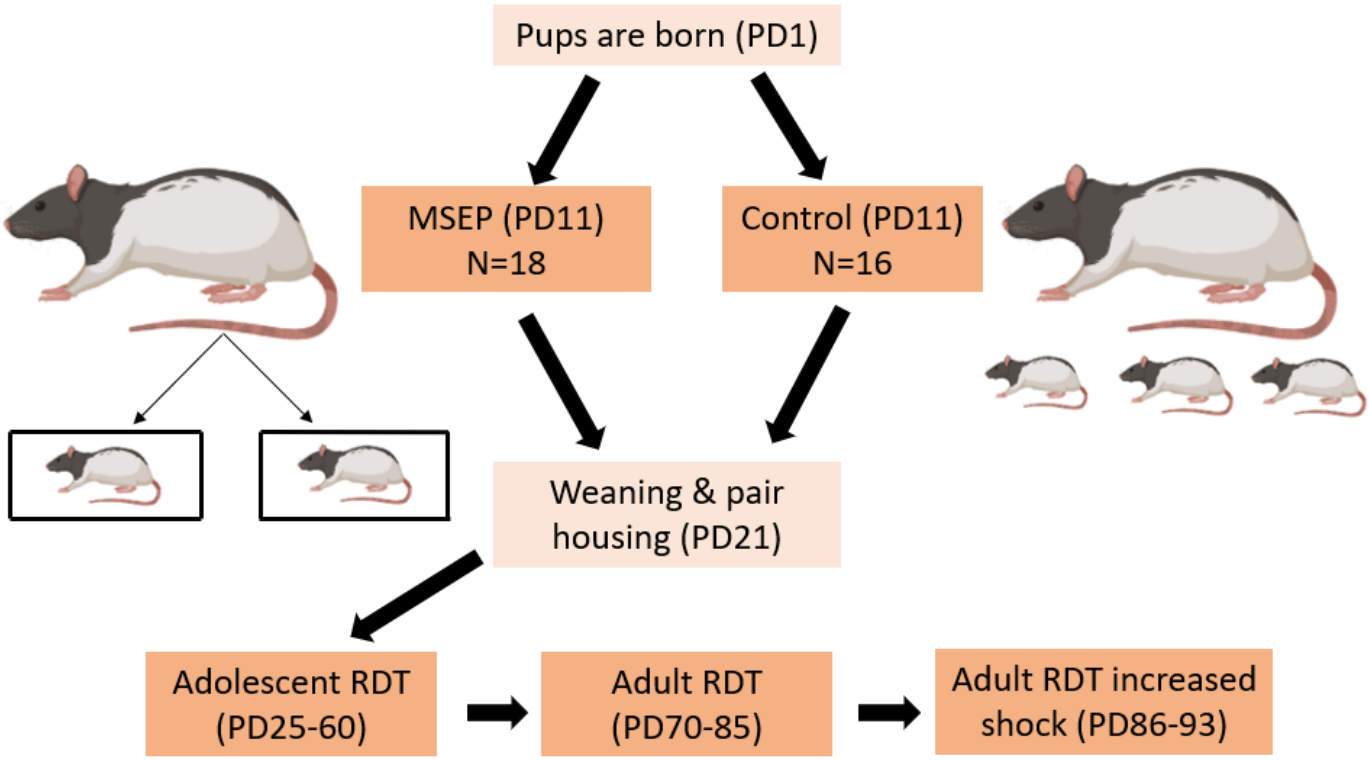


**Figure 1: Timeline of maternal separation and Risky decision-making experiments**

*Maternal Separation Protocol:*

Maternal separation was modified from Honeycutt et al (2020). Beginning at PD11, pups were separated into individual cages without food or water in a separate room for 4 hours for 10 consecutive days. Pups were weighed every other day throughout this protocol to confirm maintenance of a healthy weight. Control rats remained with their dam and litter 24 hours a day throughout this period. To minimize litter bias, one pup from each litter was swapped with another in the opposite condition. Any health issues, such as impaired movement, extreme weight loss, or aggression resulted in the animal in question being removed from the experiment.

*Risky Decision-making Shaping Procedures*

Prior to training in RDT, rats performed shaping procedures which are described in detail in Orsini and Simon (2020). Rats were first given a single session of magazine training to acquire the sounds/location of pellet delivery, wherein 38 pellets were dispensed during a 30 minute session. Then, rats underwent lever press training, learning to depress a single lever for pellet delivery on a fixed ratio-1 schedule. Rats trained on the right or left lever in separate sessions, with each phase of shaping culminating when rats performed > 30 presses in a session.

Rats were next trained in nosepoke shaping, in which they learned to poke into the lit food trough to elicit a reward-associated lever. The trough was illuminated for 10 seconds, then a poke caused extension of either the right or left lever along with extinguishment of the trough light. A press on the lever evoked a single pellet delivery as well as immediate retraction of the lever. After a 10±2 second intertrial interval (ITI), the next trial began with the opposite lever being available after the nosepoke. After >60 successful trials, rats progressed to reward magnitude discrimination, during which they learned to discriminate between levers yielding small vs large rewards. This was comparable to nosepoke shaping with two main differences: first, with each nosepoke both levers were simultaneously extended, providing rats with a choice between two options. Second, one lever produced a single pellet delivery (small reward), whereas the other delivered 3 pellets (large reward). Each session consisted of 50 trials, and rats trained until they demonstrated at least 70% choice of the large reward option.

*Risky Decision-making Task (RDT)*

Detailed RDT methodology was described in previous work (Orsini and Simon, 2020). In brief, rats were trained to choose between levers associated with a small reward (1 pellet) or a large, risky reward (3 pellets and escalating risk of 1-sec footshock). Procedure was comparable to reward magnitude training: each trial began with food trough illumination, and a nosepoke into the lit trough within 10 seconds caused both levers to extend. After rats chose between the small and large/risky

options, both levers were retracted, and the reinforcer/punishment was delivered immediately. After the outcome, the trial proceeded to a 10± second ITI followed by the next trial. If the subject failed to make a choice within 10 seconds, the trial was scored as an omission, and proceeded to the ITI.

Each session consisted of 5 blocks of 18 trials, with each block containing a different risk of shock (0,25,50,75,100%). The first 8 trials were “forced choice”, used to acclimate the rat to the new risk level, with only a single lever extended after each trough nosepoke (four trials of each lever presented in pseudorandom order). The next 10 were “free choice” trials, with both levers extended after each nosepoke and rats given a choice between options. Shock was set at an intensity of .2mA throughout adolescence and during the first RDT assessment in adulthood, then was shifted to .3mA for a second assessment in adulthood.

*Statistical Analysis*

Risky decision-making was reported as % choice of the large, risky reward averaged across the last 5 days of training. Choice latency was defined as mean time required to choose either the risky or safe lever across all trials in the final four task blocks (because no risk was associated with either option in block one). Stable performance across these sessions was confirmed by lack of effect of session and lack of interaction in a session X block mixed ANOVA. Effects of maternal separation on RDT was measured with a treatment (maternal separation vs control) X sex X block mixed ANOVA. Age effects were assessed using age (adolescent vs adult) X treatment X sex X block mixed ANOVA.

**Results**

*Maternal Separation increases Risky Decision-making in Adolescence*

Male and female rats exposed to maternal separation (MSEP) or control conditions were trained in RDT during adolescence. As seen previously with RDT (Gabriel et al., 2019; Orsini et al., 2019; Farrell et al., 2021), rats collectively shifted preference away from the large, risky reward as risk level increased ($F_{(4,120)}$=21.615*, p*<.001; Fig 2a*).* Importantly, MSEP caused a significant increase in choice of the risky option (F(1,30)=12.220, p=.001; fig 2a), as well as a significant group X risk interaction, such that controls displayed a greater shift than the MSEP group away from the large reward after the addition of risk in blocks 2-5 (F(4,120)=4.405, p=.002). There was no effect of sex on decision-making (F(1,30)=1.468, p=.235) and no sex-based interactions (ps>.585; Figure 2b-c).

We next assessed response latency, defined as average time taken to choose either the safe or risky option following lever extension during blocks 2-5 (when risk of punishment was present). Overall, there was no difference in latency to choose the risky vs safe outcome (F(1,22)=.785,

**Figure 2**

p=.385). There was a main effect of group (F(1,22)=4.773, p=.040), such that adolescent rats exposed to MSEP made choices more quickly than adolescent controls (Figure 2c). There was no lever X group interaction (F(1,22)=.005, p=.943), indicating that the reduction in response latency in MSEP rats was comparable across risky and safe choices. There was no effect of sex ((F(1,22)=2.079, p=.163), although there was a significant sex X group interaction (F(1,22)=5.227, p=.032) and near significant lever X group X sex interaction, (F(1,22)=3,164, p=.089), such that females exposed to MSEP showed increased latency to select the safe option but reduced latency to select the risky option compared to controls, whereas MSEP males showed reduced latency for either option (Figure 2d-e).

Finally, we assessed omissions, defined as trials in which rats either failed to initiate the trial or select a level within the allotted time. There was an effect of risk on omissions (F(4,128)=190.295, p<.001), such that subjects on average omitted more trials with increasing risk. There was also an effect of group (F(1,32)=8.454, p=.007), with adolescent rats exposed to MSEP omitting less trials than controls (despite increased reward consumption due to choosing the large reward more frequently than controls). There was a significant effect of sex (F(1,32) = 4.947, p=.033) and risk X sex interaction (F(4,128)=3.123, p=.017), with females omitting more trials than males.

*Maternal Separation does not affect Risky Decision-making in adulthood*

After a 10-day break, rats resumed RDT performance with the same parameters as in adolescence, and risk-taking was again measured and compared between groups on PD85. As previously, there was an effect of risk, with reduced choice of the large reward as risk of punishment escalated (F(4,120)=16.02, p<.001). Unlike during adolescence, there was no effect of MSEP on risky decision-making (F(1,30)=.255, p=.617) or group X risk interaction (F(4,120)=1.956, p=.106). Also, in contrast with adolescence, there was an effect of sex (F(1,30)=28.564, p<.001) and sex X risk interaction (F(4,120)=5.657, p<.001), such than females showed increased avoidance of large, risky rewards compared to males. There were no significant sex X risk X group or sex X group interactions (ps>.250), suggesting that the sex differences in risk taking manifest in adulthood regardless of exposure to early life MSEP.

There was no significant difference in latency to choose the safe vs risky options in adulthood (F(1,26)=2.160, p=.154). There was a non-significant trend toward MSEP reducing latency to choose either option (F(1,26)=4.423, p=.091), but no lever X group interaction (F(1,26)=.079, p=.781). Unlike in adolescence, there was a significant effect of sex on latency (F(1,26)=15.731, p<.001), such that males make decisions more quickly than females. There were no significant sex-based interactions, suggesting that both lever type and early life experience did not influence sex differences in response

**Figure 3**

latency (ps>.469). As previously, there was an effect of risk on omissions (F(4,128)=38.913, p<.001), p<.001), such that all subjects omitted more trials as risk of punishment increased. There was no effect of MSEP on omissions (F(1,32)=.952,p=.337). As in adolescence, females omitted more trials than males (F(1,32)=33.196, p<.001), but there was no sex X group interaction (F(1,32)=1.095, p=.303).

*Retesting RDT in Adults with Increased Shock Intensity*

During adult RDT, male preference for risky rewards approached ceiling levels regardless of treatment (Figure 3). It is possible that any effects of MSEP in adulthood were concealed by this near-maximal choice of the risky option. To create more parametric space for detecting potential group differences, rats were retrained in RDT with shock intensity raised from .2 to .3 mA, which has been shown to reduce risky choice(Simon et al., 2009b; Shimp et al., 2015). As anticipated, increasing the shock caused a significant reduction in risky choice (F(1,30)=53.756, p<.001). When isolating the .3 mA condition, there was a significant effect of risk (F(4,120)=66.567, p<.001), with subjects shifting preference away from large rewards with increasing risk. As with the lower shock intensity, there was no effect of MSEP on risky decision-making (F(1,30)=.095, p=.76) or risk X group interaction (F(1,30)=.012, p=.915; Figure 4a). There was an effect of sex, such that males were more risk-prone than females (F(1,30)=8.094, p=.008; Figure 4b-c). There were no other sex-based interactions (ps>.215). Therefore, the lack of MESP effects on adult risky decision-making were evident regardless of shock intensity.

There was no significant difference in latency to choose the safe vs risky options (F(1,27)=.621, p=.437; Figure 4d). However, there was a significant difference between groups (F(1,27)=6.225, p=.019), with MSEP causing increased latency to choose either option. There was no significant effect of sex (F(1,27)=.218, p=.645), and no significant interactions between any variables (ps>.653; Figure 4e-f). Trial omissions were elevated as risk of punishment increased (F(4,28)=65.768,p<.001). As with the lower shock intensity, there was no effect of early life experience on omissions (F(1,32)=.578,p=.453). Finally, females omitted significantly more trials than males (F(1,32)=16.941, p<.001), with no sex X group interaction (F(1,32)=.345, p=.561).

*Comparing Risky Decision-making in Adolescence and Adulthood*

To our knowledge, this is the first study to longitudinally test adolescent and adult punishment-based risky decision-making. Accordingly, we compared risk-taking as well as effects of MSEP on risk-taking between age groups. There was a near-significant trend of age (F(1,20)=3.227, p=.083), with adolescents demonstrating increased risk preference compared to adults. There was also a

**Figure 4**

significant main effect of sex ($F(1,20)=16.605$, $p<.001$), with males showing increased risk-taking across adulthood/adolescence.

Critically, there was a significant age X group interaction ($F(1,120)=11.502$, $p=.002$) and age X risk X group interaction ($F(4,120)=6.206$, $p<.001$), enabling individual comparisons between ages within both MSEP and control subjects (Figure 5). MSEP rats were significantly more risk-prone during adolescence than adulthood ($F(1,16)=11.718$, $p=.003$). Interestingly, there was also a significant sex X age interaction ($F(1,16)=16.574$, $p<.001$), such that MSEP-exposed males displayed consistent risk preferences across the lifespan, whereas females were riskier during adolescence than in adulthood. In control rats, there was no effect of age on risk-taking ($F(1,14)=2.898$, $p=.111$). In summary, there was no substantial difference in risky decision-making between adolescence and adulthood in subjects raised in normal laboratory conditions, but rats exposed to MSEP during development were riskier in adolescence than adulthood.

## Discussion

We determined that MSEP increases risky decision-making in both male and female rats during late adolescence (post-natal days 55-60). Additionally, adolescents exposed to MSEP made both risky and safe decisions more rapidly than controls. In adulthood, MSEP-evoked risk-taking and increased rate of decision-making were both abolished in the same subjects. While decision-making itself was not affected by MSEP, rate of decision-making slowed in MSEP subjects. Interestingly, no sex differences in risk-taking were observed during adolescence, then males shifted toward a higher risk decision-making strategy than females in adulthood. Finally, MSEP-exposed rats showed a sex-dependent reduction in risk preference from adolescence to adulthood, whereas there was no age difference in risk-taking in control rats.

### *Maternal Separation Increases Risk-taking in Adolescence*

Adolescence is a period characterized by extensive behavioral and neurobiological alterations, making the brain and behavior particularly vulnerable to early life adversity. We observed that in late adolescence (days 55-60), MSEP increased risky choice in RDT. Moreover, MSEP-evoked risk-taking was comparable between male and female rats. This was somewhat surprising, as the consequences of MSEP are often sex-specific (Spivey et al., 2009; Kunzler et al., 2015; Ganguly et al., 2019; Honeycutt et al., 2020; Zühlsdorff et al., 2022; Rincón-Cortés, 2023; Gildawie et al., 2024). This suggests that the MSEP's effects on adolescent risk-taking are likely not mediated by alterations in sex hormone transmission or other sexually dimorphic neural mechanisms.

MSEP causes alterations to several brain circuits implicated in risky decision-making during

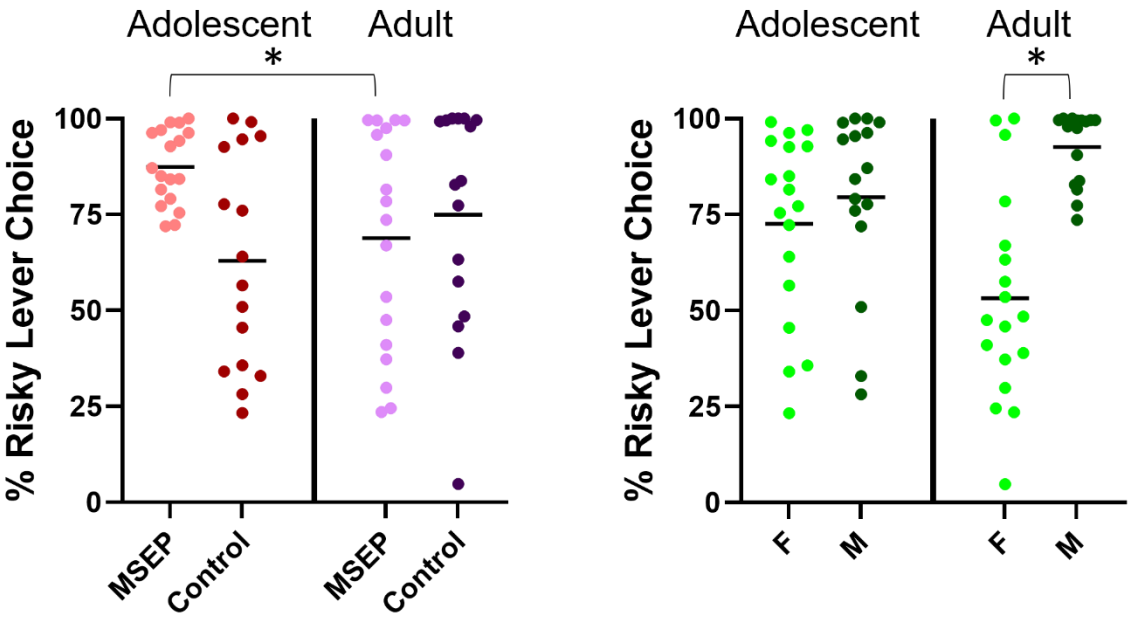
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**Figure 5**

adolescence (Orsini et al., 2015a; Rincón-Cortés, 2023). Mesolimbic dopamine release in response to an acute stressor is enhanced in adolescence (Jahng et al., 2010), which is analogous to the increased phasic mesolimbic dopamine release observed in rats with a bias toward risk-taking (Freels et al., 2020). MSEP also altered dopamine receptor expression in prefrontal cortex and striatum in adolescent females (Majcher-Maślanka et al., 2017), another biomarker of punishment-driven risk-taking (Simon et al., 2011; Mitchell et al., 2014). MSEP also causes differences in both structural and functional measures of communication between basolateral amygdala and medial prefrontal cortex (Honeycutt et al., 2020; Thomas et al., 2020), which contribute to different aspects of both punishment-based and reward omission-based risk-taking (Ghods-Sharifi et al., 2009; Onge et al., 2012; Orsini et al., 2017, 2018; Tremblay et al., 2021). Therefore, it is possible that increased adolescent risk-taking following MSEP is a result of impaired communication in cortical/striatal/limbic circuitry.

MSEP reduced latency to make both risky and safe decisions during adolescence. This reduced deliberation prior to choice may reflect reduced processing of the potential outcomes associated with each option, leading to a bias toward risky choice. It is possible that this reduced decision latency is related to MSEP altering activity in basolateral amygdala (BLA), as BLA lesions both increased choice of risky rewards and reduced the latency to make these risky choices. Additionally, during pre-choice deliberation, lateral orbitofrontal cortex signals information about impending risk, and this signaling is attenuated in risk-taking subjects (Gabriel et al., 2024). It is possible that MSEP diminishes this risk processing, leading to ongoing choice of risky options.

Risk-taking as captured in RDT is a complex phenotype that involves several other factors. It is possible that MSEP-enhanced risk-taking was driven by altered pain sensitivity, since the punishment used in RDT is risk of mild shock. Therefore, it is possible that MSEP reduces the aversive properties of the shock. However, MSEP has been shown to increase nociception in rodents, which would likely reduce rather than enhance risk-taking. Furthermore, several measures of pain tolerance and shock sensitivity are uncorrelated with risk-taking in RDT (Simon et al., 2011; Truckenbrod et al., 2023b), and administration of the analgesic drug morphine does not alter risk-taking (Mitchell et al., 2011), suggesting that RDT performance is not tightly linked to pain tolerance.

It is also possible that MSEP increased risk-taking by reducing cognitive flexibility. This would affect ability to adapt decision-making after changes in risk-level, leading to “flattening” of the decision-making curve (Figure 2). A meta-analysis determined that MSEP reduces flexibility in rodents, although these results were somewhat heterogeneous (Ou-Yang et al., 2022). Furthermore, MSEP induces reduced flexibility in post-weaning animals (day 26) but not in late adolescence/early adulthood (day 60), the time period in which risk-taking was measured in the current study (days 55-60)(Thomas et al., 2020). Finally, risk-taking rats display increased cognitive flexibility compared to

risk-averse subjects (Shimp et al., 2015), suggesting that impaired flexibility would likely manifest as reduced rather than enhanced risk-taking.

The onset of substance use disorder (SUD) often occurs in adolescence, and early life neglect is associated with increased substance use during this period. Risky decision-making is an endophenotype of SUD, and can drive ongoing drug seeking in the face of health, financial, and social consequences. It is possible that elevated risk-taking is one of the factors that promotes SUD in adolescents with early life adversity. Risk-taking in RDT is associated with a cluster of addiction relevant traits, including impulsive action (Gabriel et al., 2019, 2023), cue sensitivity (Olshavsky et al., 2014), and sensitivity to drugs of abuse (Mitchell et al., 2013; Gabriel et al., 2019; Orsini et al., 2020). In addition, risk-taking is associated with a hypersensitive mesolimbic dopamine system and reduced D2 receptor expression in dorsal striatum, both of which are observed in people with a history of substance misuse (Volkow et al., 2007; Simon et al., 2011; Freels et al., 2020). Therefore, elevated risk-taking caused by MSEP may engender a state of vulnerability to substance use and misuse in adolescence.

*MSEP-increased risk-taking does not extend into adulthood*

While MSEP increases risk-taking in adolescence, this effect is not long evident in adulthood. Moreover, the reduced latency evident after MSEP in adolescence was abolished in adulthood, providing further evidence that increased risky choice in adolescence was related to an increase in “rushed” decision-making. These data contrast with a previous study reporting increased disadvantageous choice in the rat gambling task (RGT) in adults exposed to MSEP (Cao et al., 2016). This distinction may be a result of differences in the risk of punishment used in these tasks; RDT uses a probabilistic footshock, whereas the RGT uses risk of a time out periods in which reward is no longer available. Both differences and similarities have been noted in the biological processes mediating these tasks, so the divergent effects of MSEP are not entirely unexpected. Additionally, MSEP has also been shown to increase impulsive action in the differential reinforcement of low rates of responding task (DRL) in adults (Lovic et al., 2011). Impulsive action in DRL is correlated with risk-taking in RDT; therefore, it was surprising that increased risk-taking did not manifest in adulthood in the current report. It is possible that the early training in RDT followed by re-testing in adulthood in the current study was sufficient to mask the risk-enhancing effects of MSEP. This remains to be tested by assessing RDT in naïve rather than pre-trained adults following MSEP.

Brain regions involved with regulation of risk-taking, such as prefrontal cortex and striatum (Simon et al., 2011; Orsini et al., 2015a; Freels et al., 2020; Truckenbrod et al., 2023a), are still undergoing development in adolescence. In addition, punishment-based risk-taking is modulated by dopamine transmission, and the dopamine system is still undergoing development during

adolescence (Andersen et al., 2001; Ernst et al., 2009; Walker et al., 2010; McCutcheon et al., 2012; Matthews et al., 2013; Simon and Moghaddam, 2015; Kim et al., 2016). It is possibly that this ongoing development makes these brain regions particularly vulnerable to MSEP, resulting in enhanced risk-taking. The “correction” of risk-taking to normal levels in adulthood has been reported with several other cognitive phenotypes, and suggests that task-relevant brain development is affected by MSEP, but ongoing development at the end of adolescence/young adulthood is sufficient to overcome these alterations. Therefore, future research on MSEP and risk-taking should focus on adolescence, which is already a period of vulnerability to psychiatric disorders (Simon and Moghaddam, 2015; Blakemore, 2019).

*Comparing risk-taking across the lifespan*

Adolescence is a period characterized by increased impulsivity and risk-taking (Geier et al., 2010; Sturman and Moghaddam, 2011; Doremus-Fitzwater et al., 2012; Simon and Moghaddam, 2015; Galvan and Tottenham, 2016). While punishment-based risky decision-making has been previously assessed in adolescent male rats (Mitchell et al., 2014), this study is the first to compare longitudinal measurements of risk-taking in adolescence and adulthood of male and female rats. We observed that in control subjects, risky decision-making was comparable between adolescence and adulthood. However, age differences emerged in rats exposed to MSEP, with MSEP adolescents showing greater risk-taking than adults. This suggests that increased adolescent vs adult risk-taking may not be inherent, but instead manifests after early life adversity.

Sex differences in RDT have been reported repeatedly, with females adopting a more risk-averse strategy than males (Orsini et al., 2016, 2021; Blaes et al., 2022; Gabriel et al., 2023; Truckenbrod et al., 2023b). Interestingly, there were no sex differences during adolescence regardless of early life experience. Sex differences then manifested in early adulthood, with the first adult measurement occurring only 25 days after the adolescent measurement (days 56-60 vs days 81-85). Therefore, functional sex differences within brain circuitry underlying risk and reward during decision-making may not emerge until adulthood.

*Conclusion*

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