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Adolescent Social Isolation Increases Sensitivity to Pain and Opioid Use in Adulthood in Rats

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Adolescent social stress, including isolation, is a risk factor for substance use disorder and can induce persistent behavioral changes. This study examines the impact of adolescent social isolation (SI) on opioid use and related behaviors in adulthood using WKY and DSS rat strains. We compared oxycodone intake during self-administration between rats either group-housed (GH) or SI for 6 weeks during adolescence, using PeerPub operant chambers that simultaneously record oral intake of two rats. SI rats (n = ~12/group) showed greater vulnerability to oxycodone consumption in adulthood compared to GH rats. Repeated measures mixed ANOVA revealed significant effects of treatment ($F_{1,51}=13.1$, $p=0.0007$), sex ($F_{1,51}=12.5$, $p=0.0009$), and strain ($F_{1,51}=6.83$, $p=0.012$), with a significant treatment × sex interaction ($F_{1,51}=5.12$, $p=0.028$). Session-level analyses revealed significant treatment differences for sex ($F_{16,1406}=4.7$, $p=2.28\times10^{-9}$) and strain ($F_{16,1406}=2.8$, $p=0.0002$). SI rats also showed significantly shorter baseline pain sensitivities (latencies) compared to GH rats, suggesting increased pain sensitivity prior to opioid exposure. A mixed ANOVA revealed significant differences in baseline latency between treatment groups for WKY rats ($F_{1,128}=22.84$, $p=4.75\times10^{-6}$), with significant results in the DSS group ($p=0.00014$). Strain comparisons showed WKY rats had higher baseline latency than DSS rats ($p=2.41\times10^{-6}$). These findings highlight the role of adolescent social stress in increasing vulnerability to opioid use and pain-related phenotypes.