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Lessons learned in creating selected lines for high and low delay discounting

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Delay discounting (DD) is a heritable trait (~ .4 - .5) linked to the development of various psychopathologies, including substance use disorder. Selectively breeding rodent lines exhibiting extreme DD (high or low) would provide a valuable resource to investigate DD's genetic basis. Using heterogeneous stock rats, we have completed three generations of selection. For each generation, rats' DD phenotypes were determined via an adjusting-amount procedure assessing choice between a small, immediate sucrose reward and a delayed 150 ul reward (0, 2, 4, 8, 16 or 24 second delays). Normalized-AUC (highly correlated to the hyperbolic gradient of the discounting function) was used to create 24 pairs of high-discounting and 24 pairs low-discounting rats for each generation. Data from Selection Generation 1-3 suggest little response to selection, but a shift in the overall distribution towards steeper delay discounting. One contributory to this drift appears to be the inadvertent inclusion of rats in the breeding pairs with high levels of DD assessed using less traditional measures (exponential DD rather than hyperbolic DD). Additional analyses suggest that this less traditional measure is a substantially higher heritability and the distribution differences contribute to the slow increase in overall DD. Further, our additional analyses suggest that different behavioral characteristics underlie the DD phenotype including differential responsivity to reward size versus differential responsivity to reward delay.

On-going work explores whether these are associated with different genetic profiles, and future work will examine their different relationships to substance use. Future selection efforts must distinguish between these phenotypic nuances for successful selection to occur.