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Polygenic prediction of incentive salience attribution to a reward cue using RATTACA in heterogeneous stock rats

Conditioned stimuli (“cues”) paired with rewards can acquire incentive salience, thereby becoming attractive and serving as effective conditioned reinforcers. Incentive salience can be measured during a Pavlovian conditioned approach (PavCA) procedure, in which an illuminated lever (the cue) predicts a banana-flavored food reward. While some rats (“sign-trackers”) approach the cue upon its presentation, other approach the food-delivery location (“goal-trackers”). Using PavCA GWAS data to generate polygenic prediction (also known as “RATTACA”), we selected 35 experimentally naïve male and female heterogenous stock rats with high (rST; n=18) or low (rGT; n=17) sign-tracking scores from a population of 449 rats. During eight sessions of PavCA, rSTs showed robust levels of cue-directed approach compared to rGTs, who displayed greater levels of food-cup directed approach ($p < 0.001$). By session eight, 9 of 18 rSTs and 0 of 17 rGTs met criterion for classification as sign-trackers based on a previously published PavCA Index classification method (Meyer et al., 2012), while 6 of 18 rSTs and 17 of 18 rGTs met the criterion to for classifications as goal-trackers. rSTs responded for the cue during a conditioned reinforcement test than rGTs, although this difference was more modest ($p <0.05$). These results validate RATTACA as a practical method for predicting cue-reactivity phenotypes in behaviorally naïve HS rats. This prospective selection approach can be used to study SUD vulnerability factors and in combination with experimental manipulation to determine gene x environment interactions.

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