A HIGH THROUGHPUT, FORWARD GENETIC BEHAVIORAL SCREEN IDENTIES MICE WITH ALTERED RESPONSE TO PSYCHOSTIMULANTS

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RESULTS

We have conducted a high throughput forward genetics screen in mice to identify behavioral mutants. Mice 10-15 weeks in age were measured for baseline activity and then injected with cocaine (20mg/kg, intraperitoneally) and post-injection observed activity was observed for an hour. We developed a video based screening protocol that is highly scalable and allows one technician to test over 100 mice per day for locomotor response to drugs of abuse. Over the past five years we have screened over 20,000 ENU mutagenized mice for response to cocaine. We have identified 19 heritable mutant lines with altered response to cocaine. We are currently mapping and characterizing three of these mutants.

CONCLUSIONS

One such mutant, Gridlock'd, has low response to cocaine and amphetamine. On average the response of these mice is one Standard Deviation lower than wild type animals. The quantitative nature of these mutants has presented a challenge for genetic mapping. We have used Quantitative Trait Locus (QTL) methods to map this mutant to a chromosome. We are currently fine mapping the mutant to determine the exact mutation which causes the low response phenotype.

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