Methods: Nrg1 TM HET mice failed to extinguish cocaine-seeking more often than WT mice. These findings suggest a Nrg1-mediated shift in the dose-response curve. In IVSA, Nrg1 TM HET mice failed to extinguish cocaine-seeking more often than WT mice. These findings suggest a Nrg1-mediated shift in the dose-response curve.

Discussion: The data presented suggest the Nrg1 TM mutation produces an addiction-relevant phenotype for cocaine. These findings provide the first evidence for a potential genetic link between schizophrenia and cocaine abuse and may help explain elevated susceptibility to cocaine abuse in patients.

References

M91. ADDICTION-RELEVANT BEHAVIOURS FOR COCAINE IN A NEUREGULIN 1 MUTANT MOUSE MODEL OF SCHIZOPHRENIA

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Background: Substance abuse is highly prevalent in schizophrenia patients, worsening symptoms, increasing hospitalisation, and reducing antipsychotic medication efficacy. The reason for high substance abuse rates in schizophrenia is unclear, however, it has been hypothesised that genetic predisposition for schizophrenia may increase the patients' susceptibility to addictive behaviour. Elevated addiction propensity can be examined using mouse models of genetic risk for schizophrenia. The heterozygous neuregulin 1 transmembrane domain mutant (Nrg1 TM HET) mouse shows face, construct and predictive validity for schizophrenia and displays altered behavioural and neural responses to the major psychoactive cannabis constituent. However, the rewarding properties of drugs of abuse have not been assessed in these mice.

Methods: We examined addiction-like behaviours for cocaine in adult male Nrg1 TM HET mice. Cocaine reward (5, 10, 20 mg/kg i.p.) was assessed in conditioned place preference (CPP), where the pairing of a drug with a neutral context produces a preference for the drug-paired context. Self-administration of cocaine including the motivation to do so was also examined using intravenous self-administration (IVSA; cocaine doses: 0.1, 0.5, 1 mg/kg/infusion). We also tested cessation of cocaine self-administration and relapse-like behaviour using IVSA.

Results: In CPP, Nrg1 TM HET mice did not develop a preference for lower doses of cocaine (e.g. 5–10 mg/kg cocaine) which was evident in WT mice. However, at the highest dose (20 mg/kg), Nrg1 TM HET mice showed such a preference, which was absent in WT mice. These findings suggest a Nrg1-mediated shift in the dose-response curve.

Conclusion: The data presented suggest the Nrg1 TM mutation produces an addiction-relevant phenotype for cocaine. These findings provide the first evidence for a potential genetic link between schizophrenia and cocaine abuse and may help explain elevated susceptibility to cocaine abuse in patients.