

Spontaneously Hypertensive Rat substrains show differences in premorbid addiction vulnerability traits and cocaine self-administration: Implications for a novel rat reduced complexity cross

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Manuscript Source: <https://www.biorxiv.org/content/10.1101/2021.03.06.434216v1>

Manuscript Authors: Kathleen M. Kantak, Carissa Stots, Elon Mathieson & Camron D. Bryant

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- Depending on the source of the input text, the Sentence Audit may contain occasional html artefacts that are parsed as sentences (E.g. "Download figure. Open in new tab").
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All queries, feedback or suggestions are also very welcome.

Research Paper Sections:

The sections of the research paper input text parsed in this audit.

[illegible]

Title

Spontaneously Hypertensive Rat substrains show differences in premorbid addiction vulnerability traits and cocaine self-administration: Implications for a novel rat reduced complexity cross

S1 [001] ABSTRACT

S1 [002] Forward genetic mapping of F2 crosses between closely related substrains of inbred rodents - referred to as a reduced complexity cross (RCC) - is a relatively new strategy for accelerating the pace of gene discovery for complex traits, such as drug addiction.

Forward genetic mapping ...
... of F2 crosses ...
... between closely related substrains ...
... of inbred rodents - referred ...
... to as a reduced complexity cross ...
... (RCC) ...
... - is a relatively new strategy ...
... for accelerating the pace ...
... of gene discovery ...
... for complex traits, ...
... such as drug addiction.

S1 [003] RCCs to date were generated in mice, but rats are thought to be optimal for addiction genetic studies.

RCCs ...
... to date were generated ...
... in mice, ...
... but rats are thought ...
... to be optimal ...
... for addiction genetic studies.

S1 [004] Based on past literature, one inbred Spontaneously Hypertensive Rat substrain, SHR/NCrl, is predicted to exhibit a distinct behavioral profile as it relates to cocaine vulnerability traits relative to another substrain, SHR/NHsd.

Based ...
... on past literature, ...
... one inbred Spontaneously Hypertensive Rat substrain, ...
... SHR/NCrl, ...
... is predicted ...
... to exhibit a distinct behavioral profile ...
... as it relates ...
... to cocaine vulnerability traits relative ...
... to another substrain, ...
... SHR/NHsd.

- S1 [005]** Direct substrain comparisons are a necessary first step before implementing an RCC.
- Direct substrain comparisons are a necessary first step ...
... before implementing an RCC.
- S1 [006]** We evaluated a number of premorbid addiction vulnerability traits and cocaine self-administration behaviors using a longitudinal within-subjects design.
- We evaluated a number ...
... of premorbid addiction vulnerability traits ...
... and cocaine self-administration behaviors ...
... using a longitudinal within-subjects design.
- S1 [007]** Trait impulsivity and compulsivity were greater in SHR/NCrl than SHR/NHsd, as were reactivity to sucrose reward, sensitivity to acute psychostimulant effects of cocaine, and cocaine abuse liability studied under fixed-ratio and chained schedules of cocaine self-administration.
- Trait impulsivity ...
... and compulsivity were greater ...
... in SHR/NCrl ...
... than SHR/NHsd, ...
... as were reactivity ...
... to sucrose reward, ...
... sensitivity ...
... to acute psychostimulant effects ...
... of cocaine, ...
... and cocaine abuse liability studied ...
... under fixed-ratio ...
... and chained schedules ...
... of cocaine self-administration.
- S1 [008]** Trait compulsivity correlated with the acute psychostimulant effects of cocaine, which in turn correlated with cocaine taking under the chained schedule.
- Trait compulsivity correlated ...
... with the acute psychostimulant effects ...
... of cocaine, ...
... which in turn correlated ...
... with cocaine taking ...
... under the chained schedule.
- S1 [009]** Trait compulsivity also was the best predictor of cocaine seeking responses.
- Trait compulsivity also was the best predictor ...
... of cocaine seeking responses.
- S1 [010]** Heritability estimates indicated that 22%-40% of the variances for the above phenotypes can be explained by additive genetic factors, providing sufficient genetic variance to conduct genetic mapping in F2 crosses of SHR/NCrl and SHR/NHsd.
- Heritability estimates indicated ...
... that 22%-40% ...
... of the variances ...

... for the above phenotypes can be explained ...
... by additive genetic factors, ...
... providing sufficient genetic variance ...
... to conduct genetic mapping ...
... in F2 crosses ...
... of SHR/NCrl ...
... and SHR/NHsd.

S1 [011] These results provide compelling support for using an RCC approach in SHR substrains to uncover candidate genes and variants that are of relevance to cocaine use disorders.

These results provide compelling support ...
... for ...
... using an RCC approach ...
... in SHR substrains ...
... to uncover candidate genes ...
... and variants ...
... that are ...
... of relevance ...
... to cocaine use disorders.

S1 [012] Highlights

Highlights

S1 [013] Closely related SHR substrains have distinct cocaine vulnerability traits

Closely related SHR substrains have distinct cocaine vulnerability traits

S1 [014] Inhibitory control was poorer in SHR/NCrl than SHR/NHsd

Inhibitory control was poorer ...
... in SHR/NCrl ...
... than SHR/NHsd

S1 [015] SHR/NCrl were more sucrose reactive and sensitive to acute cocaine than SHR/NHsd

SHR/NCrl were more sucrose reactive ...
... and sensitive ...
... to acute cocaine ...
... than SHR/NHsd

S1 [016] Cocaine abuse liability was greater in SHR/NCrl than SHR/NHsd

Cocaine abuse liability was greater ...
... in SHR/NCrl ...
... than SHR/NHsd

S1 [017] SHR substrains can be used in an RCC to uncover cocaine vulnerability genes & variants

SHR substrains can be used ...
... in an RCC ...
... to uncover cocaine vulnerability genes & variants

S2 [018] 1. Introduction

S2 [019] The addictions, in particular cocaine addiction, are highly heritable neuropsychiatric diseases [1, 2].

The addictions, ...
... in particular cocaine addiction, ...
... are highly heritable neuropsychiatric diseases ...
... [1, 2]...
... .

S2 [020] Given the nearly 2 million past-month cocaine users in the US, with ~1 million meeting diagnostic criteria for cocaine dependence [3], new research directed at identifying genetic variants that influence cocaine addiction vulnerability will improve diagnosis, prevention, and treatment.

Given the nearly 2 million past-month cocaine users ...
... in the US, ...
... with ~1 million meeting diagnostic criteria ...
... for cocaine dependence ...
... [3], ...
... new research directed ...
... at identifying genetic variants ...
... that influence cocaine addiction vulnerability will improve diagnosis, ...
... prevention, ...
... and treatment.

S2 [021] One of the only known genome-wide association study (GWAS) hits to date in cocaine dependence was a variant near FAM53B [4] that was functionally supported by covariance between Fam53b expression and cocaine self-administration in recombinant inbred mice [5].

One ...
... of the only known genome-wide association study ...
... (GWAS) ...
... hits ...
... to date ...
... in cocaine dependence was a variant near FAM53B ...
... [4] ...
... that was functionally supported ...
... by covariance ...
... between Fam53b expression ...
... and cocaine self-administration ...
... in recombinant inbred mice ...
... [5].

End of Sample Audit

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