

Accepted Manuscript

Title: Effects of genetic and environmental risk for schizophrenia on hippocampal activity and psychosis-like behavior in mice

Authors: Daniel Scott, Carol A. Tamminga

PII: S0166-4328(17)31276-7
DOI: <https://doi.org/10.1016/j.bbr.2017.10.039>
Reference: BBR 11159

To appear in: *Behavioural Brain Research*

Received date: 2-8-2017
Revised date: 27-10-2017
Accepted date: 31-10-2017

Please cite this article as: Scott Daniel, Tamminga Carol A. Effects of genetic and environmental risk for schizophrenia on hippocampal activity and psychosis-like behavior in mice. *Behavioural Brain Research* <https://doi.org/10.1016/j.bbr.2017.10.039>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Effects of Genetic and Environmental Risk for Schizophrenia on Hippocampal Activity and Psychosis-like Behavior in Mice

Daniel Scott, PhD* and Carol A. Tamminga, MD

Department of Psychiatry, University of Texas Southwestern Medical Center

5323 Harry Hines Blvd, Dallas TX, 75390-9127

Telephone: (214) 645-2791

Fax: (214) 645-2786

* Corresponding author: Daniel.scott2@utsouthwestern.edu

Highlights

- Maternal deprivation alters the basal levels of activity with the hippocampal subfields in mice.
- Maternal deprivation induces a state of spontaneous hyperactivity and impairs prepulse inhibition.
- Expression of a dominant negative form of Disc1 impairs cued and contextual fear conditioning.
- Disc1 deficiency does not augment the effects of maternal deprivation or vice versa.
- Maternal deprivation and Disc1 deficiency have distinct, non-overlapping effects on behavior and hippocampal activity in adult mice.

Schizophrenia is a serious mental illness most notably characterized by psychotic symptoms. In humans, psychotic disorders are associated with specific hippocampal pathology. However, animal model systems for psychosis often lack this pathology, and have been weak in providing a representation of psychosis. We utilized a double-risk model system combining genetic risk with environmental stress. We hypothesized these factors will induce hippocampal subfield pathology consistent with human findings, as well as behavioral phenotypes relevant to psychosis. To address this, we exposed wild-type and transgenic Disc1 dominant negative (Disc1-deficient) mice to maternal deprivation. In adulthood, hippocampal subfields were examined for signs of cellular and behavioral pathology associated with psychosis. Mice exposed to maternal deprivation showed a decrease in dentate gyrus activity, and an increase in CA3/CA1 activity. Furthermore, results demonstrated a differential behavioral effect between maternal deprivation and Disc1 deficiency, with maternal deprivation associated with a hyperactive phenotype and impaired prepulse inhibition, and Disc1 deficiency causing an impairment in fear conditioning. These results suggest distinct consequences of environmental and genetic risk factors contributing to psychosis, with maternal deprivation inducing a state more wholly consistent with schizophrenia psychosis. Further research is needed to determine if this pathology is causally related to a specific behavioral phenotype. The development of a strong inference animal model system for psychosis would satisfy a high medical need in schizophrenia research.

متن کامل مقاله

دریافت فوری ←

ISIArticles

مرجع مقالات تخصصی ایران

- ✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
- ✓ امکان دانلود نسخه ترجمه شده مقالات
- ✓ پذیرش سفارش ترجمه تخصصی
- ✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
- ✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
- ✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
- ✓ دانلود فوری مقاله پس از پرداخت آنلاین
- ✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات