

Plan Overview

A Data Management Plan created using DMPTool

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Title: Neurodevelopmental effects of embryonic exposure to psychotropic medications in real-world mixtures

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Template: NIH-Default DMSP

Project abstract:

Wide ranges of drugs with overlapping targets in the nervous system contaminate drinking water sources. Psychotropic medications are among the most commonly prescribed drugs in the U.S., and a significant portion of these drug residues are discharged into the receiving water bodies. These drug residues eventually reach the drinking water, cross maternal biological barriers, and can alter the embryonic nervous system. Exposure of zebrafish embryos to specific combinations of drugs has resulted in nervous system abnormalities and misexpression of genes implicated in autism, Alzheimer's, and schizophrenia. Thus, chronic exposure to sub-therapeutic doses of these drugs represents a viable risk to human mental health. With the prevalence of such disorders ever-increasing, so does the urgency of understanding how environmental exposure increases risk. This proposal addresses the long-term research goals of elucidating the molecular mechanisms underlying the environmental risks for neuropsychiatric disorders while identifying genes that contribute to normal nervous system development. The hypothesis being tested is that developmental exposure to low levels of psychoactive drugs in environmentally-relevant mixtures drives abnormal gene expression and ultimately affects nervous system function. This proposed research will use bioinformatics and predictive analytics to identify candidate genes from RNA-Seq data generated following exposure of larval zebrafish to environmentally relevant levels of psychoactive drugs found in drinking water source bodies. As a measure the functional consequences of this type of exposure, on a battery of larval behaviors that are disrupted in neurodevelopmental disorder models will be tested following drug exposure. The next phase of the current proposal will use quantitative RT-PCR and in situ hybridization to quantify and explore nervous system-specific changes in gene expression following drug exposure. By raising zebrafish in dosed water as a proxy for prenatal human exposure through contaminated

drinking water, these experiments will identify sensitive behaviors and genes that are expressed in developing neural tissues. The differential expression of each of these genes individually may have minor effects on the organism, and that the summative changes in gene expression are likely complex and varied. The final phase of this proposed research will develop a genetic loss-of-function model for one of the genes that was downregulated following exposure and evaluate the effect of this loss on behavior.

Start date: 09-01-2023

End date: 08-31-2026

Last modified: 01-18-2024

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Neurodevelopmental effects of embryonic exposure to psychotropic medications in real-world mixtures

This project will produce experimental data from the following methods: video tracking behavior, real-time quantitative polymerase chain reaction, and light microscopy. Data will be collected from a minimum of three independent experiments, with each experiment consisting of multiple groups: exposed vs. control or wild-type (retreg1+/+), heterozygous (retreg1+/-), and knockout (retreg1-/-), from these developmental stages: 2-3 days old, 5-6 days old, 17, and 30 days old. The total size of the data collected in this project is projected to be 100 GB.

We expect to generate the following data file types during this project: images (.TIFF), tabular (.CSV and .XLS), and video (.MP4 and H.264 AVC).

Raw data files will be analyzed to generate CSV files containing quantifications of behaviors and gene expression counts, and to enable statistical analysis.

In this proposed project, the cleaned, item-level spreadsheet data for all variables will be shared openly, along with example quantifications and transformations from initial raw data. Final files used to generate specific analyses to answer the Specific Aims and related results will also be shared. The rationale for sharing only cleaned data is to foster ease of data reuse.

To facilitate interpretation of the data, protocols DOIs will be created and shared from protocols.io.

Imaging data will be made available in tif format, and video data will be made available in mp4 format and will not require the use of specialized tools to be accessed or manipulated.

Data will be stored in common and open formats, such as csv for our behavioral data. Information needed to make use of this data along with references to the sources of those standardized names and metadata items will be included wherever applicable.

Data described above in the "data to be shared" section will be deposited into Murray State University's Digital Commons.

Murray State University's Digital Commons provides searchable study-level metadata for dataset discovery. [Repository] assigns DOIs as persistent identifiers and has a robust preservation plan to ensure long-term access. Data will be discoverable online through standard web search of the study-level metadata as well as the persistent pointer from the DOI to the dataset. We will include ORCID iDs for people, DOIs for outputs (e.g., datasets, protocols), and Research Resource Identifiers (RRIDs) for resources as much as possible to make data identifiable and findable.

All scientific data generated from this project will be made available as soon as possible, and no later than the time of publication or the end of the funding period, whichever comes first. The duration of preservation and sharing of the data will be a minimum of 10 years after the funding period.

There are no anticipated factors or limitations that will affect the access, distribution or reuse of the scientific data generated by the proposal.

Controlled access will not be used. The data that is shared will be shared by unrestricted download.

These experiments do not use human data.

Lead PI D.R. Weinberger, ORCID: 0000000299735685, will be responsible for the day-to-day oversight of lab/team data management activities and data sharing.

Planned Research Outputs

Data paper - "Neurodevelopmental effects of embryonic exposure to psychotropic medications in real-world mixtures"

Behavior data

Data paper - "Regulator of autophagy 1 loss-of-function affects larval behavior"

Data paper - "Developmental exposure to psychotropic drugs in mixture alters gene expression patterns in the brain"

Planned research output details

Title	Type	Anticipated release date	Initial access level	Intended repository(ies)	Anticipated file size	License	Metadata standard(s)	May contain sensitive data?	May contain PII?
Neurodevelopmental effects of embryonic exposure t ...	Data paper	Unspecified	Open	None specified		None specified	None specified	No	No
Regulator of autophagy 1 loss-of-function affects ...	Data paper	Unspecified	Open	None specified		None specified	None specified	No	No
Developmental exposure to psychotropic drugs in mi ...	Data paper	Unspecified	Open	None specified		None specified	None specified	No	No