Plan Overview

A Data Management Plan created using DeiC DMP

Title: Clinical and functional characterization of GABAAR-receptor related disorders: translating genetic diagnostics into personalized treatment

Creator:nazanin Azarinejad Mohammadi

Principal Investigator: nazanin Azarinejad Mohammadi

Data Manager: nazanin Azarinejad Mohammadi

Affiliation: Syddansk Universitet / University of Southern Denmark

Template: DCC Template

Project abstract:

Developmental and Epileptic Encephalopathies (DEEs) are rare and severe neurological conditions often associated with intellectual disability, developmental delay, autism spectrum disorders and movement disorders. Seizures often begin in early infancy, and patients are often resistant to antiepileptic treatment. Genetic factors play a major role in the underlying cause of many DEEs, and the identification of the causative genes have disclosed unique information on the different pathomechanisms and opened novel therapeutic perspectives. Recently there has been a plethora of pathogenic variants identified in the γ-aminobutyric acid type A receptor (GABAAR) that causes DEE. This receptor is important as it helps to maintain normal brain activity and variants in GABAAR genes will cause changes to normal brain function. The overall aim of this proposal is to establish specific correlations between phenotype, genotype, functional effects and therapeutic response to translate genetic diagnostics into therapy. Knowing the functional effect of a genetic variant can assist clinicians to avoid ineffective or even disease-aggravating treatments. Our findings will help change the current paradigm of treating patients with DEE currently uses a trial-and-error approach to one that utilizes precision medicine based on a patient's genetic, functional and clinical diagnoses.

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Data Collection

What data will you collect or create?

Sub-project 1: Gathering phenotype information from a larger group of patients with GABAAR variants in a database, we will determine any correlations between the pharmacophenomic data, the genotypes, the cluster of mutations in the protein domains, and the paralog preservation score.

Sub-poject 2: Determine the function of 25 unique *GABRB2* variants. These represent variants in the different functional parts of a GABAAR subunit as well as different subunit types. Variants in α- and β- subunits will be evaluated as single- and double-subunit mutant receptors, while variants in the γ2-subunits will be evaluated as single-subunit mutated receptors only. Each mutant receptor will be expressed in Xenopus oocytes, the gold standard expression system for this type of study and two-electrode voltage clamp methods will be used to assess function.

Sub-project 3: Explore the rational use of selected FDA/EMA approved drugs, and for testing, we have chosen both marketed and experimental drugs.

How will the data be collected or created?

Data for sub-project 1, will be collected by sending question formular to the researchers/doctors who are responsible for each patient carrying the target mutation. And anonymous data about each variants phenotype will be plottet in a safe database in redcap.

Data for sub-projects 2 and 3 will be created in labratory and the results will be saved in Filadelfia hospitals safe serves.

Documentation and Metadata

What documentation and metadata will accompany the data?

The created database in redcap or artikels published based on laboratory data will be published in nonpublic journals to provide information about the effect of the varaints in ooccyttes.

Ethics and Legal Compliance

How will you manage any ethical issues?

All procedures performed in studies involving human participants were in accordance with the ethical standards of the National Committee on Health Research Ethics (file no. H-2-2010-122) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was reported to the data-protection agency.

How will you manage copyright and Intellectual Property Rights (IPR) issues?

Storage and Backup

How will the data be stored and backed up during the research?

The data for laboratory experiments will be be saved in Filadelfia hospitals server, so that they will have a backed up data for me during my research. And the data collected for the sub-project 1 will be stored also in hospitalt server.

How will you manage access and security?

Our data does not contain any personal information at all, that would need protected platforms for sharing between collaborators. Therefore usual dropbox can be a way to share data only with collaborators.

Selection and Preservation

Which data are of long-term value and should be retained, shared, and/or preserved?

All the data collected and obtained are going to be published and also saved in the safe database platform RedCap, which is fully secure. Evendough there is no personal information about patientsa or their families.

What is the long-term preservation plan for the dataset?

For the sub-project 2, every reseracher has already got ligal promission from the patients and their family to be able to use their disease related information for research based on listed lows for each country.

Data Sharing

How will you share the data?

By publishing the data in specific journals, which are avalible for researchers.

Are any restrictions on data sharing required?

Question not answered.

Responsibilities and Resources

Who will be responsible for data management?

Mostly the Phd student (which is me), but my supervisors will also be responsible for provide me platforms and relevant help and guidlines to how to manage my obtained data.

What resources will you require to deliver your plan?

I need resourses such as a safe server to save and storage my data, which our hospital provide. And some softwares and data-analysis programes as well which all are provided from my superviseors.