ME-CFS26-002 - MEndelian Randomisation for Evaluating Medicines and Approved Pharmacotherapies in ME/CFS

Zusammenfassung

ME/CFS presents two major challenges for patients and clinicians: the absence of established biomarkers and the lack of disease-modifying treatments. This lab-rotation project focuses on the latter by applying Mendelian randomisation (MR) to evaluate opportunities for drug repurposing in ME/CFS.

Recent genome-wide association studies have generated robust summary statistics for ME/CFS, enabling the application of modern genetic epidemiology methods. Building on observed genetic correlations between ME/CFS, migraine, and irritable bowel syndrome (IBS), we will apply a drug-target MR framework to assess whether genetically proxied perturbation of selected drug targets influences ME/CFS risk.

We will focus on a predefined set of drugs approved for migraine or IBS, including agents targeting CGRP signalling, the renin–angiotensin system, and gastrointestinal epithelial and neuronal pathways. Mendelian randomisation analyses will use ME/CFS genome-wide association summary statistics as the primary outcome, including analyses stratified by sex, infection history, as well as long COVID GWAS data. For each drug target, we will construct genetic instruments using cis-eQTLs, cis-pQTLs where available, functional coding variants, and selected downstream proxy traits that reflect target modulation. Causal inference will start with colocalisation analyses to assess shared genetic signals, followed by cis-MR. Sensitivity analyses will address directionality, pleiotropy, and potential confounding.

The primary outcome of this work will be a genetically informed evaluation of whether modulation of specific drug targets is likely to increase or decrease ME/CFS risk, thereby providing evidence to support or deprioritise selected drug repurposing hypotheses. More broadly, this project aims to establish a rigorous and reusable analytical pipeline for drug-target MR in ME/CFS, laying the groundwork for future causal investigations and informed translational research in this field.

Wissenschaftliche Disziplinen:
Genetics (50%) | Bioinformatics (30%) | Bioinformatics (20%)

Keywords:
Genetic epidemiologyMendelian randomisationDrug repurposingCausal inferenceTranslational genetics

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Weiterführende Links zu den beteiligten Personen und zum Projekt finden Sie unter
https://www.wwtf.at/funding/programmes/ei/ME-CFS26-002/