ME-CFS24-002 - Genetic architecture of chronic fatigue syndrome

Zusammenfassung

Currently, there is no consensus on the genetic foundations of ME/CFS, although its heritability estimated at up to 50%. While a large-scale GWAS is ongoing in a dedicated ME/CFS cohort (DECODE-ME), our project will complement this by focusing on rare genetic variants. Thus, the aim of this research project is to provide a list of causal genes for ME/CFS to facilitate further testing and characterization in collaboration with clinical researchers and wet lab biologists.

This opportunity arises from the recent availability of whole genome sequencing data from large-scale biobanks such as UK Biobank and All of Us. We can now categorize all protein-altering variants within a gene or other genomic structures like transcription factor binding sites and evaluate their collective impact on ME/CFS. We will utilize the International Consensus Criteria to define cases, however we will also conduct sensitivity analyses around the phenotype definition, and extend our analyses to include long COVID phenotypes within the cohorts mentioned above.

Our primary analysis will be a meta-analysis of data from the UK Biobank and All of Us, which we will, depending on availability, also attempt to replicate using imputed data from the DECODE-ME cohort. This will not only provide the most extensive analysis of rare variants in ME/CFS to date enhancing our knowledge of the condition's causal genes and pathways, but it will also establish a dataspace and collaborative framework for clustering, factor analysis, and other exploratory and epidemiological studies, which we think are essential to fully understand this complex condition. These analyses could also inform subsequent rounds of genetic association tests. Ultimately, the outcomes of these tests may enable stratification of patients and facilitate the categorization of patients into specific subgroups.

Wissenschaftliche Disziplinen:
Genetics (60%) | Epidemiology (30%) | Data science (10%)

Keywords:
rare genetic variantsUKBiobankwhole genome sequencinggenome-wide association study

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Weiterführende Links zu den beteiligten Personen und zum Projekt finden Sie unter
https://wwtf.at/funding/programmes/ei/ME-CFS24-002/