AMBER: Antidepressant Medications: Biology, Exposure and Response

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AMBER

Antidepressant Medications: Biology, Exposure & Response

COLLABORATE WITH US

BACKGROUND

- Depression is a highly prevalent global disorder, with both pharmacological and psychological treatments available.
- Substantial progress has been made into how genetics contribute to the risk of developing depression, but this has not translated into treatments.
- Only one-third of patients respond to the first drug prescribed, and our poor mechanistic understanding of antidepressant actions and treatment response has limited personalised treatment[1].

The AMBER project (2023-2028) will use causal inference, electronic health records, and genomic data to advance our understanding of antidepressant mechanisms and individual response variations

PROJECT APPROACH

Patient engagement on ANTIDEPRESSANT TREATMENT

- Convene a Lived Experience Advisory Panel, who will interact regularly with the other work-packages, to guide the entire programme.
- Participatory Research exploring:
  - attitudes to personalised medicine in the depression treatment pathway
  - the clinical experiences of people with 'difficult-to-treat' depression.
- Community engagement to explore the lack of diversity in mental health research participants.

Sue Fletcher-Watson, Iona Beange, Cristina Douglas & Mark Somerville

Robust and reproducible ANTIDEPRESSANT RESPONSE & EXPOSURE phenotypes

- Use real world data from electronic health care records to inform and derive novel antidepressant exposure and response phenotypes.
- Explore advantages of combining information from structured and unstructured ('free text') clinical data to refine phenotypes.
- Validate, refine and disseminate code for wider use.

Heather Whalley, Matthew Iveson, Arlene Casey & Matúš Falis

Genetic signatures of ANTIDEPRESSANT RESPONSE

- Establish collaboration and data sharing for clinical studies.
- Define and apply electronic health record algorithms for antidepressant response and resistance.
- Perform genome-wide analysis of antidepressant response to identify genetic associations, polygenic profiles and biological pathways.

Cathryn Lewis, Oliver Pain, Michelle Kamp & Chris Wai Hang Lo

Cross-projects

Naomi Wray, Clara Albiñana & Alicia Walker

Genetic signatures of ANTIDEPRESSANT EXPOSURE

- Identify genomic datasets with antidepressant exposure.
- Conduct genome-wide association studies of antidepressant exposure.
- Conduct DNA methylation, proteomic and metabolomic association studies of antidepressant exposure.
- Apply causal inference methods to identify causal effects of antidepressants on molecular phenotypes.

Andrew McIntosh, Mark Adams, Amelia Edmondson-Stait & Megan Calnan

CELLULAR GENOMIC STUDIES on ANTIDEPRESSANT TREATMENT

- Generate gene expression signatures for antidepressants in human cell lines.
- Use comparative and network-based analyses to understand biological pathways affected by SSRIs
- Analyse SSRI gene signatures in responder and non-responder patient cell lines to assess feasibility of using patient cell line gene expression assays to predict treatment response.

Sonia Shah, Quan Nguyen, Anjali Henders & David Brici

COLLABORATIVE

Conducted in partnership with individuals with lived experience, we aim to foster trust, enhance patient relevance and impactful dissemination of findings.

OPEN & TRANSPARENT

A core component will be sharing of code, methods for best practice, and guidance for phenotype ascertainment from linked clinical data.

SUMMARY

- The AMBER project will integrate clinical, genomic, and patient-participatory research to provide insights into antidepressant action and response, enhance understanding of drug mechanisms and biological pathways, and develop predictive models for personalised prescribing to improve patient outcomes.

References:

1. Trivedi MH et al. 2006. Evaluation of Outcomes With Citalopram for Depression Using Measurement-Based Care in STAR*D: Implications for Clinical Practice. Am J Psychiatry;163(1):28–40.

CONTACT DETAILS

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