based planning, had signal for treatment response (β=2.29, SE=1.17, p=.05).
Conclusions: Self-report measures were the most predictive of treatment response, over and beyond task-based cognitive measures. The next step is for machine learning models (i.e., elastic net regression, random forest) to test the predictive power of an algorithm based on these features.
Funding Source: MQ: transforming mental health (MQ16IP13)
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Keywords: Treatment Prediction, Depression, Internet-Based Methodology, Internet-Based Cognitive Behavioural Therapy

A Reinforcement Learning Framework to Illuminate Change Mechanisms Underlying Specific Psychotherapy Interventions

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Background: Advances in reinforcement learning and Bayesian inference could help illuminate the change processes underlying specific psychotherapy interventions.
Methods: We built a reinforcement learning agent who could learn from the environment using both model-based and model-free algorithms. It made inferences about the value of the current state with an arbitration function integrating model-based and model-free values in a time- and uncertainty-dependent manner. Similar to situations of patients with negative experiences, the agent first learned in an environment with positive and negative outcomes in different states. Subsequently, the environment changed such that all states led to positive outcomes. To assess how interventions helped the agent to adapt best, we operationalized behavioral therapies as exposures to the states previously leading to negative outcomes to experience their current positive nature, cognitive restructuring as an instructed change in the reward matrix of the model-based part of the agent, and the "being mode" in mindfulness with its focus on the current experience as an increase of the relative impact of the current reward in the state value inference process.
Results: In line with core findings by Furukawa et al. (2021), the largest individual patient meta-analysis to date, simulations showed that our agent qualitive and quantitative benefited most from behavioral therapies, fared well after mindfulness and cognitive restructuring, but was also prone to relapse after cognitive restructuring when faced with stress for a wide range of parameter settings.
Conclusions: The proposed framework might help to develop new theory-driven behavioral tasks to predict treatment response to the specific interventions.
Funding Source: NIH: R01 (Mood) - 10012117
Keywords: Mathematical Modeling, Reinforcement Learning Framework, Psychotherapy, Exposure Therapy, Cognitive Restructuring

SYMPOSIUM
Uncovering Novel Drug Targets for Psychiatric Illnesses by Harnessing Large-Scale Genomic and Brain Omics Data

Co-Chairs: Aliza Wingo, Panos Roussos

Multi-Ancestry eQTL Analysis of Human Brain Identifies Candidate Causal Variants for Psychiatric Disorders

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Background: Large-scale, genome-wide association studies (GWAS) have identified hundreds of loci associated with psychiatric traits. Yet identification of the variants, genes and molecular mechanisms underlying these traits remains challenging. Integration of GWAS with expression quantitative trait loci (eQTLs) and identification of shared genetic architecture have been widely adopted to nominate genes and candidate causal variants.
Methods: We developed the multivariate multiple QTL approach and performed a large-scale, multi-ancestry eQTL meta-analysis to increase power and fine-mapping resolution. Analysis of 3,983 RNA-seq data from post mortem brain samples of from 2,119 donors of diverse ancestry gave an effective sample size of 3,154.
Results: Joint statistical fine-mapping of eQTL and GWAS identified 329 variant-trait pairs for 24 brain-related traits driven by 204 unique candidate causal variants for 189 unique genes.
Conclusions: This integrative analysis identifies candidate causal variants and elucidates potential regulatory mechanisms for genes underlying schizophrenia and bipolar disorder.
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Keywords: Expression Quantitative Trait Loci (eQTL), Gene Expression, Mixed-Effect Model, Brain Tissue

Integrating Human Brain Proteomes With GWAS Results to Identify Causal Brain Proteins for the Major Psychiatric Disorders

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Background: Major psychiatric disorders such as major depressive disorder (MDD), bipolar disorder, schizophrenia, anxiety disorders, PTSD, and alcohol use disorder affect approximately 25% of the population annually; however, their treatments are effective in only a subset of the patients, highlighting a pressing need for more effective treatments.