Shared Genetic Architecture between Substance-Use Disorders and Psychiatric Disorders

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Motivation

• Many individuals with psychiatric disorders also exhibit substance abuse disorders

• More than 80% of individuals with schizophrenia are nicotine dependent (de Leon et al., Schizophrenia Research (2005))

• 25% of patients with major depressive disorder also exhibit alcohol use disorder (Melartin et al., J Clin Psychiatry (2002))

• Better understanding of common neurological mechanisms can lead to better targeted treatment
Hi-C coupled MAGMA (aka H-MAGMA)

Problem: The Majority of these variants are not in genes (Edwards et al., Cell (2013))
Hi-C coupled MAGMA (aka H-MAGMA)

Pleiotropic Gene - A single gene that can affect more than one trait
Number Of Pleiotropic Genes For Different Neuronal Subtypes

DA - Dopaminergic Neurons
neun - Cortical Neurons
ADHD - Attention Deficit Hyperactivity Disorder
MDD - Major Depressive Disorder
SCZ - Schizophrenia
CPD - Cigarettes Per Day
PAU - Problematic Alcohol Use
Central Nervous System Cell Types
Radial Glia-Like
Neuroblast
Neuronal Progenitor
Oligodendrocyte Precursor Cells
Dopaminergic Neurons
Endothelial
GABAergic Neurons
Microglia
Oculomotor and Trochlear Nucleus
Pericytes
Red Nucleus
Serotonergic Neurons

ADHD_VS_CPD
ADHD_VS_PAU
MDD_VS_CPD
MDD_VS_PAU
SCZ_VS_CPD
SCZ_VS_PAU

Normalized Expression by Midbrain Cell Type
Conclusion

• More pleiotropic genes found using Cortical Neuron-specific H-MAGMA for Alcohol Use Disorder and Major Depressive Disorder

• More pleiotropic genes found using Dopaminergic Neuron-specific H-MAGMA for Nicotine Addiction and Schizophrenia

• Cellular expression profiles highlight excitatory neurons as the primary cell type for pleiotropy between substance use and psychiatric disorders in the cortex, and Dopaminergic, GABAergic, and Serotonergic neurons in the midbrain.
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