Precision Psychiatry Through Intermediate Phenotypes

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Precision psychiatry seeks to redefine mental disorders through mechanistic, biologically grounded constructs rather than descriptive categories. Guided by the Research Domain Criteria (RDoC) framework, my research behavioral genetics, neuroimaging, and causal inference to uncover pathways linking genomic variation to brain and behavior.

A central focus is on delay discounting (DD), a quantitative measure of intertemporal choice rooted in behavioural economics. Genome-wide and multivariate analyses show that DD has a polygenic architecture with estimated chip-based heritability between 10–20%, and shared genetic influences across executive function, reward sensitivity, and externalizing traits. Polygenic scores for DD predict both substance use and behavioral addiction phenotypes, supporting its role as a transdiagnostic intermediate phenotype that captures shared vulnerability to diverse forms of dysregulated reward behavior. Building on this foundation, we mapped the comorbidity structure of substance use disorders (SUDs) and other psychiatric conditions to the polygenic profiles of intermediate phenotypes such as DD. These analyses reveal that co-occurrence across psychiatric domains reflects overlapping polygenic liabilities for core regulatory processes rather than disorder-specific mechanisms. Complementary efforts extend toward identifying neural correlates of addiction liability using integrative genetic–neuroimaging approaches, including reverse Mendelian randomization to explore potential causal pathways from genetic risk to brain structure and function.

These efforts collectively demonstrate the potential of intermediate phenotypes as a scaffold for linking genomic architecture, neural circuitry, and behavioral regulation. This research program operationalizes the RDoC vision, translating biologically grounded constructs into empirically testable models that trace how genetic variation shapes neural systems and behavior.