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Executive Function and Impulsivity Predict Distinct Genetic Variance in Internalizing Problems, Externalizing Problems, Thought Disorders, and Compulsive Disorders: A Genomic Structural Equation Modeling Study

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Abstract

Individual differences in self-control predict many health and life outcomes. Building on twin literature, we used genomic structural equation modeling to test the hypothesis that genetic influences on executive function and impulsivity predict independent variance in mental health and other outcomes. The impulsivity factor (comprising urgency, lack of premeditation, and other facets) was only modestly genetically correlated with low executive function (r_g=.13). Controlling for impulsivity, low executive function was genetically associated with increased internalizing (β_g=.15), externalizing (β_g=.13), thought disorders (β_g=.38), compulsive disorders (β_g=.22), and chronotype (β_g=.11). Controlling for executive function, impulsivity was positively genetically associated with internalizing (β_g=.36), externalizing (β_g=.55), body mass index (β_g=.26), and insomnia (β_g=.35), and negatively genetically associated with compulsive disorders (β_g= −.17). Executive function and impulsivity were both genetically correlated with general cognitive ability and educational attainment. This work suggests that executive function and impulsivity are genetically separable and show independent associations with mental health.

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Conflict of Interest

P.F and S.L.E. are employed by and hold stock or stock options in 23andMe, Inc. The other authors report no conflict of interest.

Keywords

executive control; genomic SEM; UPPS-P Impulsive Behavior Scale; Barratt Impulsiveness Scale

Introduction

The ability to exert control over one's own thoughts, attention, and actions is integral to daily life. Measurement of "self-control" is varied, but typically includes either computerized or behavioral tasks that assess executive function or attentional control abilities (Miyake & Friedman, 2012; Miyake et al., 2000), or questionnaires that assess the ability to exert attentional or cognitive control in everyday situations, such as measures of impulsivity (Lynam et al., 2006; Whiteside & Lynam, 2001). In both cases, measures of self-control are associated with a range of health and life outcomes (Diamond, 2013; Sharma et al., 2014), including mental health traits such as internalizing (e.g., anxiety, depression) or externalizing (e.g., substance use, ADHD) problems (Eisenberg et al., 2019; Friedman et al., 2020). Different measures of self-control are often only modestly phenotypically and genetically correlated with one another (Cyders & Coskunpinar, 2011; Freis et al., 2022; Friedman et al., 2020; Sharma et al., 2014), and predict distinct genetic variance in mental health outcomes (Freis et al., 2022; Friedman et al., 2020; Shields et al., 2022).

We sought to further evaluate the differential relevance of various measures of self-control to mental health using results from large-scale genome-wide association studies (**GWASs**). Using genomic structural equation modeling (**SEM**), which applies SEM methods to GWAS results, we examined the genetic overlap among measures of executive function and impulsivity and tested whether each construct predicts unique genetic variance in latent variables capturing four broad domains of psychopathology and related traits (internalizing problems, externalizing problems, thought disorders, and compulsive disorders). We also examined how genetic influences on executive function and impulsivity relate to other relevant cognitive, social, and neurological traits, including general cognitive ability, educational attainment, body mass index (**BMI**), chronotype, and insomnia.

Self-Control: Importance and Measurement Challenges

Individuals exert self-control in many ways. From a cognitive perspective, individual differences in self-control are frequently described with the construct of executive function, which captures a broad set of abilities including the ability to stop a dominant or prepotent response (inhibition; e.g., the antisaccade task), the ability to flexibly switch between tasks or mental representation (shifting; e.g., task switching paradigms), and the ability to monitor and manipulate information in working memory (working memory updating; e.g., the *n*-back task) (Friedman & Miyake, 2017; Miyake & Friedman, 2012; Miyake et al., 2000). Although individual executive function measures are not highly correlated with one another (Miyake et al., 2000), latent variables capturing inhibition, shifting, and working memory updating processes are strongly correlated with one another (Friedman & Miyake, 2017; Karr et al., 2018), reflecting the fact that they share considerable common variance. This common variance (referred to here as "common executive function") correlates with mental health outcomes such as anxiety, depression, substance use, and psychopathology (Friedman

et al., 2020; Gustavson, Franz, Panizzon, et al., 2019; Gustavson et al., 2017; Snyder et al., 2015). Common executive function is also highly heritable, and demonstrates strong longitudinal stability across adolescence, early adulthood, and middle age (Friedman et al., 2016; Gustavson et al., 2018).

From a social and personality psychology perspective, self-control is needed in everyday life to successfully plan (i.e., premeditation), resist temptations or strong emotions (impulsive urgency), ignore distractions, make progress on difficult or frustrating tasks (e.g., avoiding procrastination), and act in a general organized manner. Varying constructs are used to tap into these self-control traits, including impulsivity (Barratt, 1993; Lynam et al., 2006), conscientiousness (Costa & McCrae, 1992), grit (Duckworth & Quinn, 2009), and self-regulation (Tangney et al., 2004). These measures typically correlate highly with one another and capture a common set of genetic influences (Gustavson et al., 2014; Takahashi et al., 2021). Other related self-report and behavioral measures are available, such as delay discounting (Matta et al., 2012; Moreira & Barbosa, 2019) or delay of gratification (Mischel & Baker, 1975). However, these constructs often show small (or divergent) phenotypic and genetic associations with everyday self-control traits (Gustavson et al., 2020; Murphy & Mackillop, 2012; Reynolds et al., 2006), and current GWAS of delay discounting are based on a relatively small number of subjects (Sanchez-Roige et al., 2018). Therefore, these constructs are not considered here.

In the current investigation, we focused on comparing executive function with “impulsivity” because it is arguably the most well-studied and comprehensive example of self-control. The UPPS-P model (and corresponding scale) (Lynam et al., 2006; Whiteside & Lynam, 2001) posits that impulsivity consists of lack of premeditation (i.e., acting without thinking), impulsive urgency (i.e., control over emotions or urges), lack of perseverance (i.e., giving up easily), and sensation seeking. The Barratt Impulsiveness Scale is another well-established instrument that focuses more specifically on the tendency to act without premeditation, but includes multiple subscales: attention, motor, and non-planning (Barratt, 1993; Patton et al., 1995). Common variance across the impulsivity facets (hereafter, “common impulsivity”) is heritable, and explains a large portion of their correlations with both internalizing and externalizing problems (Gustavson, Franz, Kremen, et al., 2019).

Given that both executive function and impulsivity capture the construct of self-control and relate to similar mental health outcomes, it is natural to expect that they would correlate highly with one another. However, substantial evidence suggests these measures are only weakly correlated (Cyders & Coskunpinar, 2011; Duckworth & Kern, 2011; Sharma et al., 2014). Such low correlations may reflect reliability and/or measurement issues in one or both sets of measures (Enkavi et al., 2019; Hedge et al., 2018). However, recent phenotypic and twin investigations have observed similarly low associations even when constructs are assessed using latent variables (Freis et al., 2022; Friedman et al., 2020; Harden et al., 2017; Snyder et al., 2021). For example, Friedman et al. (2020) demonstrated that a common executive function factor (based on 9 tasks) was only modestly phenotypically ($r = -.20$ to $-.11$) and genetically correlated ($r_g = -.44$ to $-.04$) with five impulsivity dimensions (measured using the UPPS-P). Moreover, Friedman et al. (2020) showed that impulsivity and executive function predict distinct variance in traits related to mental health. Thus,

executive function and impulsivity may simply reflect separable domains of self-control (Friedman & Gustavson, 2022).

Genetic Influences Underlying Executive Function, Impulsivity and Mental Health

Two commonly studied mental health correlates of executive function and impulsivity are internalizing and externalizing problems. Internalizing problems include mood and anxiety disorders as well as post-traumatic stress disorder (PTSD), with common genetic and non-genetic influences explaining much of the overlap among these disorders (Caspi et al., 2014; Kotov et al., 2017). Externalizing problems include substance use, conduct disorder, attention-deficit hyperactivity disorder (ADHD), and antisocial personality disorder, which share genetic variance (Kotov et al., 2017; Linner et al., 2021). Importantly, failures of self-control have been linked to both internalizing and externalizing problems (Freis et al., 2022; Friedman et al., 2020; Linner et al., 2021; Nigg, 2017).

There is also substantial comorbidity among thought disorders (sometimes termed as ‘psychotic disorders’), defined here as the overlap between schizophrenia and bipolar disorder (Grotzinger et al., 2022; Kotov et al., 2017; Yalincetin et al., 2017). This common variance underlying thought disorders has been also conceptualized as “cognitive dysregulation,” suggesting a link to executive function and potentially impulsivity (Kotov et al., 2017).

Similarly, there is shared variance among obsessive compulsive disorder (**OCD**) and anorexia nervosa, as both disorders are characterized by fearful obsessive thoughts, ritualism, and meticulousness (Bastiani et al., 1996; Kotov et al., 2017). Hereafter, use the term ‘compulsive disorders’ to represent this shared variance. There is evidence that common executive function is genetically linked to both thought and compulsive disorders (Hatoum et al., 2023). However, findings for impulsivity are mixed, particularly for compulsive disorders. Namely, while some have proposed compulsive disorders may be related to *lower* levels of impulsivity (as opposed to high impulsivity like other psychiatric disorders), current evidence is inconclusive regarding whether any phenotypic or genetic association exists (for review, see Howard et al. (2020)).

Better understanding how and why executive function and impulsivity relate to one another and predict mental health will be important in constructing a comprehensive theory of self-control and will improve our understanding of psychiatric disorders. Advances in statistical genetics have enabled researchers to estimate genetic correlations between pairs of traits – even when the traits were measured in non-overlapping samples (Bulik-Sullivan et al., 2015). Moreover, many of these methods only require GWAS summary statistics, which greatly facilitates efforts to aggregate and analyze genetically informative data. With the recent availability of large-scale GWASs of executive function, impulsivity, and mental health, there is now an unprecedented opportunity to investigate how these complex traits are related to one another at the genetic level.

Genomic SEM (Grotzinger et al., 2019) provides an effective statistical framework for such a study. This method applies SEM techniques to genetic correlation matrices derived from GWAS summary statistics. It allows researchers to move beyond pairwise combinations of

traits and into the multivariate space, enabling theoretically motivated path models to be formally tested. As many GWASs are now based on hundreds of thousands of subjects, this method can reliably estimate latent factor models at the genetic level, capturing shared genetic influences on psychopathology (and related traits) and examining their relationships with other traits (e.g., Grotzinger et al., 2022; Linner et al., 2021; Mallard et al., 2022). Using large-scale (N>100,000) GWASs of impulsivity (Sanchez-Roige et al., 2019; Sanchez-Roige et al., 2023) and common executive function (Hatoum et al., 2023), here we apply genomic SEM to examine how these traits predict genetic variance in psychopathology and related traits. This approach synergizes with existing twin research while not being subject to the same assumptions (e.g., the equal-environments assumption), providing a complementary and converging method to understand genetic associations (Friedman et al., 2021).

The Current Study

The current study had 3 main goals (see Figure 1 for a summary). First, we used genomic SEM to estimate the genetic relationships between executive function and impulsivity. Common executive function was based on a GWAS of a factor score comprising 5 tasks from the UK Biobank (Hatoum et al., 2023) while common impulsivity was based on a factor comprising subscales of the UPPS-P and BIS scales (e.g., including measures of impulsive urgency, lack of premeditation/planning, attentional and motor impulsivity, and lack of perseverance), expanding on our previous model (Gustavson et al., 2020). In our current models, we allowed for unique associations between impulsive urgency and other constructs as earlier work has argued urgency may play an especially large role in internalizing problems (Berg et al., 2015; Carver & Johnson, 2018; Johnson et al., 2013). Consistent with earlier phenotypic and twin investigations, we hypothesized that executive function and impulsivity would have only modest shared genetic influences.

The second goal was to evaluate whether executive function and impulsivity predict distinct genetic variance in psychopathology and related traits, focusing on latent genetic factors for internalizing problems, externalizing problems, thought disorders, and compulsive disorders, building on prior twin studies (Freis et al., 2022; Friedman et al., 2020). We hypothesized that both sets of measures would predict variance in latent factors of psychopathology and related traits. We also hypothesized that variance unique to impulsive urgency would show a particularly strong association with internalizing, reflecting the unique emotional control abilities captured by this facet of impulsivity (Gustavson et al., 2020).

Finally, we examined whether executive function and impulsivity predict distinct genetic influences on the other relevant cognitive, educational, and health traits. We prioritized traits that have been linked to executive function and/or impulsivity and that rely on more objective experiences (rather than retrospective judgments), including general cognitive ability, educational attainment, body mass index (**BMI**), and two sleep traits (insomnia and chronotype). General cognitive ability was included because it is strongly genetically correlated with intelligence in family studies (Gustavson et al., 2022) and GWASs (Hatoum et al., 2023). Executive function and impulsivity may also be genetically linked with educational attainment and BMI given their links with cognition, income, life milestones,

and obesity (Eisenberg et al., 2019). Finally, chronotype and insomnia reflect distinct aspects of sleep health that are also differentially genetically related to mental health traits (Morrison et al., 2022) and therefore may relate to executive function and/or impulsivity (e.g., Gillett et al., 2021; Tai et al., 2022).

Transparency and Openness

Preregistration:

This study was not preregistered

Data, materials, code, and online resources:

The R data files containing the genomic SEM matrices for all analyses are displayed at the following link (https://osf.io/nfzxs/), which allows for replication and analyses of competing models without obtaining the source data.

Reporting:

This study involved analyses of existing data rather than new data collection.

Ethical approval:

Analyses were based on publicly available, de-identified GWAS summary statistics which contain no subject-level information, so no ethical approval was required.

Method

Genome-wide association studies

All GWAS summary statistics were based on individuals of European ancestry (based on genotype data). These datasets have been extensively described elsewhere and are summarized below and in supplemental Table S1. We accessed publicly available GWAS summary statistics for all traits (except impulsivity and loneliness, which were obtained in collaboration with 23andMe, Inc.). We used the largest, most-representative, public versions of the GWAS summary statistics, focusing on GWASs of N>150,000 individuals where possible (i.e., all constructs except compulsive disorders). Ns reported below reflect the data analyzed here. For internalizing and externalizing measures, this involved a combination of case-control studies (e.g., major depressive disorder; **MDD**) and related dimensional measures (e.g., loneliness, neuroticism). Thus, we refer to these factors as capturing psychopathology and related traits. Strong genetic correlations among these measures within each domain (i.e., Table S2) and earlier work using these measures (e.g., Linner et al., 2021) justify including both sets of measures for the latent factors.

Executive function.—We focused on a single GWAS of common executive function ability based on individuals from the UK Biobank (N=427,037) (Hatoum et al., 2023). This GWAS was based on a factor score created from five neuropsychological/cognitive tasks including trail-making, symbol-digit substitution, backward digit span, prospective memory, and pair matching tests. These tasks capture a range of executive function processes

including response inhibition, interference control, task-set switching, and working memory updating.

Impulsivity.—GWASs of impulsivity were initially published based on a sample of about 22,000 individuals (Sanchez-Roige et al., 2019), but the current study utilized updated summary statistics based on a sample about six times larger (Sanchez-Roige et al., 2023). These association results included measures from the UPPS-P Impulsive Behavior Scale (Cyders et al., 2014; Whiteside & Lynam, 2001) and the BIS (Patton et al., 1995). The 20-item brief version UPPS-P Impulsive Behavior Scale includes 4 items for each of the 5 subscales ("lack of premeditation", N=132,667; "lack of perseverance", N=133,517; "positive urgency", N=132,132; "negative urgency", N=132,559; "sensation seeking", N=132,395). The 30-item BIS is comprised of three subscales ("attentional", N=124,739; "motor", N=124,104; "nonplanning", N=123,509).

Internalizing.—We used summary statistics from five independent GWASs: loneliness (N=511,280) (Abdellaoui et al., 2019), MDD (N=500,199) (Howard et al., 2018), neuroticism (N=523,783) (Baselmans et al., 2019), subjective well-being (N=204,966) (Okbay et al., 2016), and post-traumatic stress disorder (**PTSD**, N=174,659) (Nievergelt et al., 2019).

Externalizing.—The model of externalizing problems was based on a recent genomic SEM investigation by the Externalizing Consortium (Linner et al., 2021). This model included GWASs of attention-deficit/hyperactivity disorder (**ADHD**; N=53,293) (Demontis et al., 2019), lifetime cannabis use (N=162,082) (Pasman et al., 2018), lifetime smoking initiation (N=632,802) (Liu et al., 2019), reverse-coded age at first sexual intercourse (N=317,694) (Linner et al., 2021), number of sexual partners (N=370,711) (Linner et al., 2021), and general risk tolerance (N=939,908) (Linnér et al., 2019). We recreated the model from Linner et al. (2021), with two exceptions. First, we used only the publicly available versions of the summary statistics files for these traits. Second, we replaced the GWAS of problematic alcohol use with an updated GWAS (N=160,824) (Mallard et al., 2022). After doing so, it was no longer necessary to include a residual correlation between problematic alcohol use and smoking initiation.

Thought disorders and compulsive disorders.—We derived the model of thought disorders and compulsive disorders based on Hatoum et al. (2022), which was similar to other recent multivariate genetic models of these traits (Grotzinger et al., 2022; Lee et al., 2019). The thought disorder factor was based on GWASs of schizophrenia (N=175,799) (Trubetskoy et al., 2022) and bipolar disorder (N=413,466) (Mullins et al., 2021) from the Psychiatric Genomics Consortium. The compulsive disorder factor was based on GWASs of OCD (N=9,725) (Arnold et al., 2018) and anorexia nervosa (N=72,517) (Watson et al., 2019).

Other cognitive, educational and health traits.—We used summary statistics from GWASs of general cognitive ability (N=300,486) (Davies et al., 2018), educational attainment (N=765,283) (Okbay et al., 2022), and health, including BMI, (N=681,275)

(Yengo et al., 2018), morningness preference (N=449,732) (Jones et al., 2019), and insomnia (N=453,379) (Lane et al., 2019).

Data Analyses

All analyses were conducted in R version 4.1.1 (R Core Team, 2022). We used the genomic SEM package version 0.0.4 (Grotzinger et al., 2019), which applies SEM methods to GWAS summary statistics. Genomic SEM leverages linkage disequilibrium score regression (Bulik-Sullivan et al., 2015) to generate a genetic correlation matrix between all traits for which summary statistics are available. Genomic SEM adjusts for sample overlap where relevant by estimating a sampling covariance matrix that indexes the extent to which sampling errors of the estimates are associated (Grotzinger et al., 2019). We reversed statistics related to executive function so that the magnitude of associations can be interpreted in the same direction as those for impulsivity (psychopathology and related traits are generally associated with lower executive function but higher levels of impulsivity).

SEMs are fit to the data using genomic SEM, which draws on functionality from the *lavaan* R package (Rosseel, 2012). In these analyses, we used the default diagonally weighted least squares (**DWLS**) estimation method. Model fit was determined based on chi-square tests (χ^2), the comparative fit index (**CFI**), the Akaike information criterion (**AIC**), and the standardized root mean square residual (**SRMR**). Good-fitting models are expected to have CFI > .95, SRMR < .08 and smaller AIC values than competing nested models (Hu & Bentler, 1998). Good-fitting models also traditionally have non-significant χ^2 statistics. However, because χ^2 statistics are sensitive to large sample sizes such as those used in this study, we focused on other fit indices. Moreover, studies using genomic SEM based on these large-scale GWASs have generally used more relaxed thresholds for other fit statistics such as CFI >.90 (Linner et al., 2021); we adopted this threshold for acceptable fit in the current study. Significance of individual parameter estimates were established with 95% confidence intervals (CIs). When fitting models with only 2 indicators (i.e., thought disorders and compulsive disorders), the two factor loadings were constrained to be equal to ensure the factor was locally identified.

Model-Fitting Approach

First, we separately fit confirmatory factor models of impulsivity and psychopathology-related traits. For impulsivity, we first fit a five-factor model based on prior work (Gustavson et al., 2020). Using this model as a baseline, we constructed a final confirmatory model that captured common variance across impulsivity facets and urgency-specific impulsivity, after excluding facets that did not correlate well with other impulsivity facets (i.e., sensation seeking, described below). Next, we evaluated preliminary associations between executive function, impulsivity and other traits by fitting two correlational models: (a) a model with impulsivity, executive function and our psychopathology (and related traits) factors, and (b) a model with impulsivity, executive function, and the other individual GWASs examined here. Finally, to test our hypotheses concerning whether impulsivity and executive function predicted unique variance in the other outcomes, we refit these same two models but replaced the correlational paths among key constructs with regression paths from the outcomes onto the impulsivity and executive function factors. Models were estimated

separately for psychopathology and related traits vs. other cognitive, education, and health outcomes to simplify the model and aid in convergence.

Overlap With Prior Publications

GWAS summary statistics for almost all traits examined here were obtained from prior studies. Earlier investigations using impulsivity summary statistics from a much smaller GWASs (Sanchez-Roige et al., 2019) examined how some impulsivity traits examined here were associated with internalizing (Gustavson et al., 2020), externalizing (Linner et al., 2021), and thought disorder (Mallard et al., 2022) latent factors, but did not control for executive function. Genetic correlations between common executive function and many psychopathology traits were also reported in the GWAS of common executive function (Hatoum et al., 2023), which also demonstrated that these associations were independent from those with general cognitive ability. However, this earlier work did not control for impulsivity. The current study also uses modified models of internalizing (i.e., expanded to include more traits), externalizing (i.e., based on only publicly available summary statistics) and thought disorders (i.e., including a more recent GWAS of schizophrenia), compared to prior investigations. Finally, analyses comparing how executive function and impulsivity relate to other traits (e.g., educational attainment, BMI, sleep), controlling for one another, represent entirely novel analyses.

Results

The full genetic correlation matrix among all study variables is displayed in the supplement (Table S2).

Latent Variable Models of Impulsivity and Psychopathology-Related Traits

Figure 2a displays our final common factor model of impulsivity, $\chi^2(13)=233.76$, $p<.001$, CFI=.949, SRMR=.077. The common impulsivity factor successfully captured the shared variance across individual UPPS-P and BIS subscales. Additionally, to capture the particularly high correlation among UPPS-P negative urgency and UPPS-P positive urgency subscales (and subsequently examine how this variance is related to psychopathology and related traits), we included a second latent factor called “urgency-specific impulsivity”, which was fixed to be uncorrelated with genetic variance in common impulsivity. This factor was necessary for good model fit, $\chi^2(1)=161.30$, $p<.001$. We also fit a five factor model of impulsivity akin to the UPPS-P model (with BIS subscales included as indices of lack of premeditation), which had comparable fit to the two-factor model, $\chi^2(14)=302.63$, $p<.001$, CFI=.945, SRMR=.074 (see Supplementary Figure S1). As observed in prior studies, sensation seeking was uncorrelated with many other facets of impulsivity (e.g., $r_g= -.08$ with negative urgency, $r_g=.01$ with lack of perseverance), which justified its exclusion from the final model (Figure 2a). Supplemental analyses display associations between impulsivity and other traits of interest using this five-factor model (Table S3).

Our model of psychopathology and related traits is displayed in Figure 2b, $\chi^2(98)=1458.74$, $p=<.001$, CFI=.902, SRMR=.106. This model includes one residual correlation between lifetime cannabis use and the age at first intercourse ($r_g= -.29$), which was included

in Linner et al., (2021). We also allowed PTSD to load on both the internalizing and externalizing latent factors, as it appeared more highly correlated with externalizing measures than other internalizing measures were (see Table S2), and is consistent with prior associations between PTSD and externalizing (e.g., Smoller, 2016). This factor loading from externalizing to PTSD could not be removed without significantly impacting model fit, $\chi^2(1)=43.04$, $p=<.001$.

Association Between Executive Function and Impulsivity Factors

Table 1 displays the genetic correlation between executive function and impulsivity, as well as their associations with all other traits. As we anticipated, low common executive function was only weakly correlated with the common impulsivity factor, $r_g=.13$, 95% CI [.07, .20], and was uncorrelated with the urgency-specific impulsivity factor, $r_g=.00$, 95% CI = [−.08, .09].

Associations Among Executive Function, Impulsivity, and Psychopathology-Related Traits

To test the hypothesis that executive function and impulsivity predict independent genetic variance in psychopathology, we fit a regression model in which the four latent psychopathology and related trait factors were regressed on common executive function, common impulsivity, and urgency-specific impulsivity (see Figure S2 for a path model). Results are displayed in Figure 3 (with standardized beta estimates and R^2 values displayed in Table S4).

The internalizing factor was significantly predicted by low common executive function and both impulsivity factors, with the strongest prediction from urgency-specific impulsivity, $\beta_g=.55$, 95% CI [.39, .70]. In total, almost half of the genetic variance in internalizing problems was explained by executive function and impulsivity, $R^2=.46$. The externalizing factor was also predicted by common executive function and common impulsivity, but not urgency-specific impulsivity, explaining one-third of the variance, $R^2=.34$. In this case, common impulsivity explained the most variance, $\beta_g=.55$, 95% CI [.45, .65].

Thought disorders were predicted by common executive function and urgency-specific impulsivity, explaining 16% of its variance. The strongest prediction was by low common executive function, $\beta_g= .38$, 95% CI [.32, .45]. Compulsive disorders were predicted by low common executive function and common impulsivity, explaining 9% of its variance. Prediction was strongest for low common executive function, $\beta_g= .22$, 95% CI [.12, .32]. Additionally, of note, genetic influences on common impulsivity were associated with less genetic risk for compulsive disorders, $\beta_g= -.17$, 95% CI [−.31, −.04].

Genetic Associations with Other Cognitive, Educational and Health Traits

In the regression model from Figure 3, low common executive function was highly genetically associated with general cognitive ability, $\beta_g= -.76$, 95% CI [.72, .80], but some additional variance in general cognitive ability was also predicted by common impulsivity, $\beta_g= -.11$, 95% CI [−.17, −.06]. Educational attainment was genetically associated with low common executive function, $\beta_g= -.33$, 95% CI [−.28, −.37] and common impulsivity to nearly the same extent, $\beta_g= -.30$ 95% CI [−.35, −.24], explaining 22% of its variance.

BMI was predicted by both higher common impulsivity, β_g= .26, 95% CI [.21, .32], and urgency-specific impulsivity, β_g= .15, 95% CI [.04, .25], explaining 9% of its variance. Low common executive function was also weakly associated with a preference for morningness, β_g= .11, 95% CI [.07, .15], whereas insomnia was predicted by common impulsivity, β_g= .35, 95% CI [.28, .42], and urgency-specific impulsivity, β_g= .18, 95% CI [.08, .27], explaining 16% of its variance.

Discussion

Our study leveraged results from large-scale GWASs to better understand the genetic influences underlying traits related to self-control and their relationship with psychopathology and related outcomes. While we observed consistently that low executive function was genetically associated with all four factors capturing psychopathology and related traits, we found that common impulsivity was *positively* genetically associated with internalizing and externalizing and *negatively* genetically associated with compulsive disorders. Urgency-specific impulsivity was genetically associated with internalizing psychopathology and thought disorders. Finally, while genetic influences on low common executive function and high common impulsivity were similarly (and independently) associated with educational attainment, the two factors were differentially related to other cognitive and health traits. These findings align with the idea that executive function and impulsivity are distinct constructs with differential genetic relationships with psychopathology and other outcomes (Friedman & Gustavson, 2022).

Genetic Structure of Executive Function and Impulsivity

Low common executive function was only weakly genetically correlated with high common impulsivity (r_g= .13), consistent with earlier twin and phenotypic studies (Freis et al., 2022; Friedman et al., 2020). There are multiple explanations for why executive function and impulsivity tap into distinct constructs, including that executive functions are typically assessed using tasks where goals, cues, and feedback tend to be clear, and exertion of control happens across very short time-spans (i.e., milliseconds). Impulsivity, by contrast, is often measured via questionnaires, captures self-control in everyday situations, over long time-spans, and may be influenced by one's meta-cognitive awareness of their own (and others') behaviors (Caswell et al., 2015; Friedman & Gustavson, 2022). Common executive function was also uncorrelated with urgency-specific impulsivity, consistent with the idea that control over emotions may be another defining dimension separating executive function from impulsivity (Friedman & Gustavson, 2022).

This study also contributes to our understanding of the genomic structure of impulsivity. The common impulsivity factor examined here explained substantial variance across nearly all UPPS-P and BIS subscales, aligning with prior twin investigations (Gustavson, Franz, Kremen, et al., 2019; Gustavson et al., 2014). However, it is also important to recognize the multi-faceted nature of impulsivity. Here, results indicated positive and negative urgency shared unique genetic influences that were highly relevant to internalizing problems (and somewhat relevant to thought disorders, BMI, and insomnia), implying that further genome-wide investigation of these measures may yield insight into the biology underlying

emotional control. Furthermore, sensation seeking was uncorrelated with many other facets of impulsivity, aligning with a growing body of phenotypic and genetic evidence that sensation seeking is an independent construct that does not capture self-control processes (Gustavson et al., 2020; Murphy & Mackillop, 2012; Zuckerman & Glicksohn, 2016). Finally, lack of perseverance loaded only modestly on the common impulsivity factor, consistent with its relatively weak associations with the other mental health traits examined here (see Table S3). For compulsive disorders only, lack of perseverance was associated with a similar strength as other impulsivity facets, but post-hoc analyses suggested there were no significant residual association between lack of perseverance and compulsive disorders (β=.12, p=.067). Thus, like sensation seeking, lack of perseverance may capture little genetic overlap with other impulsivity facets.

Relationship of Executive Function and Impulsivity to Psychopathology and Related Traits

Common executive function and common impulsivity were differentially associated with aspects of psychopathology-related traits, cognition, and health. This result aligns with recent theoretical frameworks such as the Hierarchical Taxonomy of Psychopathology (HiTOP) (Kotov et al., 2017). The HiTOP framework characterizes externalizing as "impulsivity" and "distractibility" while describing thought and compulsive disorders as characterized by "cognitive dysregulation" (Kotov et al., 2017). Such characterizations are consistent with our findings that common impulsivity was the strongest predictor of externalizing, whereas low common executive function was the strongest predictor of thought disorders.

These findings could also be interpreted in light of the National Institute of Mental Health's Research Domain Criteria (RdoC) (Insel et al., 2010) in which impulsivity, executive function, and related measures are classified within the same system of "cognitive control." However, as these measures clearly capture different sets of genetic risk factors that are relevant to psychopathology and related traits, it will be important to further explore both domains to better understand how genetic risk factors influence psychopathology and health. Multivariate GWAS methods such as "GWAS by subtraction" (Demange et al., 2021) may be useful in parsing genetic influences on psychopathology into genetic risk factors explained by self-control traits from other genetic risk factors on psychopathology.

Finally, while we focused on four distinct domains of psychopathology, these domains are highly correlated (sometimes referred to as the p-factor). Our results that common executive function was genetically associated with all four latent psychopathology factors are consistent with prior phenotypic studies demonstrating that executive functions are associated with common variance across psychopathology (Caspi et al., 2014; Harden et al., 2019). However, the fact that common impulsivity was *positively* genetically correlated with some factors (i.e., internalizing and externalizing), but *negatively* correlated with others (i.e., compulsive disorders) suggests that impulsivity does not reflect a common liability for mental health outcomes, and that further compartmentalizing impulsivity may help us better understand its role in specific psychiatric conditions.

Additional Implications for the Self-Control-Related Traits

Unsurprisingly, low common executive function was strongly genetically correlated with general cognitive ability (β_g= −.76), but common impulsivity also demonstrated a small association with general cognitive ability even when controlling for executive function (β_g= −.11). In contrast, low executive function and high impulsivity genetic influences explained a relatively equal amount of unique variance in educational attainment (β_g= −.33 and −.30, respectively). These results suggest that both aspects of (genetically influenced) self-control may support educational attainment. For example, the short-term attentional control abilities related to common executive function may be more relevant to performance on exams and standardized tests while the long-term control abilities captured by (low) common impulsivity may be more necessary to effectively complete course assignments and persevere through stressful situations.

Results for BMI revealed genetic associations with impulsivity factors only. These findings align with evidence that self-reported measures of self-control predict obesity more strongly than executive function tasks (Eisenberg et al., 2019). Nevertheless, the lack of genetic association between BMI and executive function is somewhat surprising given phenotypic evidence linking executive function with obesity (Eisenberg et al., 2019), suggesting such phenotypic associations between BMI and executive function could be a consequence of an environmental correlation.

Finally, executive function was the only trait to weakly predict chronotype (in this case, eveningness) while both impulsivity factors predicted insomnia. Morrison et al. (2022) found sleep health to be composed of six correlated but distinct genetic domains. Controlling for other sleep health domains, chronotype was not associated with any factors of psychopathology, whereas insomnia was associated with internalizing, externalizing and thought disorders (Morrison et al., 2022). Because insomnia can be highly comorbid with psychiatric disorders and impulsivity is a key component of many psychopathologies, our finding that impulsivity predicted insomnia is consistent. However, the lack of association between impulsivity and chronotype is inconsistent with some phenotypic studies linking it with eveningness preference (Gillett et al., 2021; Hasler et al., 2022). These results help characterize both the genetic divergence of executive function and impulsivity and sleep health domains.

Strengths and Limitations

Our approach leveraged data from publicly available GWASs, most of which were based on hundreds of thousands of subjects. However, these findings based on individuals of European ancestry may not generalize to individuals of other backgrounds. This limitation reflects a general underrepresentation of non-European populations in the field of human genetics, which can be alleviated by expanding GWAS efforts. In addition, many GWASs used here were derived from population-based cohorts, such as 23andMe, that generally represent older participants with higher socioeconomic status than the general population (Sanchez-Roige et al., 2019), which may introduce biases due to gene-environment correlations (Abdellaoui et al., 2022; Howe et al., 2022) and reduce generalizability. The

GWASs of compulsive disorders (OCD, anorexia nervosa) were also based on much smaller samples than the other traits.

Second, the associations examined here are based purely on genetic data, which may differ from those of environmental nature. Historically, however, relationships among complex traits tend to be similar across the genetic, environmental, and phenotypic levels (Plomin et al., 2016; Sodini et al., 2018), suggesting the trends observed here using purely genetic data should align well with large-scale phenotypic investigations.

Third, our latent factors capturing internalizing and externalizing included a mix of case-control studies and related dimensional measures (e.g., neuroticism and loneliness), as these were the largest GWASs currently available. These different sets of measures were substantially genetically correlated with one another (see Table S1), but as more GWASs are published it will be important to evaluate whether diagnosis-based measures of internalizing and externalizing capture some potentially different sets of genetic influences as dimensional measures. Relatedly, the negative urgency facet of impulsivity was modeled after neuroticism (Lynam et al., 2006), which may have inflated our estimate of the strong overlap among urgency-specific impulsivity and internalizing. However, post-hoc analyses removing neuroticism from the model revealed very similar associations between internalizing problems and urgency-specific impulsivity (β= .52) as the model in Figure 3, suggesting that item overlap among these measures had little impact on our estimates.

Conclusion

In summary, executive function and impulsivity are weakly related at the genetic level. Both traits predict independent genetic variance in psychopathology and related traits, as well as other traits related to cognition, education, and health. Better understanding what is captured by these different facets of self-control will improve our understanding of risk and treatment for mental health conditions, and improved general well-being.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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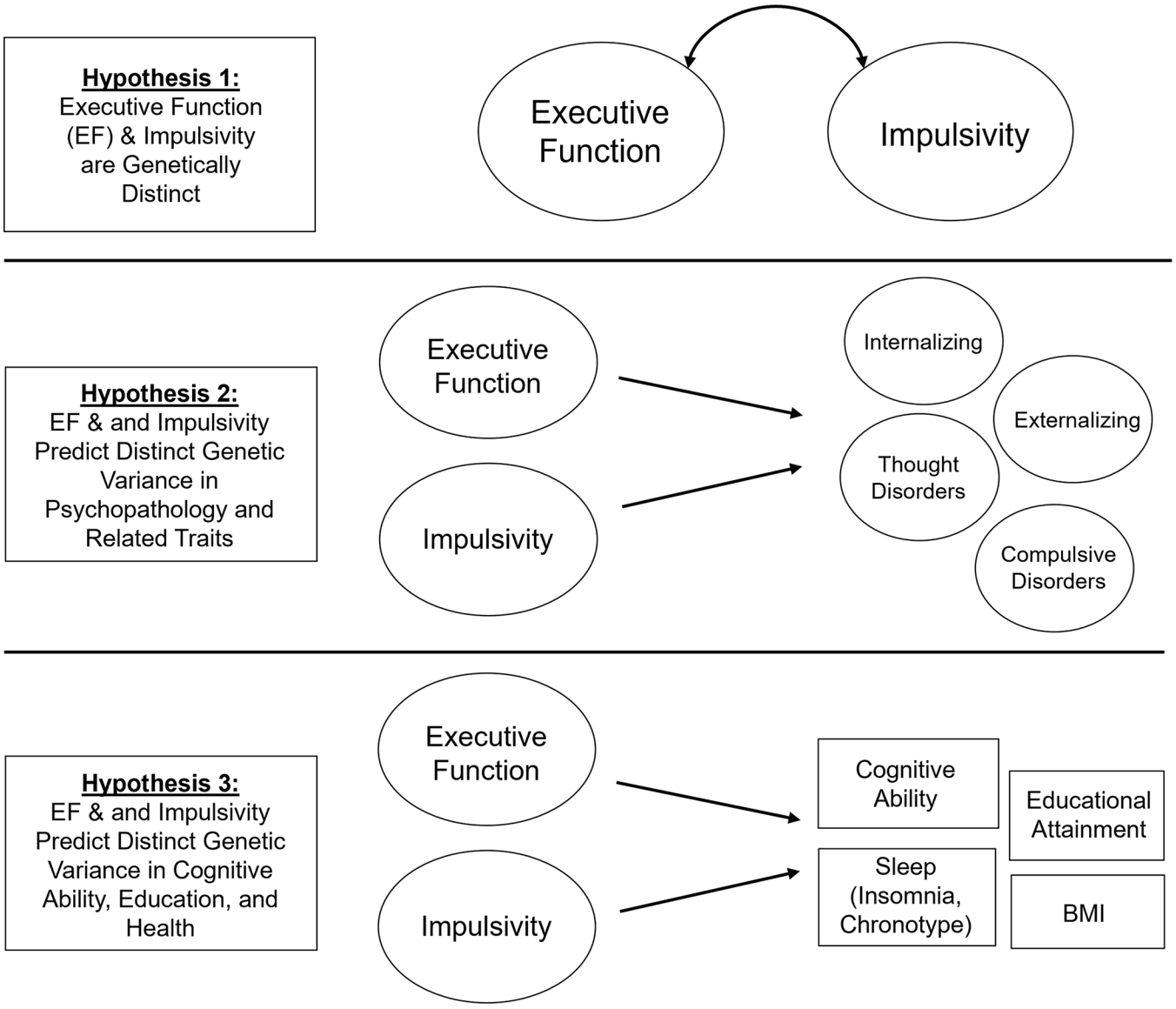

Figure 1.

Visual representation of the study goals and hypotheses. In all models, data are based on summary statistics from existing large-scale genome-wide associations studies (GWASs). First, we examine whether there are any common genetic influences on executive function (based on a GWAS of a single phenotypic factor score derived from 5 executive function tests) and impulsivity (a two-factor model based on 7 individual summary statistics). Second, we examine whether both executive function and impulsivity predict distinct genetic influences on four latent factors capturing psychopathology and related traits (2–8 GWASs per factor). Third, we test a similar hypothesis that executive function and impulsivity also predict distinct genetic influences on other individual GWASs capturing general cognitive ability, educational attainment, sleep (chronotype, insomnia), and body mass index (BMI).

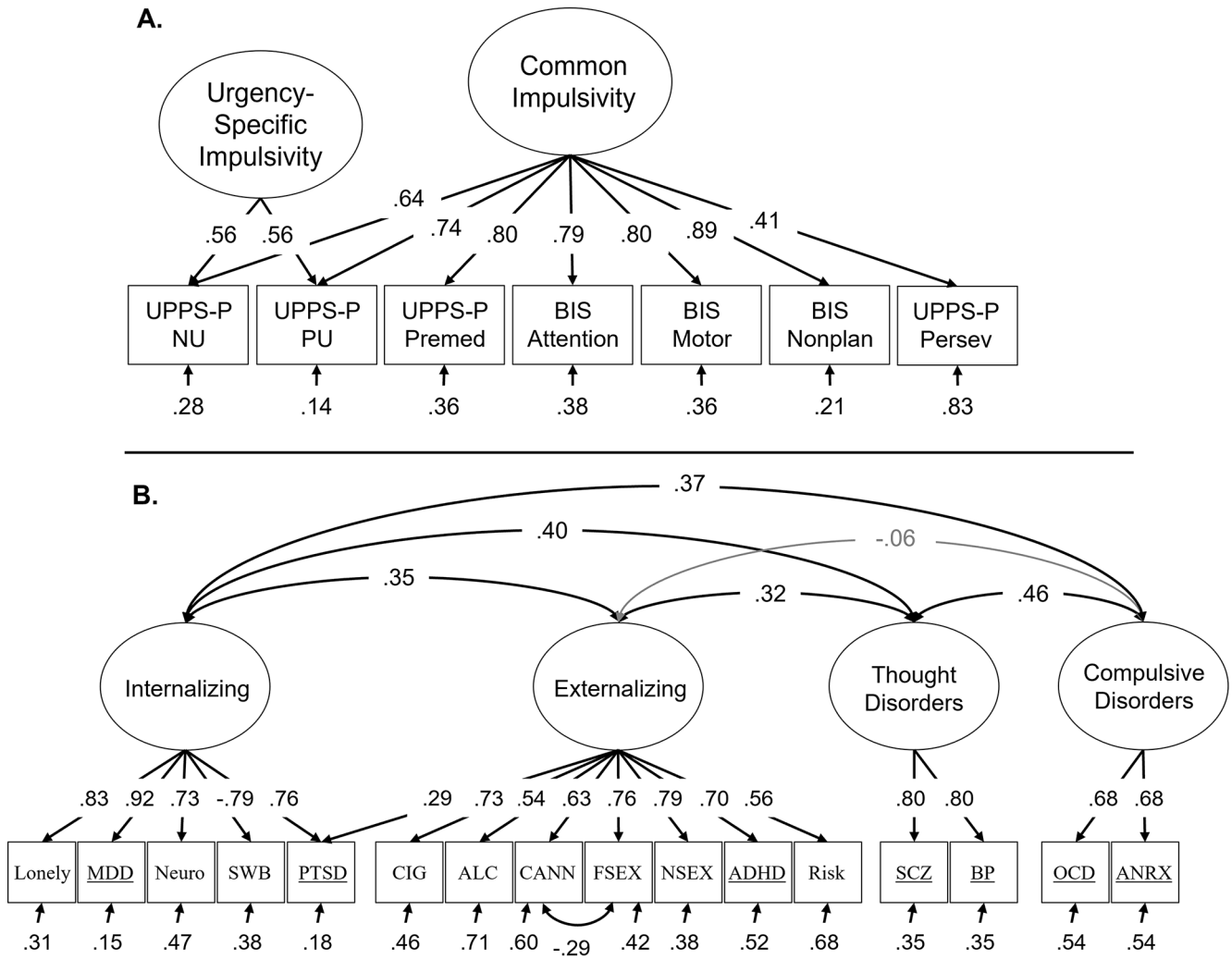

Figure 2:

(A) Two factor model of impulsivity traits and (B) four factor model of psychopathology and related traits. Boxes indicate genome-wide association study summary statistics and ovals indicate standardized latent variables. Arrows below boxes indicate residual variances. Significant correlations among latent variables are displayed with black text and lines (p<.05). Underlined measures (in Model B) display case-control studies; all other summary statistics were based on continuous measures. Model fit for A: $\chi^2(13)=233.76$, p<.001, CFI=.949, SRMR=.077. Model fit for B: $\chi^2(98)=1458.74$, p=<.001, CFI=.902, SRMR=.106. UPPS-P = UPPS-P Impulsive behavior scale; NU = negative urgency subscale; PU = positive urgency subscale; Premed = lack of premeditation; Persev = lack of perseverance subscale; BIS = Barratt Impulsiveness Scale; Lonely=Loneliness; MDD=Major depressive disorder; Neuro=Neuroticism; SWM=subjective wellbeing; PTSD=post-traumatic stress disorder; CIG=lifetime smoking initiation; ALC=problematic alcohol use; CANN=lifetime cannabis use; FSEX=reverse-coded age at first sexual intercourse; NSEX=number of sexual partners; ADHD=attention-deficit hyperactivity

disorder; SCZ=schizophrenia; BP=bipolar disorder; OCD=obsessive compulsive disorder; ANRX=anorexia.

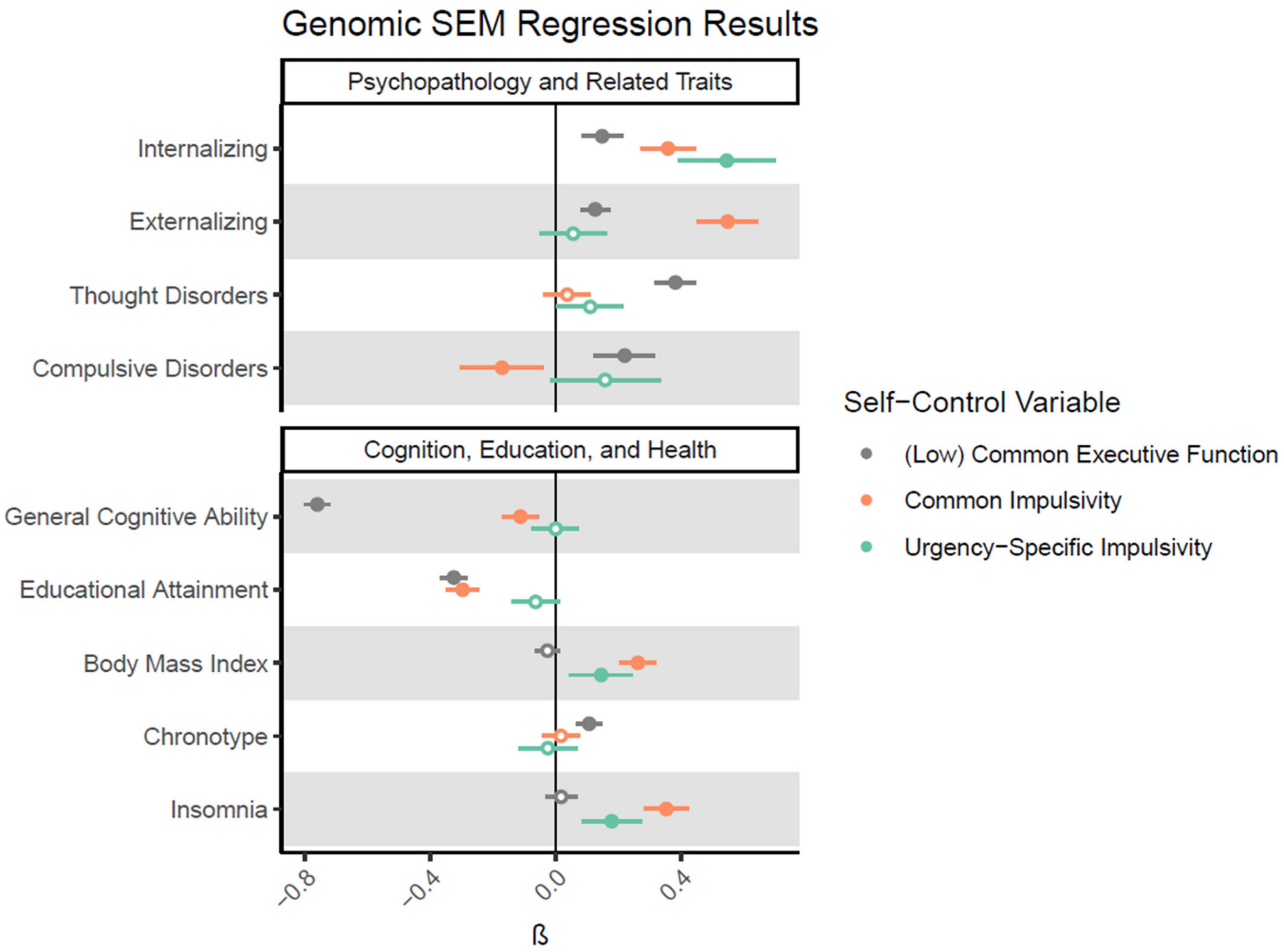

Figure 3:

Standardized associations (and standard errors) between low common executive function, common impulsivity, urgency-specific impulsivity (controlling for one another), and the other constructs of the study. Estimates from these regressions are displayed in Supplemental Table S4. Significant associations are indicated with a filled-in circle (p<.05). Model fit was identical to the correlational models from Table 1.

Table 1:

Genetic Correlations (r_g) Among Executive Function, Impulsivity, Psychopathology, and Other Study Measures

Construct	(Low) Common Executive Function		Common Impulsivity		Urgency-Specific Impulsivity	
	r_g	95% CI	r_g	95% CI	r_g	95% CI
Psychopathology						
Internalizing Problems	**0.20**	**[.16, .24]**	**0.38**	**[.31, .44]**	**0.55**	**[.45, .65]**
Externalizing Problems	**0.19**	**[.16, .23]**	**0.56**	**[.50, .63]**	0.06	[−.05, .17]
Thought Disorders	**0.39**	**[.34, .44]**	**0.08**	**[.01, .15]**	**0.12**	[.01, .22]
Compulsive Disorders	**0.20**	**[.12, .29]**	**−0.15**	**[−.27, −.02]**	0.16	[−.01, .33]
Cognitive						
(Low) Common Executive Function	–	–	**0.13**	**[.07, .20]**	0.00	[−.08, .09]
General Cognitive Ability	**−0.78**	**[−.83, −.72]**	**−0.21**	**[−.15, −.27]**	0.00	[−.08, .09]
Education & Health						
Educational Attainment	**−0.37**	**[−.40, −.33]**	**−0.34**	**[−.40, −.29]**	−0.07	[−.14, .01]
Body Mass Index	0.01	[−.02, .04]	**0.26**	**[.20, .31]**	**0.14**	**[.04, .25]**
Chronotype	**0.11**	**[.07, .15]**	0.03	[−.03, .09]	−0.03	[−.12, .07]
Insomnia	**0.06**	**[.02, .11]**	**0.36**	**[.29, .42]**	**0.18**	**[.08, .27]**

Note: Genetic correlations between executive function, impulsivity, and all psychopathology factors were estimated in the context of a single model, $\chi^2(232)=6935.80$, $p=<.001$, CFI=.845, SRMR=.108. Genetic correlations among executive function, impulsivity, and the cognitive, education, and health traits were estimated in a separate model, $\chi^2(43)=1164.72$, $p=<.001$, CFI=.916, SRMR=.092. Significant genetic correlations are displayed in bold (95% CI does not include 0).