

psychopathology, personality and genetics

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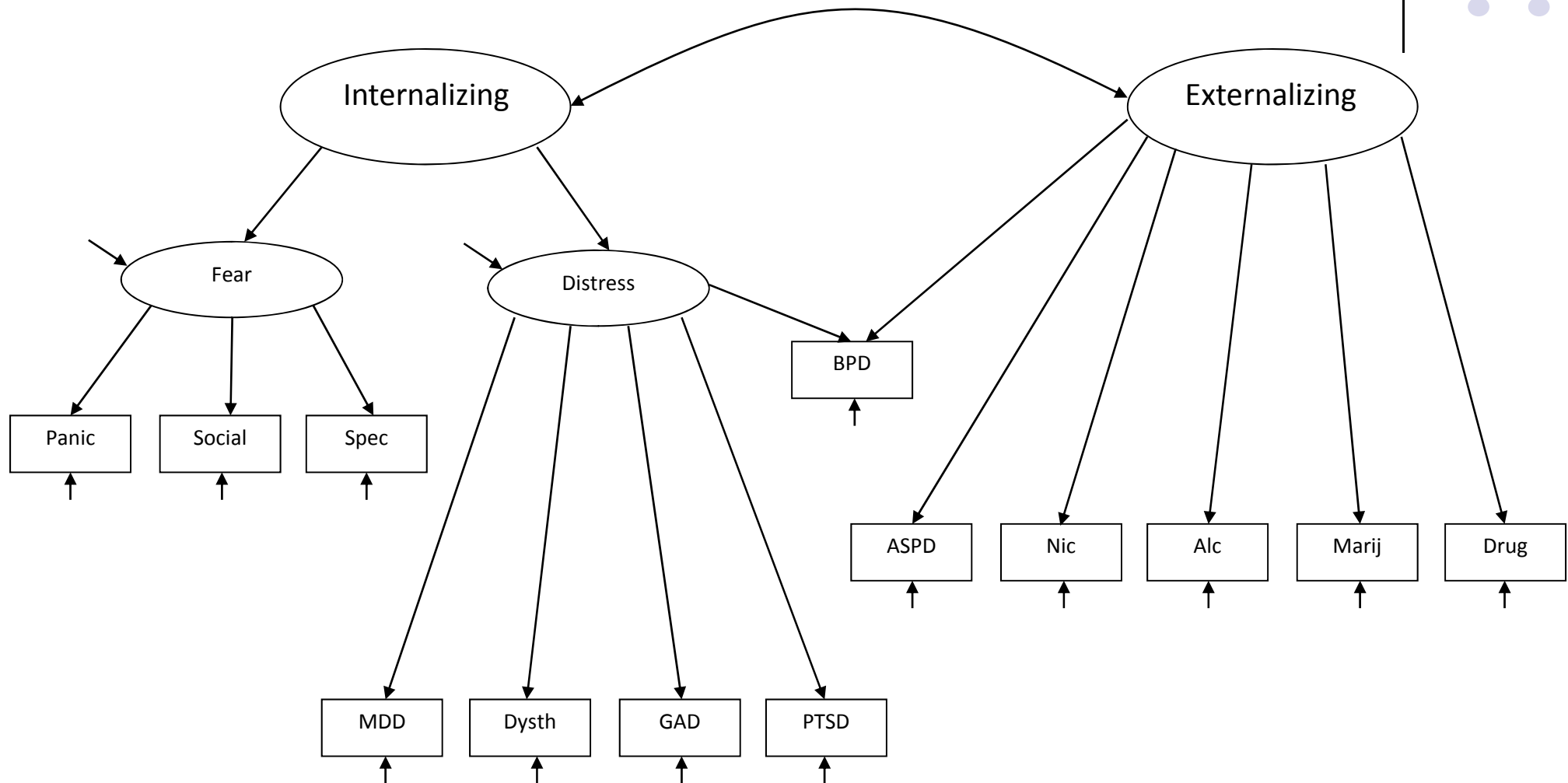
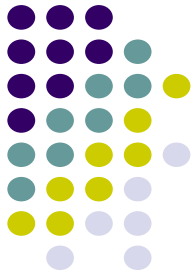
psychopathology



- has typically been thought of in terms of
- 297
- putatively discrete
- and separate categories
- that are polythetic
 - multiple combinations of criteria -> same diagnosis
- and each category is typically studied by different people publishing in different journals attending different scientific meetings funded by different parts of NIH (and so on)
- is this an accurate model of psychopathological variation?
 - and a good way to work on the problem?

a dimensional-spectrum model of common forms of psychopathology

Eaton, Krueger, Keyes, Skodol, Markon, Grant, & Hasin, 2010, *Psychol Med*



some things we've learned



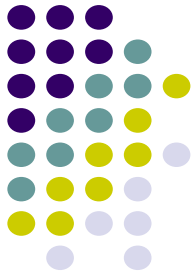
- i. the latent spectrum variables are continuous
 - as opposed to being discrete
 - via direct comparison of models with categorical vs. continuous latent variables
- ii. the phenotypic correlations among indicators are (primarily) genetically mediated
 - the latent variables appear more heritable than the indicator diagnoses
 - especially externalizing (> internalizing)
 - there are residual genetic effects on the indicators
 - alcohol is a good example
 - but the residuals are smaller effects

some things we've learned

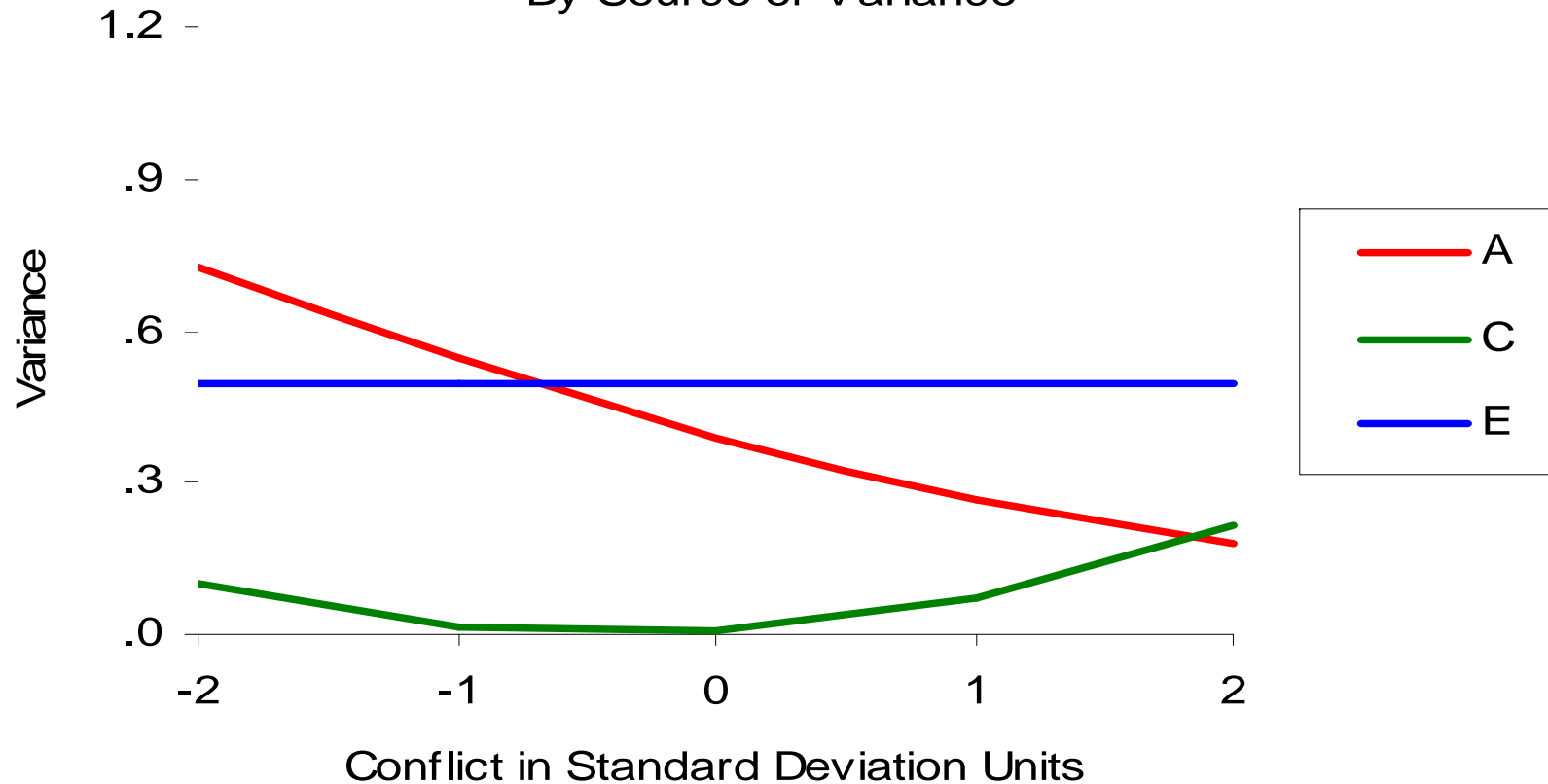


- iii. personality is at the core of the spectrums
 - dispositions function like diagnoses as indicators
 - genetically correlated with diagnoses
 - controlling for dispositions reduces “comorbidity”
- iv. this model is likely to frame key aspects of the DSM-5 meta-structure
- ***upshot: personality dispositions are key variables in behavioral public health***
 - the social costs of psychopathology are unequivocal
 - negative emotionality (neuroticism) is at the core of internalizing
 - disinhibition (un-conscientious dis-agreeableness) is at the core of externalizing
 - understanding the etiology and neurobiology of these dispositions is important

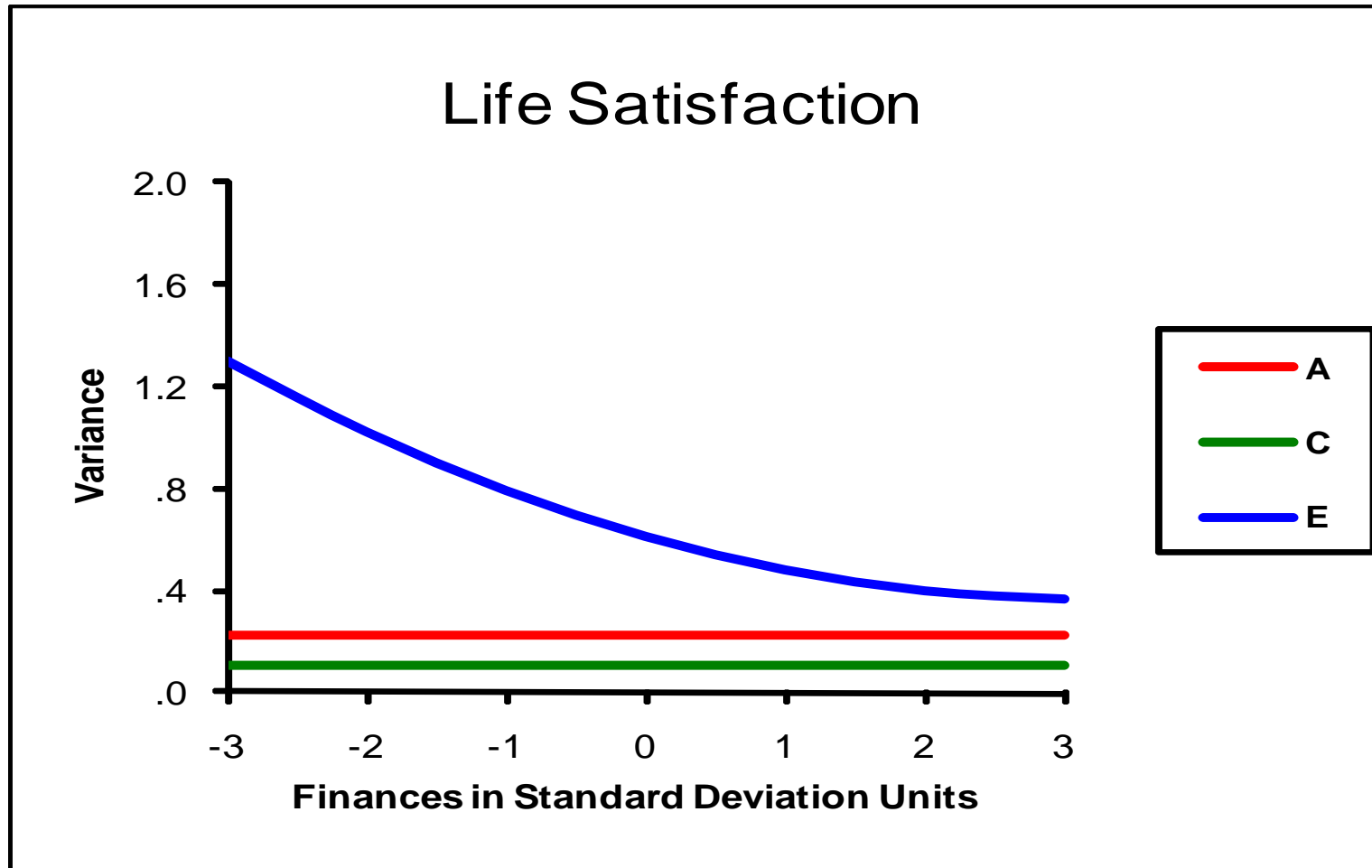
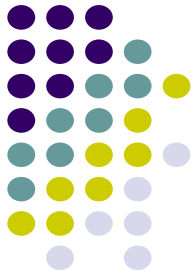
etiology of negative emotionality varies as a function of family conflict



Variance in MPQ Negative Emotionality as a Function of
Parental Conflict at Age 17
By Source of Variance



finances moderate etiology of life satisfaction



Variance in Life Satisfaction as a Function of Finances, by source of variance.

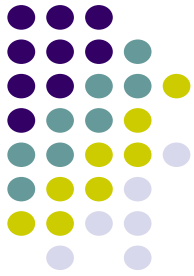
meta analytic GWAS of personality

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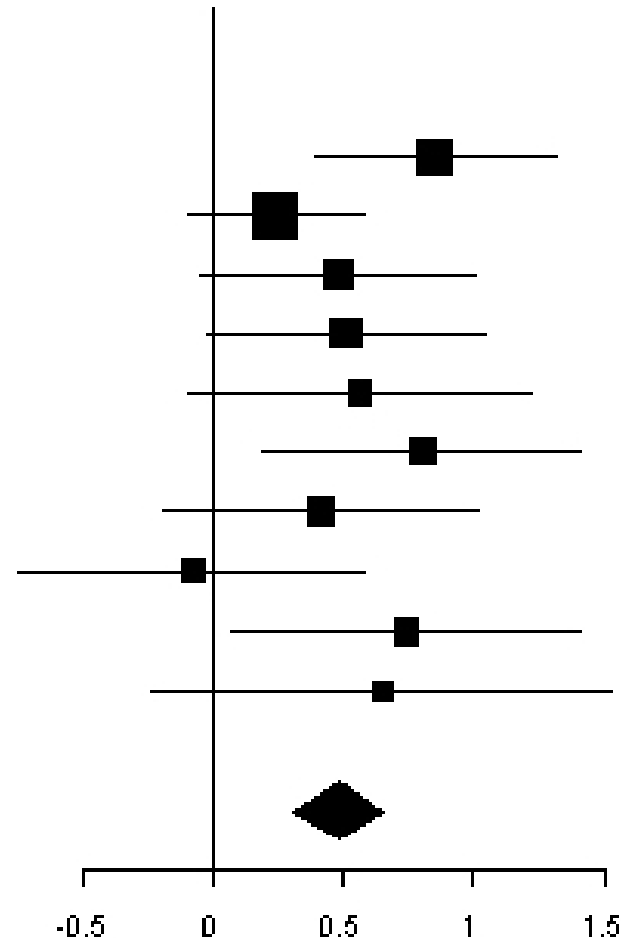


- 17,375 unrelated individuals of European ancestry from Europe, the United States and Australia
- 10 contributing studies
- genotyping platforms rendered commensurate via imputation
 - ~2.5M common SNPs included in HapMap, using the HapMap phase II CEU data as the reference sample
 - ~2,500,000 data points per person
- phenotypes are NEO-FFI (Five Factor Model; FFM) scales
 - Openness ,Conscientiousness, Extraversion, Agreeableness, Neuroticism
 - OCEAN

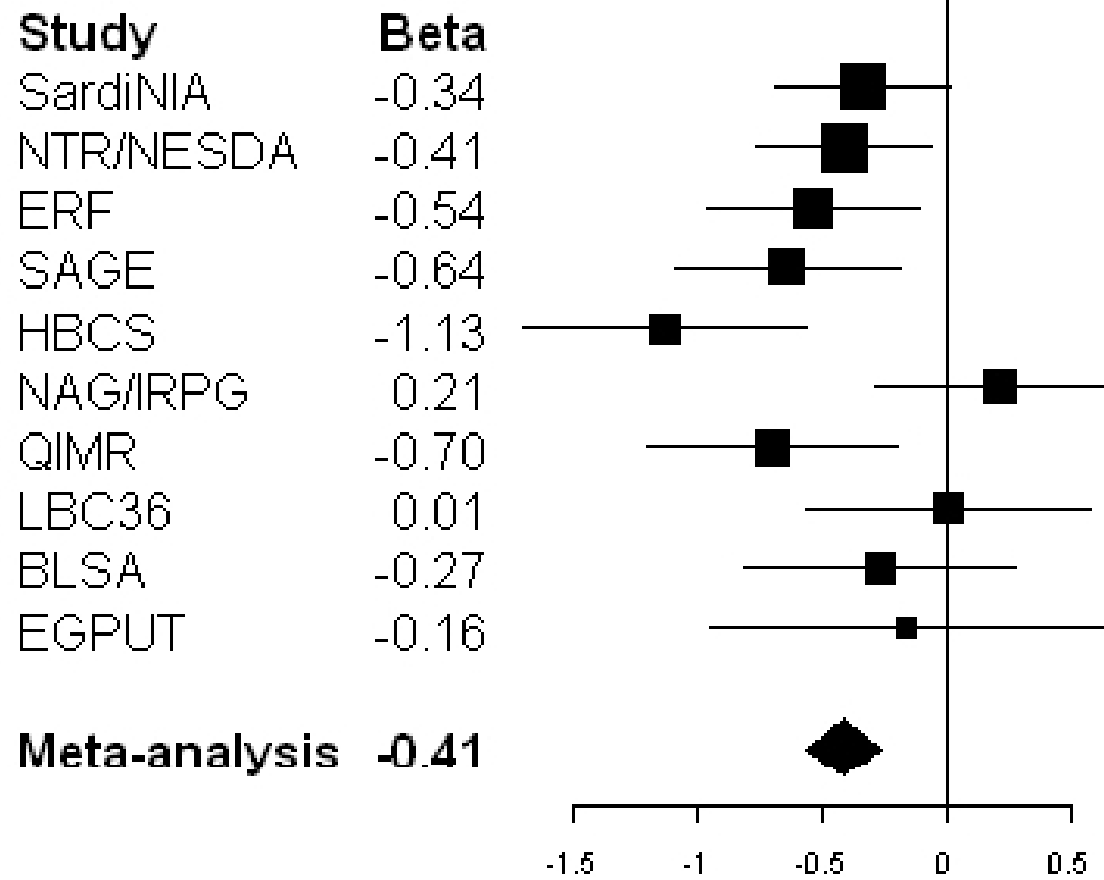
FFM meta analysis : snp on chromosome 5 for openness



Study	Beta
SardiNIA	0.85
NTR/NESDA	0.24
ERF	0.48
SAGE	0.51
HBCS	0.56
NAG/IRPG	0.80
QIMR	0.41
LBC36	-0.08
BLSA	0.74
EGPUT	0.65
Meta-analysis	0.48

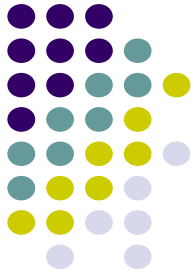
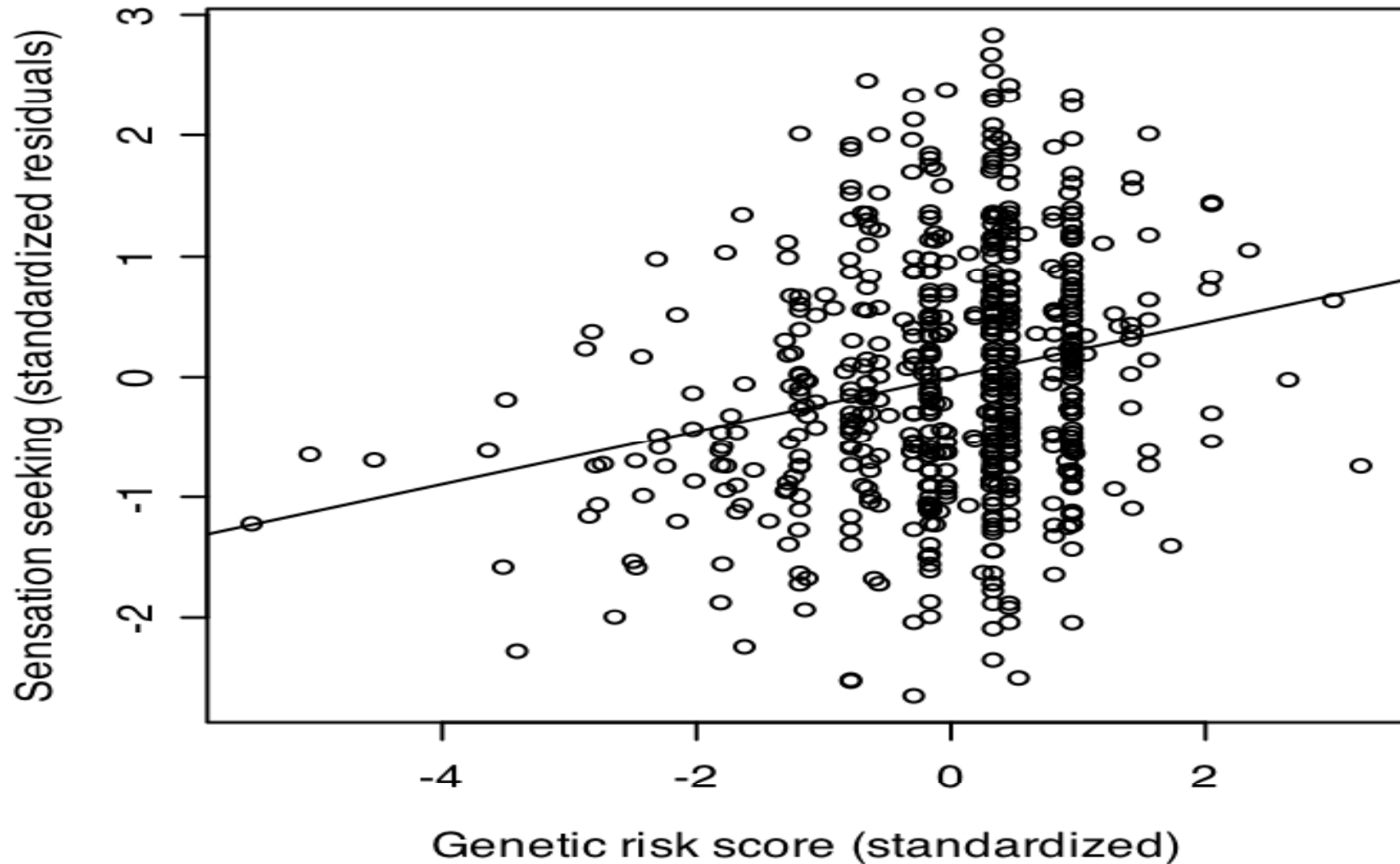


FFM meta analysis : snp on chromosome 18 for conscientiousness



aggregate of 12 snps in the dopamine (DA) system predicts sensation seeking

Derringer J, Krueger RF, Dick DM, Saccone S, Grucza RA, Agrawal A, ... Bierut LJ, 2010, *Psychol Sci*



genetics of personality and psychopathology: ongoing steps



- whole genome approaches will (and should) continue
 - much of what is found in “medical” molecular genetics would not have been predicted from a candidate approach
- candidate sets of variants for association can be pursued simultaneously
 - neurobiological variables are key intermediate phenotypes
- twin research continues to offer valuable insights
 - can study G-E processes at an aggregate level

full moderator model (cholesky with moderation effects; 17 parameter estimates)

