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Genetic risk for mental illness, and much more

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There are many different types of genetic risk for mental illness.
Neuropsychiatric disorders are highly heritable

Gottesman 1991
Cowan, Kopnisky, Hyman 2002

Sullivan, Daly, O’Donovan 2012

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Neuropsychiatric disorders have a negative impact on fecundity

From: Fecundity of Patients With Schizophrenia, Autism, Bipolar Disorder, Depression, Anorexia Nervosa, or Substance Abuse vs Their Unaffected Siblings

Only alleles with weak effects can become common because of natural selection.

Common variants risk factors, individually, have small effect sizes.

Slide courtesy of Mark Daly

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Common polygenic risk

Common polygenic risk for neuropsychiatric disorders is present in all of us to some degree.
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The exception of *de novo* variation

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Polygenic risk

Continuously distributed and present in everyone to some degree

De novo variation

A binary variable: presence/absence of a de novo variant from a class associated with disease risk
Genetic risk factors for mental illness relate to many other behavioral and developmental traits
De novo variants with large effects are also strongly associated with intellectual disability, epilepsy, motor delays, and other indicators of global neurodevelopmental impact.

Weiner et al. 2017

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Common polygenic risk is comparatively neurologically gentle

Genetic risk for ASDs and Bipolar Disorder is positively associated with cognitive ability in the general population

Bulik-Sullivan and Finucane et al. 2015

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Genetic risk factors for mental illness, especially those that run in families, are associated with many positive human traits.
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becomes

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An old idea, particularly with regard to unaffected family members

Skuse et al. JAACAP 2011

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**Genetic Correlation**

- PGC ASD SCDC, p=0.006
- iPSYCH ASD SCDC, p=0.001
- PGC ASD SCZ, p=5.63e-07
- PGC ASD MDD, p=0.096
- PGC ASD BPD, p=0.134

Robinson, St. Pourcain et al., 2016

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Genetic Risk Factor

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Thanks

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