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# Genetic risk for mental illness, and much more

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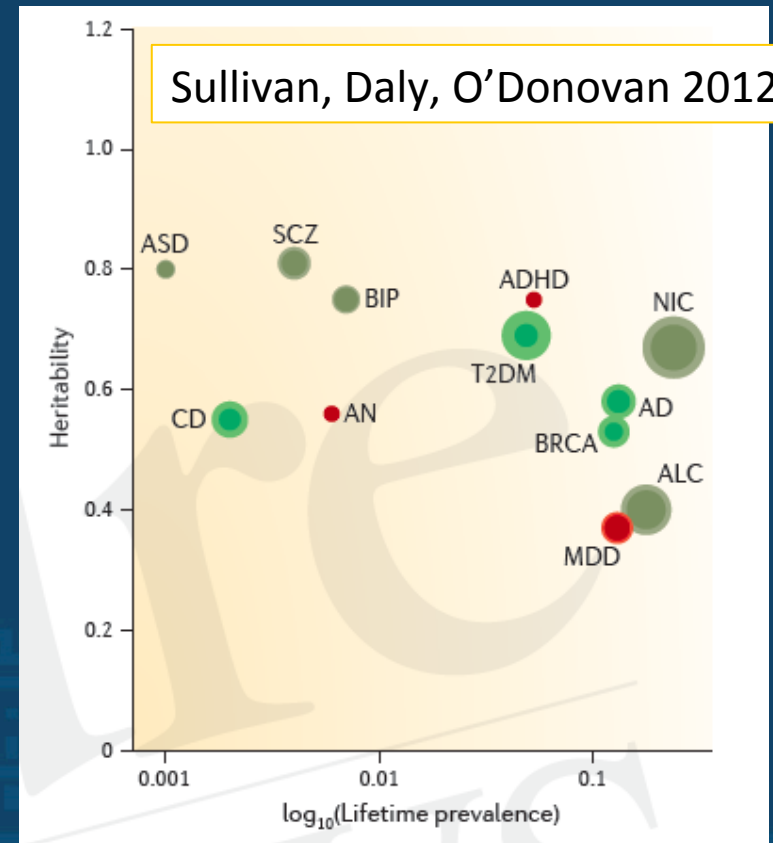
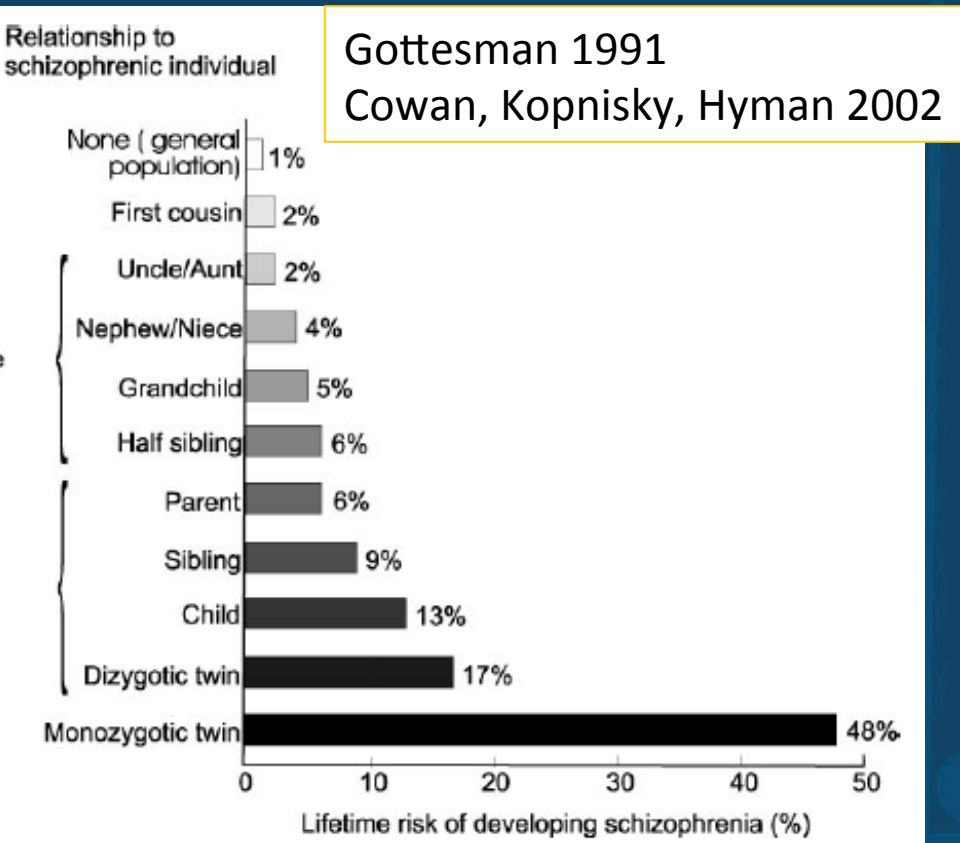
**#NAMIcon17**

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There are many different types of genetic risk for mental illness

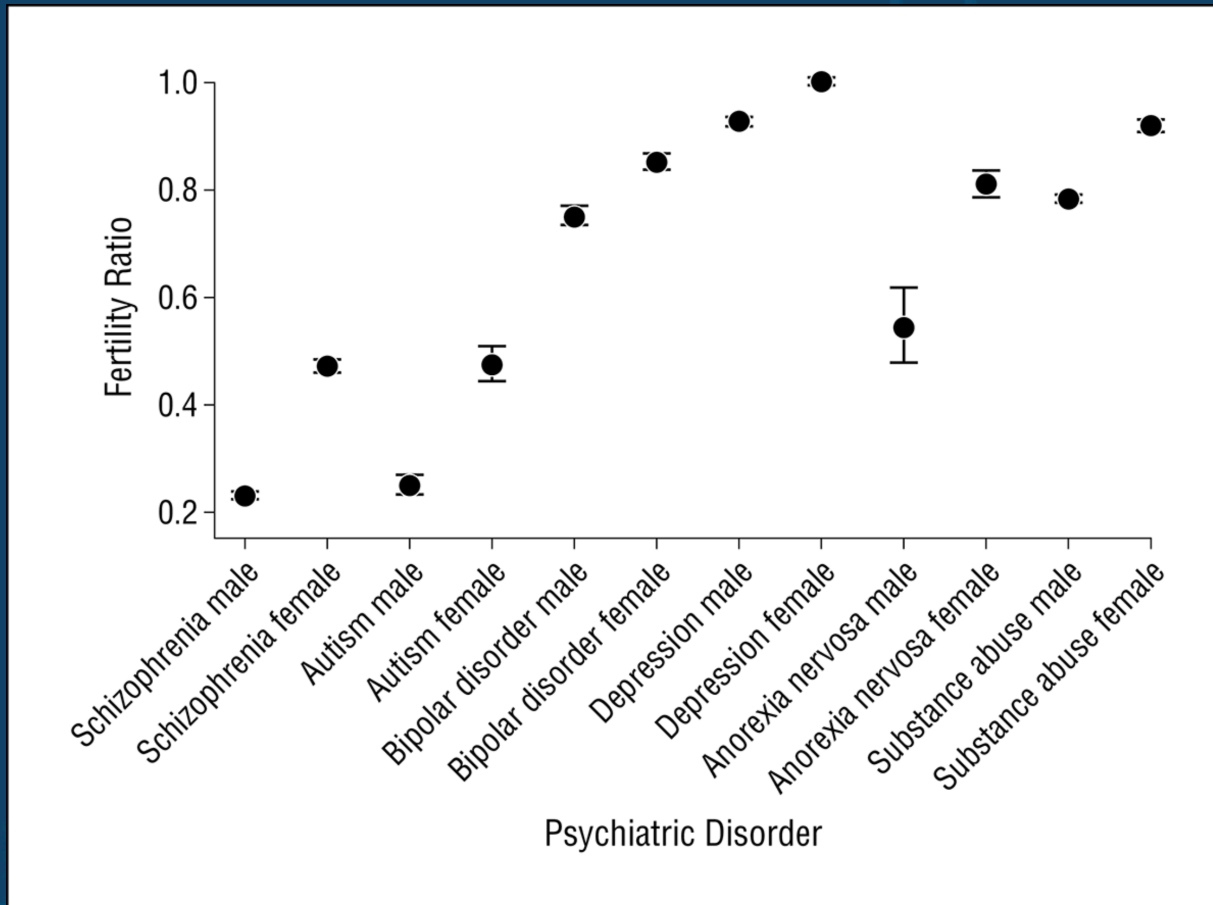
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## Neuropsychiatric disorders are highly heritable



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## Neuropsychiatric disorders have a negative impact on fecundity

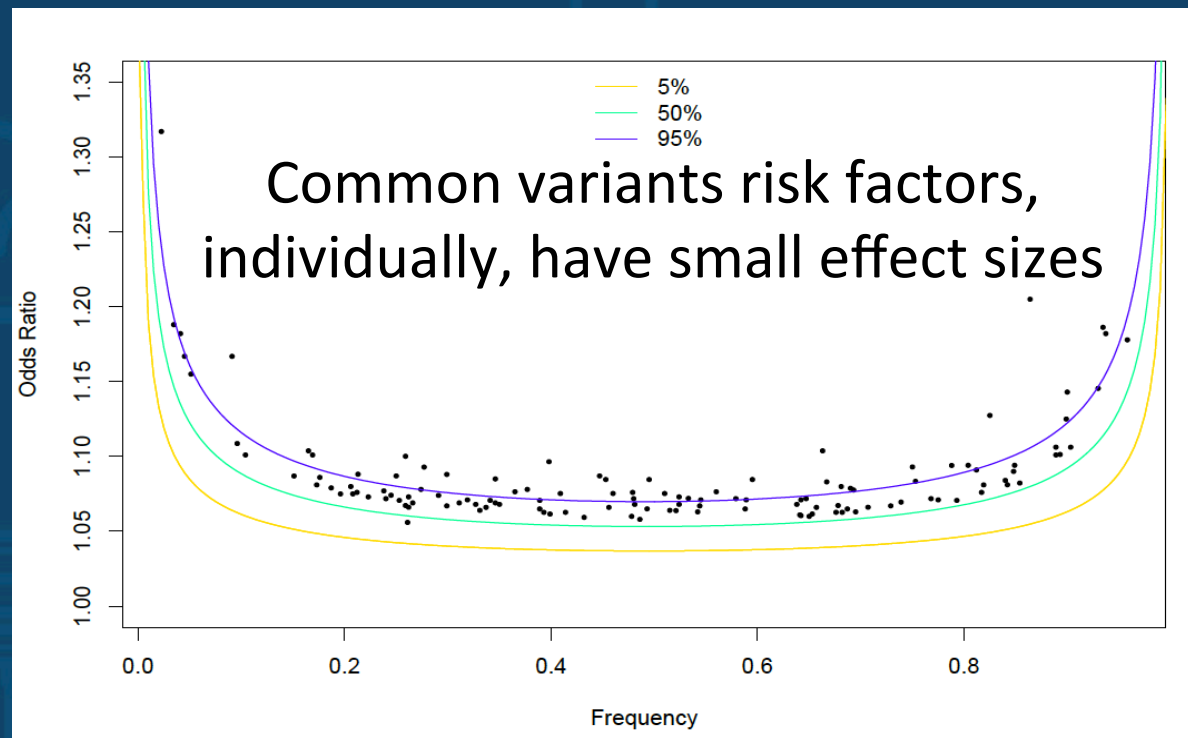


From: **Fecundity of Patients With Schizophrenia, Autism, Bipolar Disorder, Depression, Anorexia Nervosa, or Substance Abuse vs Their Unaffected Siblings**

JAMA Psychiatry. 2013;70(1):22-30.  
doi:10.1001/jamapsychiatry.2013.268

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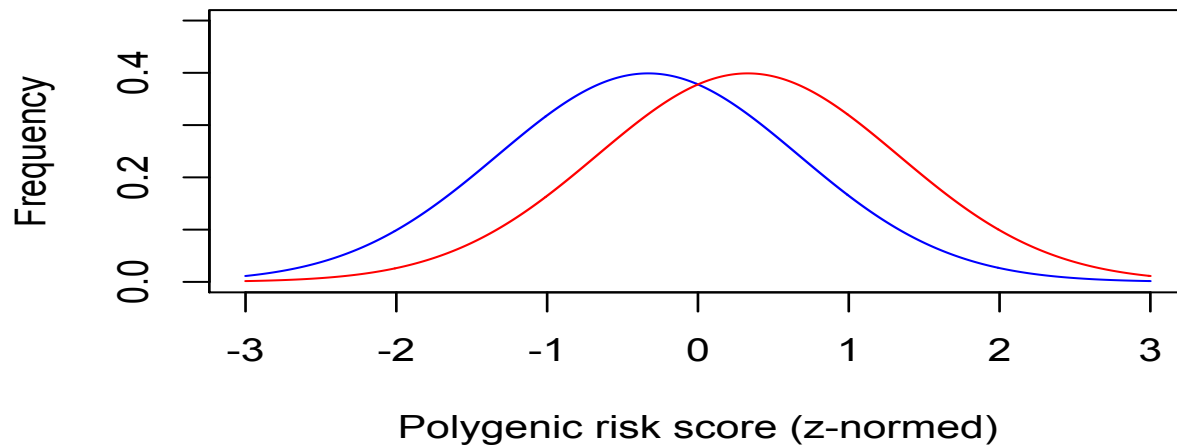
Only alleles with weak effects can become common because of natural selection



Slide courtesy of Mark Daly

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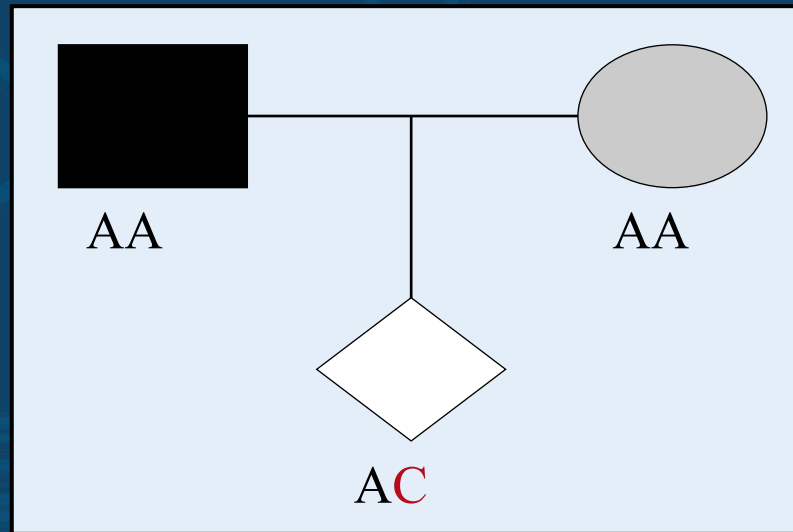
## Common polygenic risk



Common polygenic risk for neuropsychiatric disorders is present in all of us to some degree

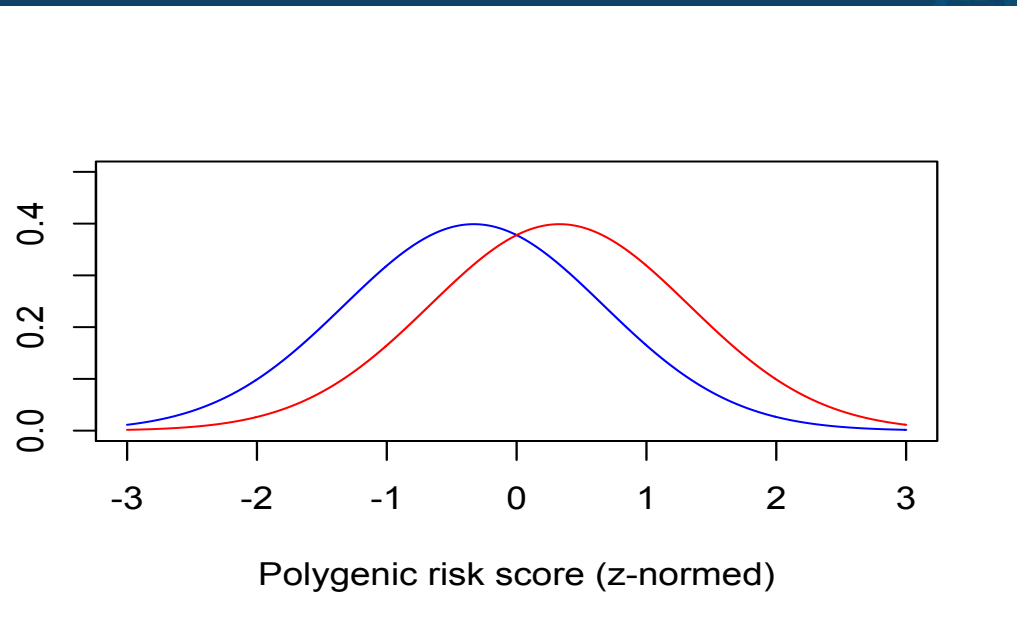
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The exception of  
*de novo* variation



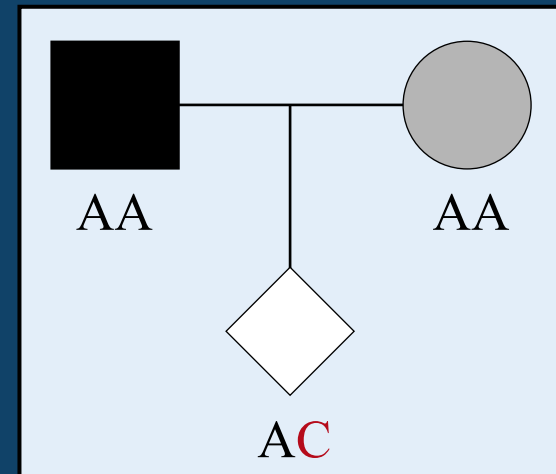
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## Polygenic risk



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



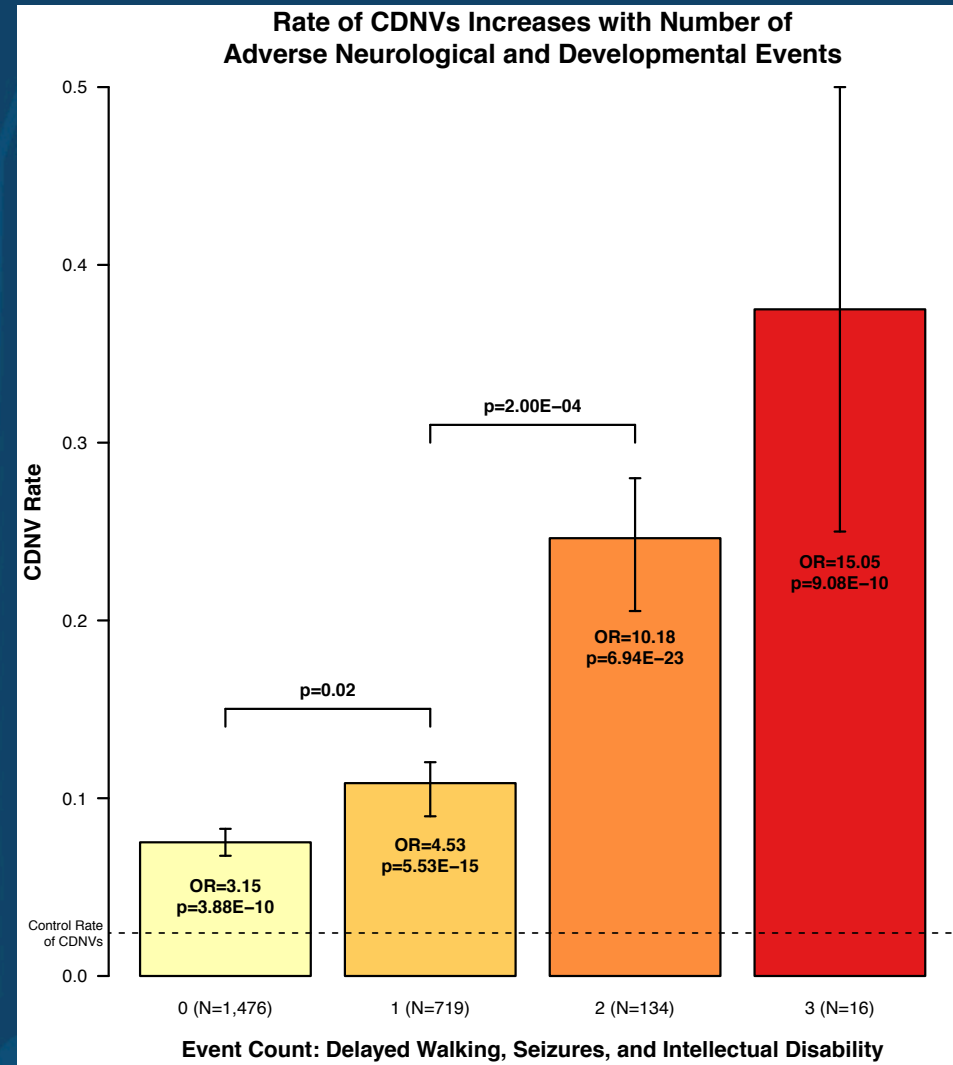
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Genetic risk factors for mental illness  
relate to many other behavioral and  
developmental traits

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De novo variants with large effects are also strongly associated with intellectual disability, epilepsy, motor delays, and other indicators of global neurodevelopmental impact

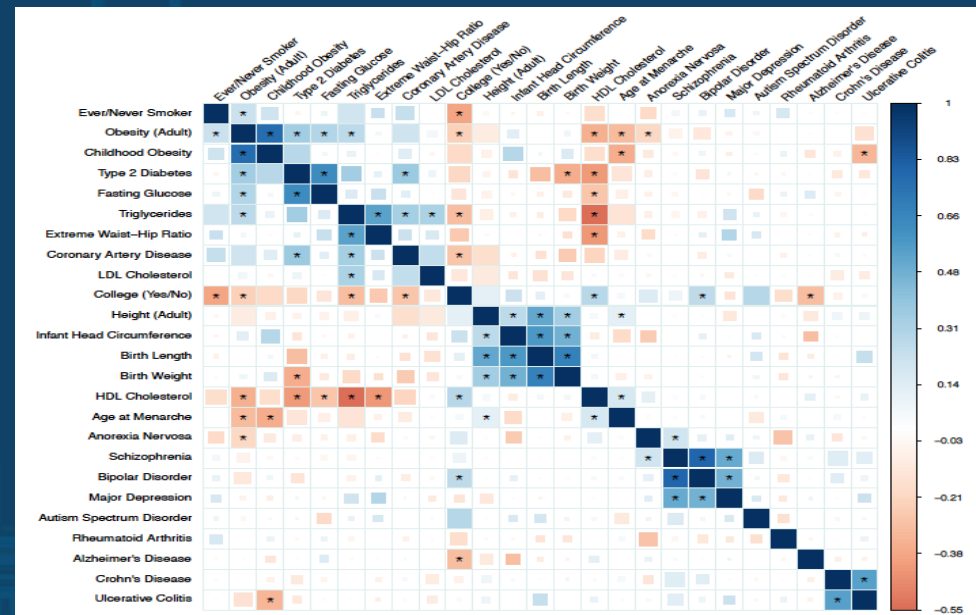
Weiner et al. 2017



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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

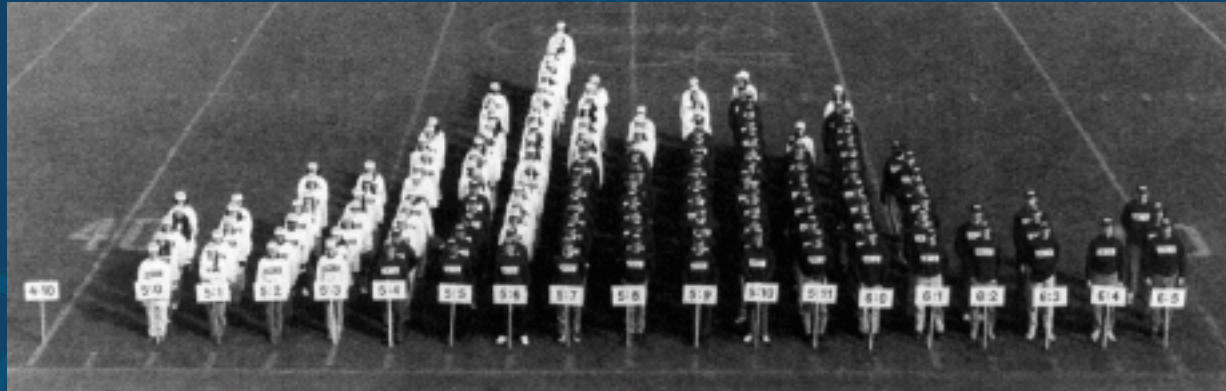


Bulik-Sullivan and Finucane et al. 2015

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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

Controls

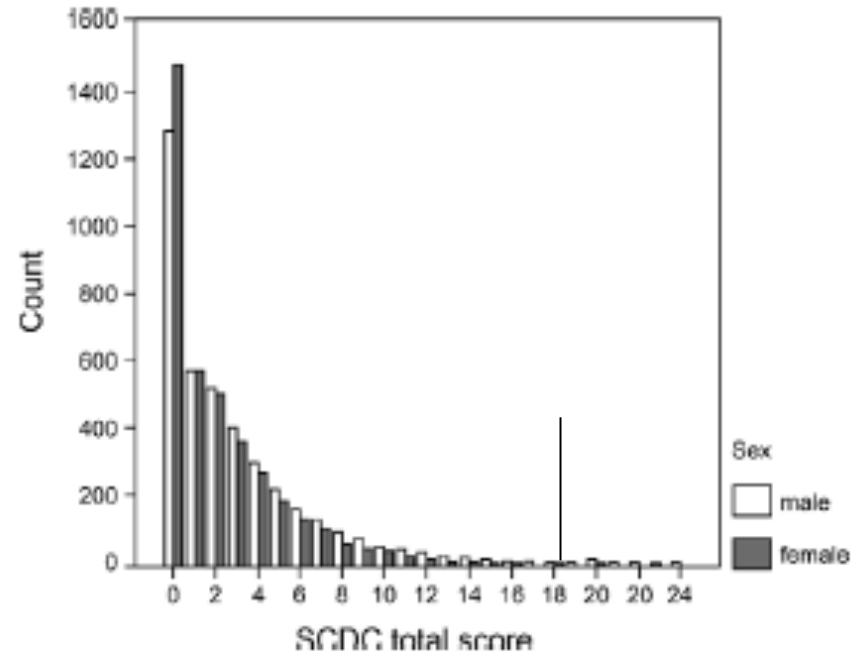
Cases

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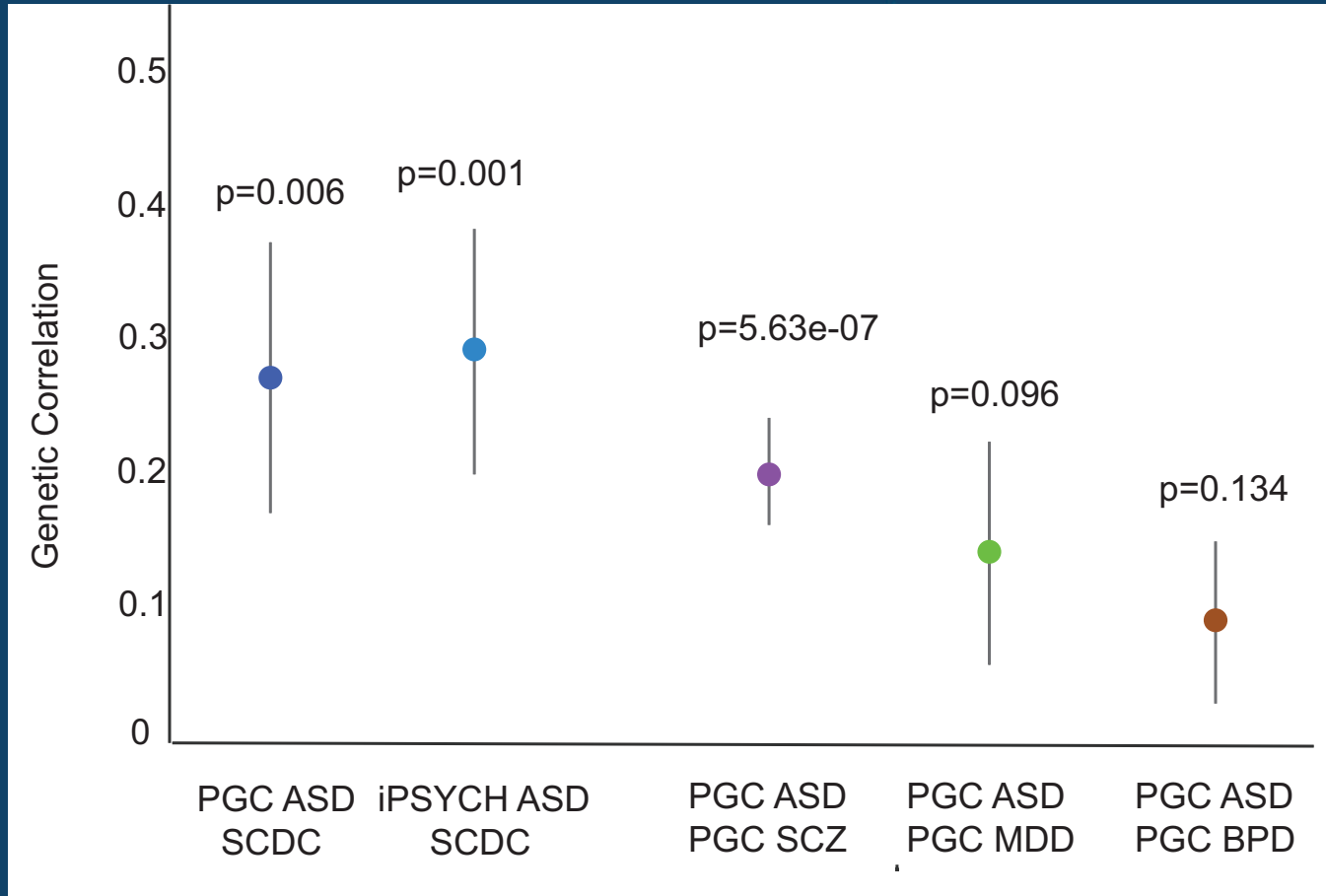
Skuse et al. JAACAP 2011

An old idea, particularly  
with regard to  
unaffected family  
members



**Fig. 1** Distribution of Social Communication Disorders Checklist (SCDC) scores as a function of sex ( $n = 8,094$ ).

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Robinson, St. Pourcain et al., 2016

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Genetic Risk Factor





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## Thanks

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