



Genetic and Environmental Contributions to Anxiety

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Disclosures

I have the following relevant financial relationship with a commercial interest to disclose:

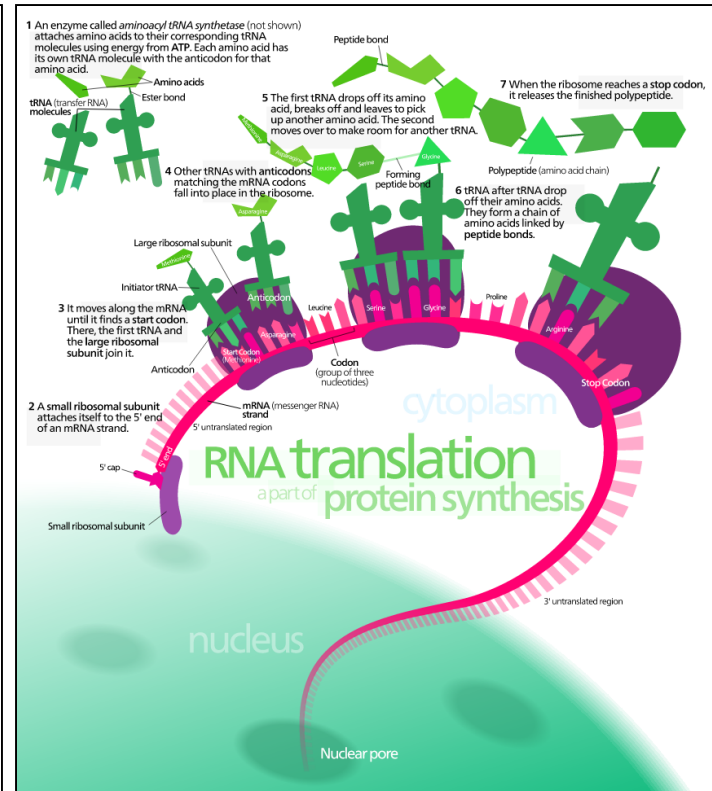
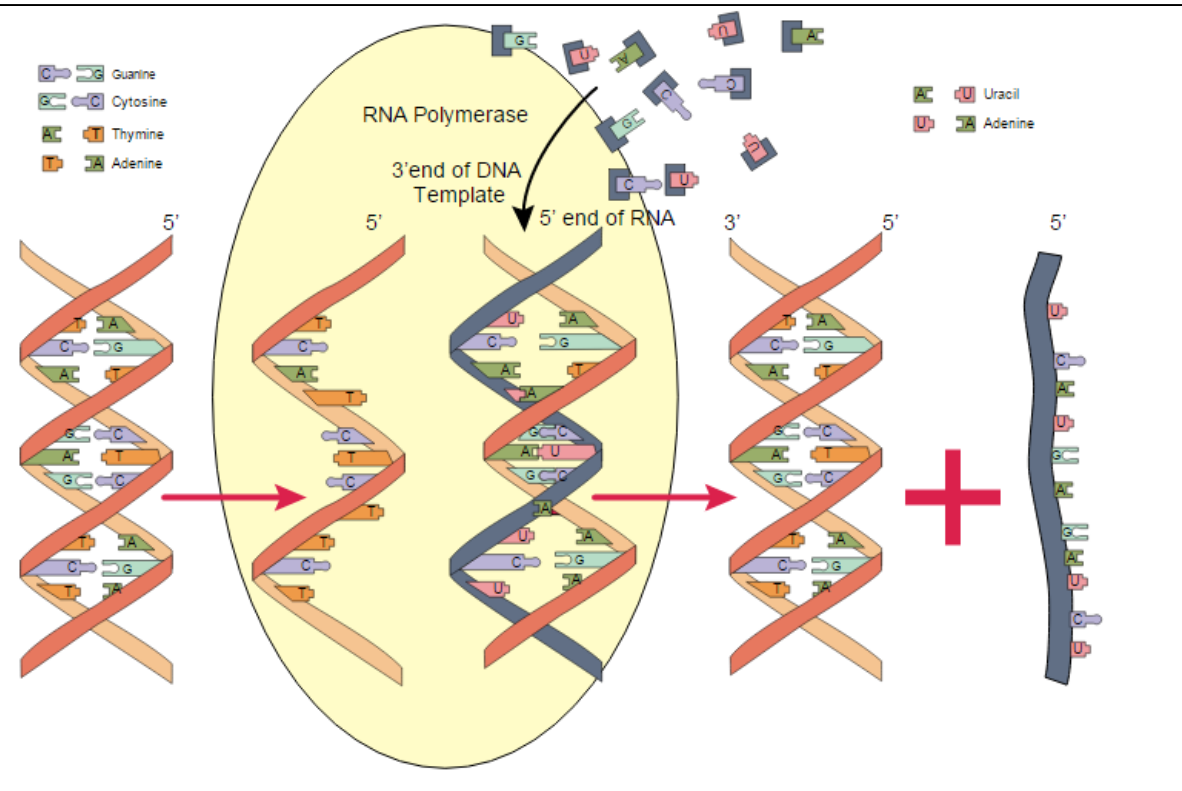
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- **Ownership Equity (Partner):** WISER Systems, LLC

Objectives

- By the end of this brief session, you will be able to:
 - Describe the basic concepts of genetics and genetic epidemiology
 - Discuss the heritability of anxiety disorders
 - Discuss gene x environment interactions and correlations as they related to anxiety disorders
 - Explain specific genes associated with anxiety disorders

Central Dogma

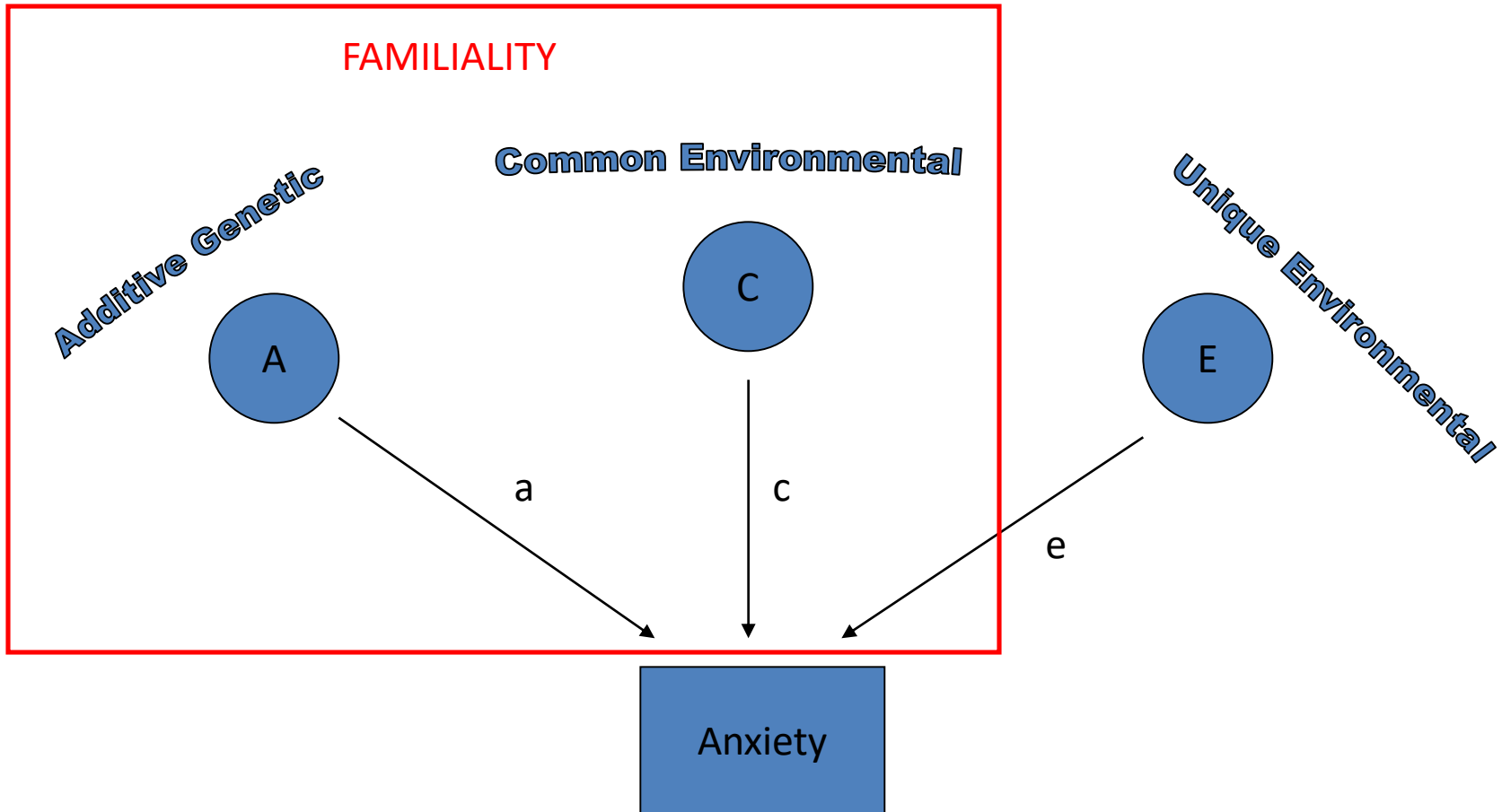
- DNA → RNA → Protein



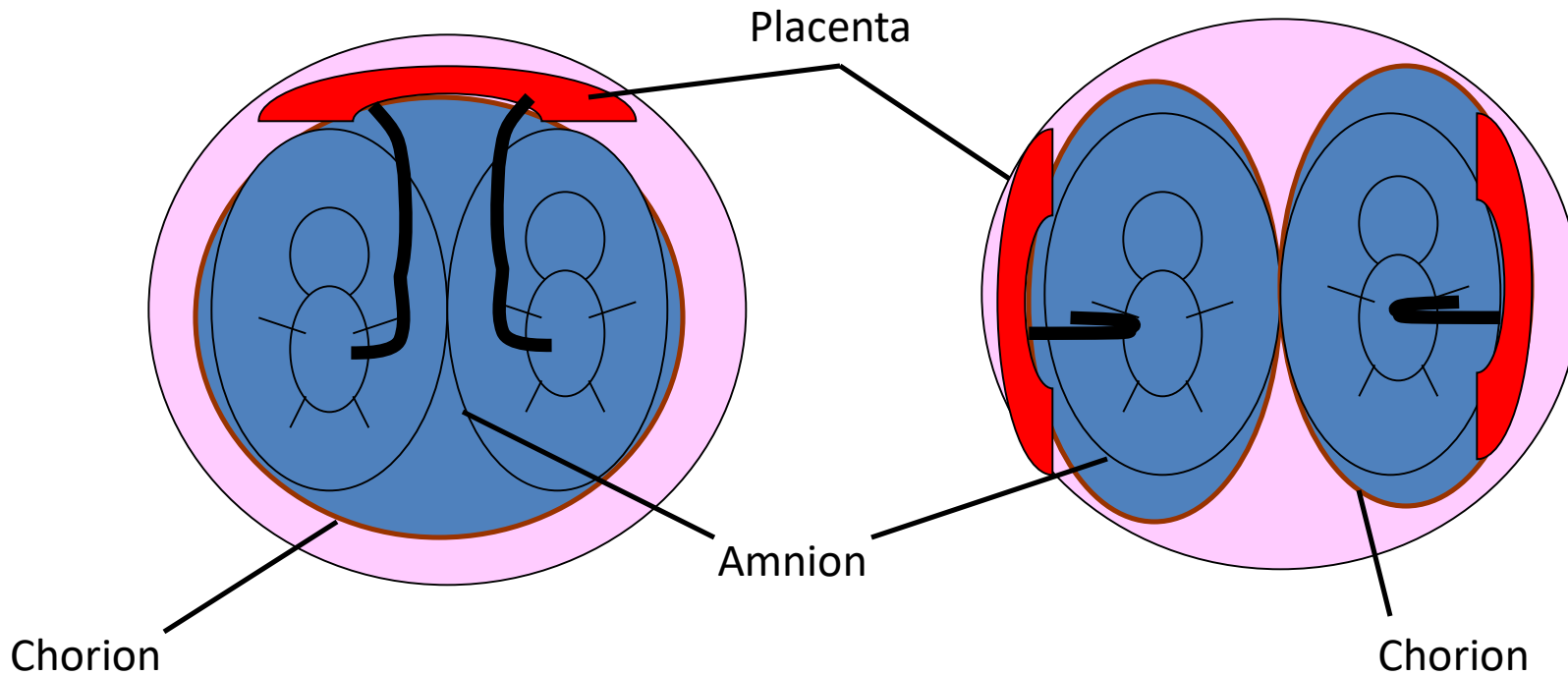
"Rna syn" by Fred the Oyster. The source code of this SVG is valid. This vector graphics image was created with Adobe Illustrator.. Licensed under GFDL via Wikimedia Commons - https://commons.wikimedia.org/wiki/File:Rna_syn.svg#/media/File:Rna_syn.svg

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Genetic and Environmental Contributions to SUD



Twin Studies



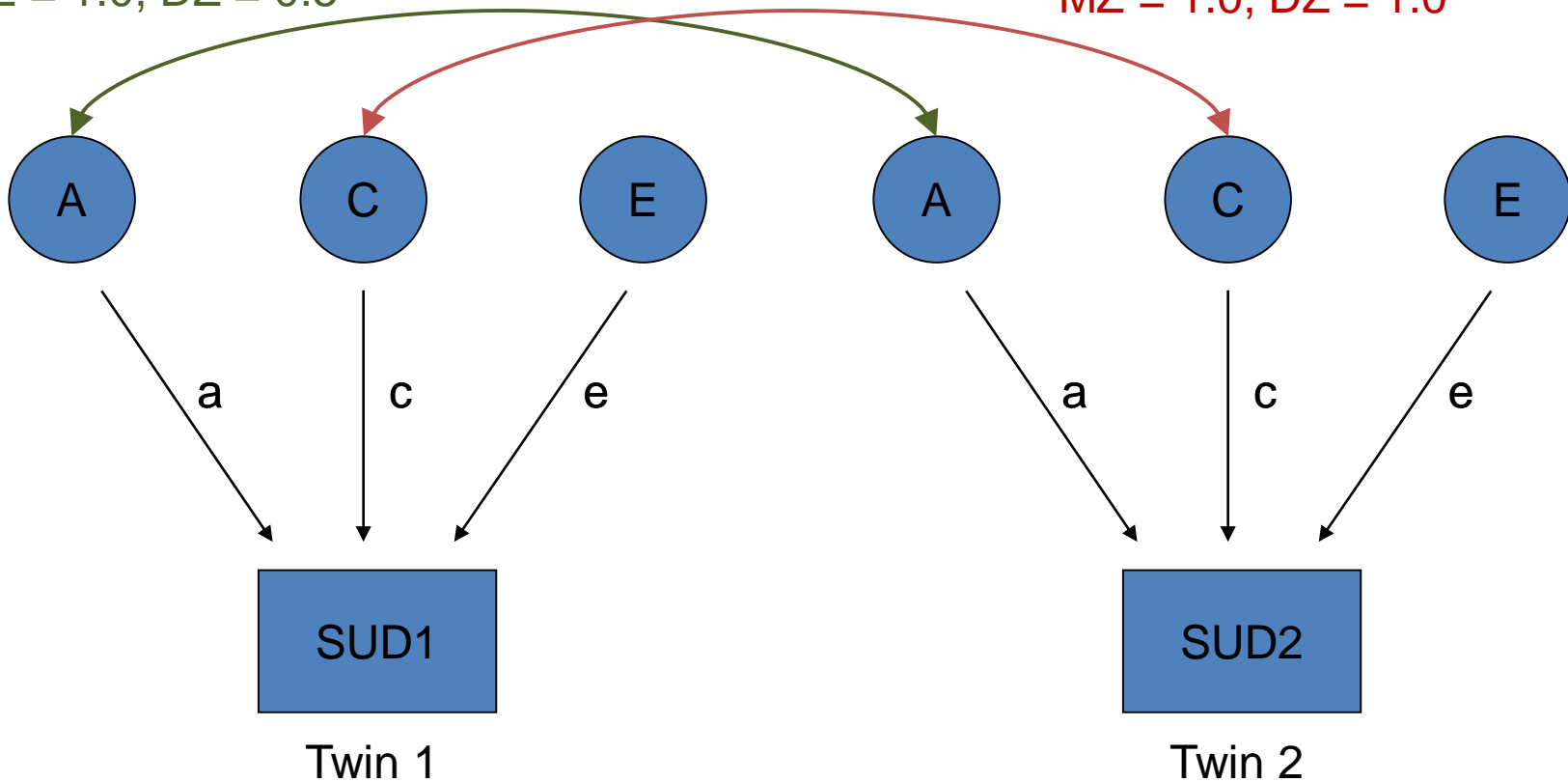
Monozygotic (MZ) twins
Share 100% of DNA

Dizygotic (DZ) twins
Share 50% of DNA

Twin Models

MZ = 1.0, DZ = 0.5

MZ = 1.0, DZ = 1.0



Heritability of Anxiety Disorders

Table 1. Summary and meta-analysis of twin studies for anxiety disorders

Disorder	Reference	Number of studies	N	Sex	a ²	c ²	e ²
PD	Hettema <i>et al.</i> , ⁹ 2001	3	9007	M, F	0.43 (0.32–0.53)	–	0.57 (0.47–0.68)
Agoraphobia	Kendler <i>et al.</i> , ¹⁰ 1992	1	2163	F	0.39	–	0.61
	Kendler <i>et al.</i> , ¹¹ 2001	1	2396	M	0.37	–	0.63
GAD	Hettema <i>et al.</i> , ⁹ 2001	2	12 924	M	0.32 (0.24–0.39)	–	0.68 (0.61–0.76)
SAD	Scaini <i>et al.</i> , ¹² 2014	5	20 433	M, F	0.27 (0.12–0.42)	0.04 (–0.01–0.09)	0.69 (0.59–0.79)
Animal phobia	Van Houtem <i>et al.</i> , ¹³ 2013	5	17 904	M, F	0.32 (0.22–0.44)	–	–
Situational phobia	Van Houtem <i>et al.</i> , ¹³ 2013	4	16 474	M, F	0.25 (0–33)	–	–
Blood-injury-injection phobia	Van Houtem <i>et al.</i> , ¹³ 2013	3	10 741	M, F	0.33 (0.28–0.63)	–	–

Confidence intervals are shown in parentheses.

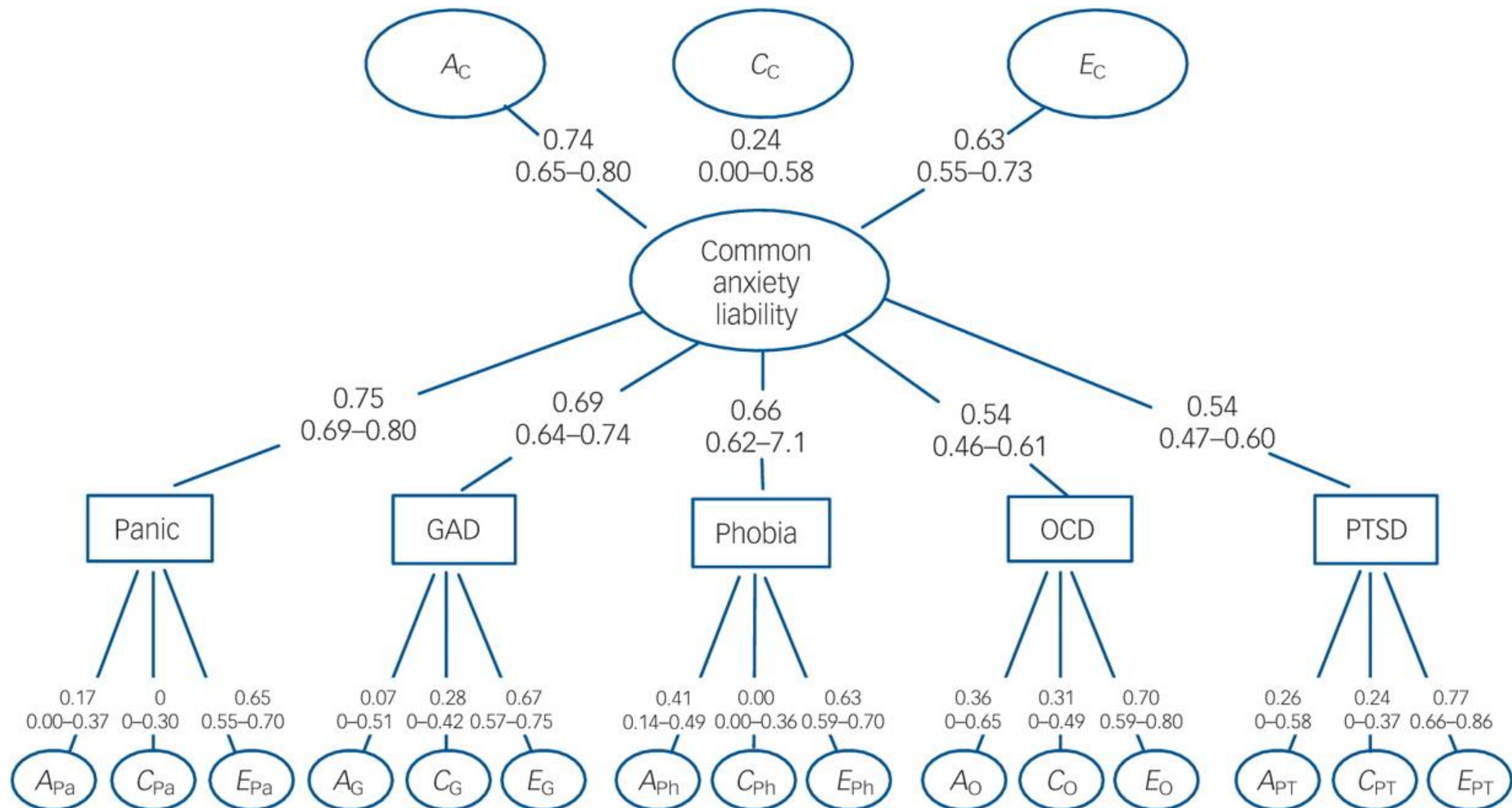
Additive genetic effects (a²) represent the genetic component of variance due to the average effects of single alleles and are known as heritability; shared environment effects (c²) are explained by events that happen to both twins, affecting them in the same way; non-shared environment effects (e²) are explained by events that occur to one twin but not the other, or events that affect either twin in a different way.

GAD, generalized anxiety disorder; PD, panic disorder; SAD, social anxiety disorder.

Heritabilities range from 20-50% for the anxiety disorders, with the highest heritability for panic

From Shimada-Sugimoto, Otowa, & Hettema (2015)

How Specific is the Heritability?



From Tambs et al (2009)

The Environment



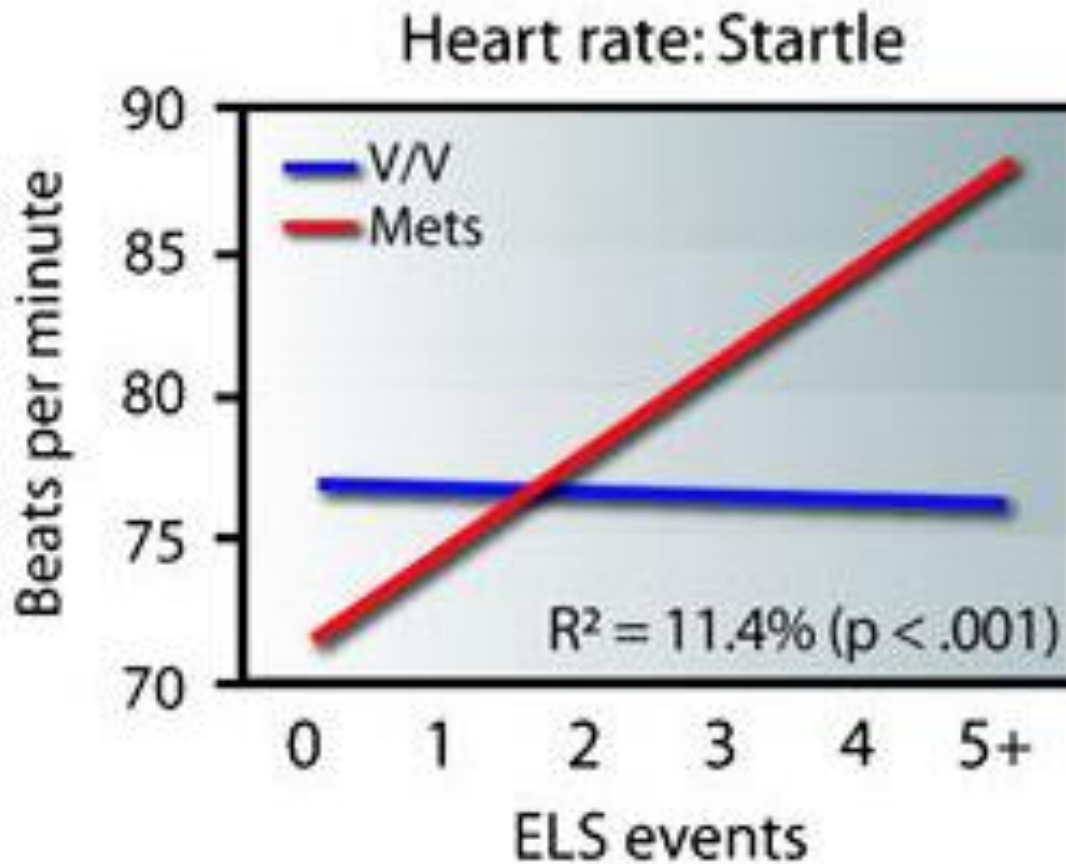
“What is inherited is the manner of reaction to a given environment”

- Dr. Elmer G. Heyne (1912 – 1997), Wheat Geneticist

Possible Roles for the Environment

- Direct effects on initiation and maintenance of anxiety
 - Especially true for disorders such as phobias, PTSD, Acute Stress Disorder, panic
- Gene-environment correlation
 - Genetic factors associated with anxiety and with environments that promote them are correlated
 - For example, parents who are more anxiety prone are more likely to set up a anxiogenic environment for their children
- Gene-environment interaction
 - Genetic risk only evident when placed in a fertile environment

Gene–Environment Interaction



Data from Gatt et al (2009)

Specific Molecular Genetic Risks

- Broad heritabilities not useful clinically
- Are there specific genes that place one at risk?
- Results from either:
 - Candidate gene studies: studies that examine specific genes thought to be associated
 - Genome-Wide Association Studies (GWAS): studies that look at markers across the entire genome
 - There have been 13 published GWAS indexed in PubMed in just the past 12 months

Molecular Genetic Findings

- Single-nucleotide polymorphisms (SNPs) from GWAS most likely to be involved:
 - *TMEM132D* on 12q24.3– associated with panic disorder (with replication). Is involved with oligodendrocyte differentiation.
 - *SLC6A4* – Serotonin transporter gene associated in family studies and candidate gene studies.
 - *MAGI1* – Associated in meta-analyses with neuroticism. Involved in protecting DNA against alkylating agents.
- SNP-based polygenic risk scores have been shown to be predictive of neuroticism

Summary

- Anxiety disorders are heritable, but probably due to multiple genes with additive effects
- There are likely gene-environment correlations and interactions involved in the expression of anxiety disorders
- Thus far, there are no reliable markers for predicting anxiety disorders using genetics

Thank you!

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