

Some Extensions to GCTA

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Methods for Human Complex Traits

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“Quantitative Genetics”

Estimates genetic (and environmental) contribution to variation by regressing measures of phenotypic similarity on genetic (and environmental) similarity

Classical Approach (Fisher, Wright, Falconer, Mather etc.)

Estimates genetic correlation from expected genetic resemblance based on genetic relatedness (MZ, DZ twins, siblings, half-siblings, cousins etc.)

“GCTA”

“Genome-Wide Complex Trait Analysis”

Visscher, Yang, Lee, Goddard

Estimates genetic correlation from empirical genetic resemblance of “unrelated” individuals based on identity by state across using genome-wide single nucleotide polymorphisms (“SNPs”)

Basic GCTA Model

$$V = G + E$$

V=Phenotypic variance between individuals

G=(Additive) genetic variance

E=(Unique) environmental variance

$$\Sigma = \mathbf{A}G + \mathbf{I}E$$

Where Σ = expected phenotypic covariance matrix between individuals; $\mathbf{A}$ = empirical genetic relatedness matrix between individuals

BUT....

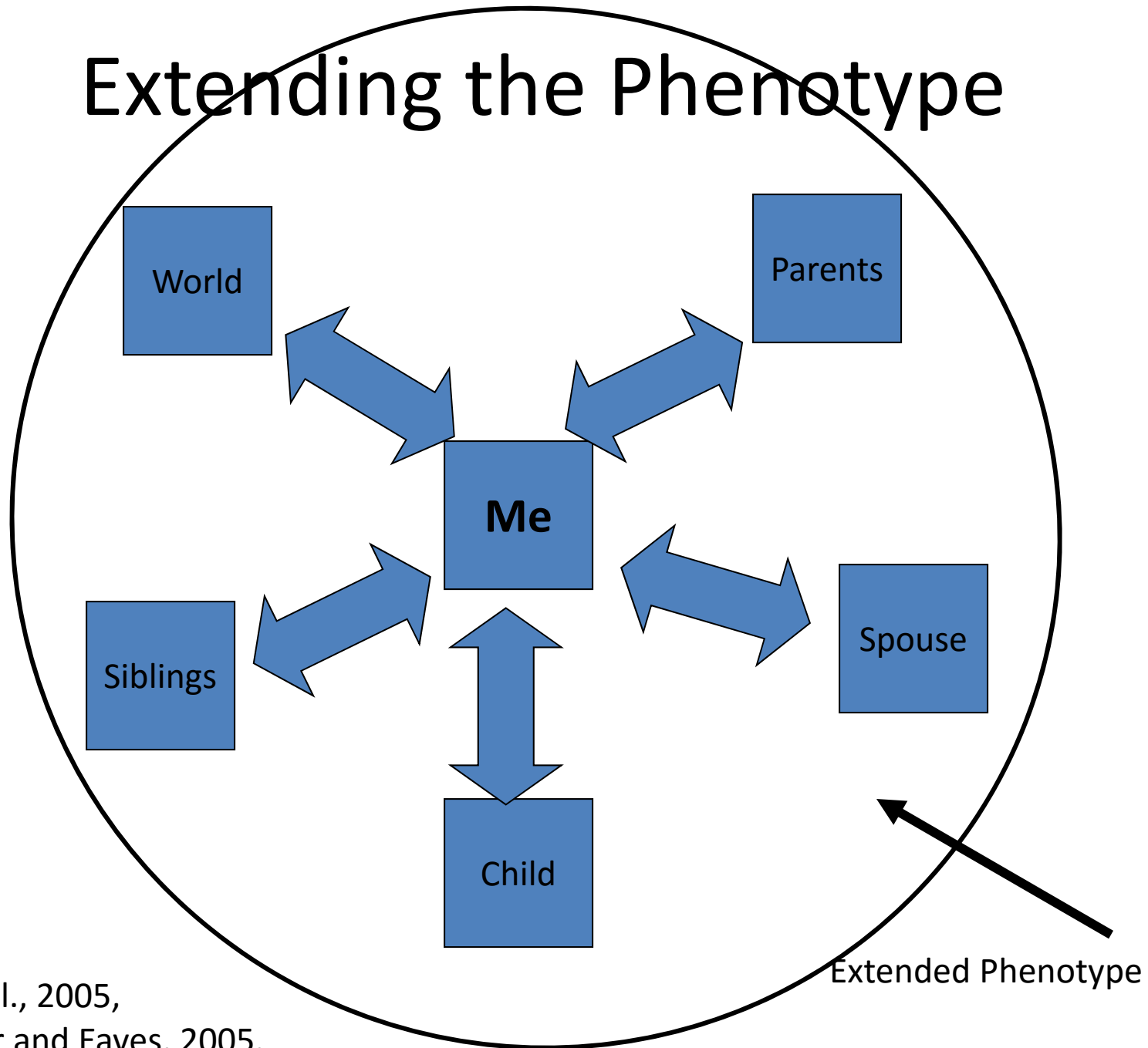
Humans are “More than”
individual packets of DNA – have
families, feet, brains and
communities

Genetic Effects on Behavioral
phenotype extend beyond
individual

Questions for GCTA:

- 1. **What can go wrong with GCTA** if you ignore other genetic and environmental processes known to affect variation in natural populations and human traits? [Negative heuristic]
- 2 **How might GCTA be enhanced** to encompass some of the subtleties of quantitative inheritance recognized in plant and animal species and human kinship studies? [Positive heuristic]

Extending the Phenotype



Eaves et al., 2005,
In Kendler and Eaves, 2005.

Can analyze in family studies
e.g. twins and kinships of twins

