Environmental influences from the perspective of behavior genetics

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Twin studies of common phenotypes: MZ twins

Phenotype	rMZ	
BMI (age 20 yrs)	.80	[Fabsitz et al, 1992]
IQ (age 7 years)	.76	[Bishop et al, 2001]
Alcohol, ever use (girls, 13-16)	.84	[Maes et al, 1999]
Alcohol use without permission	.80	
Depression (Finns, female)	.43	[Wamboldt et al, 2000]
Atopy (Finns, female)	.30	
Heart rate, resting (age 7)	.65	[VanHulle et al, 2000]
HDL cholesterol (14 years)	.81	[Nance et al, 1998]
Neuroticism (females, Australia)	.50	[Eaves et al, 1998]
Extraversion (females, Australia)	.52	

Twin studies of common phenotypes: DZ twins

Phenotype	rDZ	
BMI (age 20 yrs)	.42	[Fabsitz et al, 1992]
IQ (age 7 years)	.40	[Bishop et al, 2001]
Alcohol, ever use (girls, 13-16)	.75	[Maes et al, 1999]
Alcohol use without permission	.42	
Depression (Finns, female)	.16	[Wamboldt et al, 2000]
Atopy (Finns, female)	.15	
Heart rate, resting (age 7)	.44	[VanHulle et al, 2000]
HDL cholesterol (14 years)	.21	[Nance et al, 1998]
Neuroticism (females, Australia)	.24	[Eaves et al, 1998]
Extraversion (females, Australia)	.16	

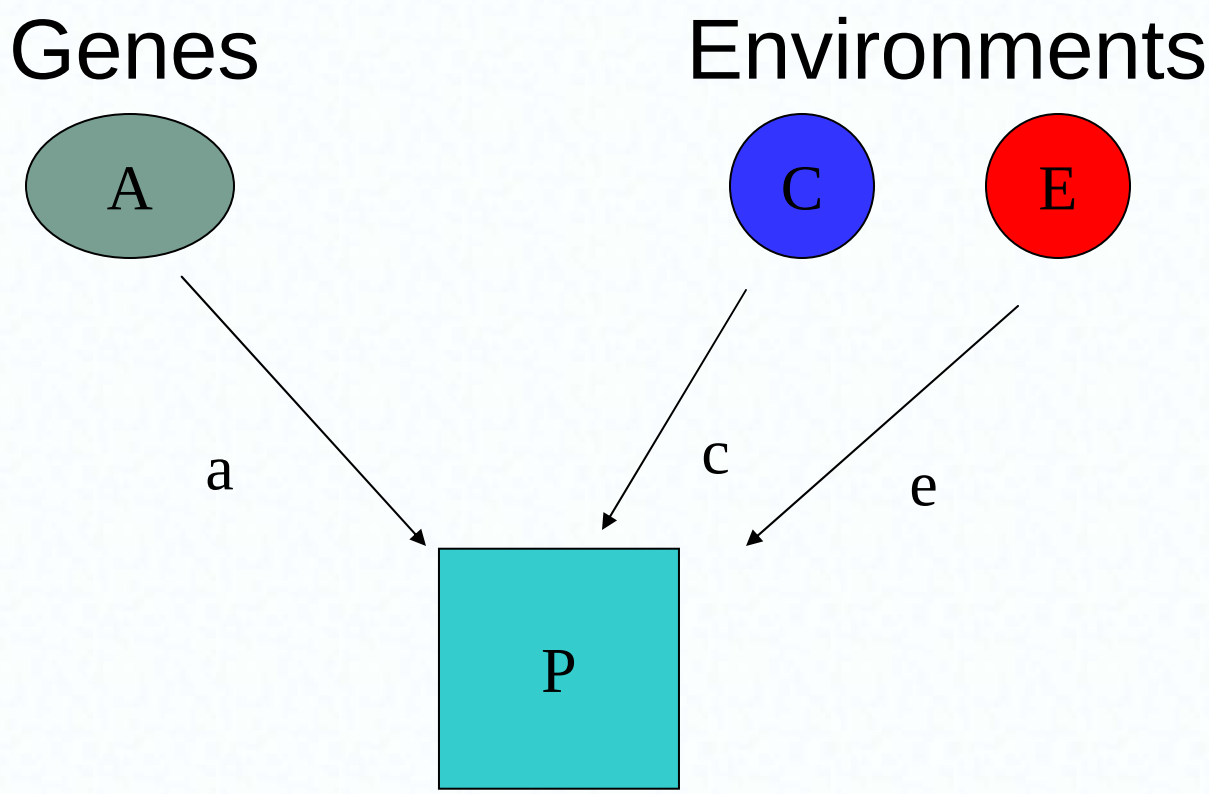
Twin studies of common phenotypes

Phenotype	rMZ	rDZ	
BMI (age 20 yrs)	.80	.42	[Fabsitz et al, 1992]
IQ (age 7 years)	.76	.40	[Bishop et al, 2001]
Alcohol, ever use (girls, 13-16)	.84	.75	[Maes et al, 1999]
Alcohol use without permission	.80	.42	
Depression (Finns, female)	.43	.16	[Wamboldt et al, 2000]
Atopy (Finns, female)	.30	.15	
Heart rate, resting (age 7)	.65	.44	[VanHulle et al, 2000]
HDL cholesterol (14 years)	.81	.21	[Nance et al, 1998]
Neuroticism (females, Australia)	.50	.24	[Eaves et al, 1998]
Extraversion (females, Australia)	.52	.16	

- Environmental variation is partitioned into
- C: shared environmental variation. I.e. shared by family members or common to family members, making them more similar to each other. (This may include shared errors of measurement.)
- E: non-shared environmental variation. I.e. specific to individuals, even in the same household, making them different from each other. (This may include random measurement error).

- The (additive) genetic variation is often referred to simply by the letter A.

Correlation	Average |difference| sd units	BMI (sd=3)	IQ (sd=15)	% of popn. |difference|
0.0	1.13	3.4	17.0	100%
0.2	1.01	3.0	15.2	89%
0.4	0.88	2.6	13.1	78%
0.6	0.71	2.1	10.7	63%
0.8	0.51	1.5	7.6	45%
1.0	0.00	0.0	0.0	0%


Genes
Environments
A
C
E
a
c
e
P

With some simplifying assumptions:

- Heritability = 2 (rMZ – rDZ)
- Shared environment = 2 rDZ – rMZ
- Non-shared environment = 1 - rMZ

Twin studies of common phenotypes

Phenotype	Genetic	Environmental	
		Shared	Non-shared
BMI (age 20 yrs)	.76	.04	.20
IQ (age 7 years)	.72	.04	.24
Alcohol, ever use (girls, 13-16)	.18	.66	.16
Alcohol use without permission	.76	.04	.20
Depression (Finns, female)	.43	---	.57
Atopy (Finns, female)	.30	.00	.70
Heart rate, resting (age 7)	.42	.23	.35
HDL cholesterol (14 years)	.81	---	.19
Neuroticism (females, Australia)	.50	---	.50
Extraversion (females, Australia)	.52	---	.48

Individuals who share their family environment (C) and are genetically identical across the entire genome are quite similar, but not identical.

Individuals who share their family environment (C) but only half of their genes are somewhat similar but often very different.

Environmental differences within families (E) *may* be as important as environmental differences between families.

Genetic and environmental influences may change, and change in importance across the life span

- Two illustrative examples:
- BMI
- Substance use and abuse

NHLBI twin study of obesity

(Fabsitz, Carmelli, and Hewitt, 1992)

Age (yrs)	rMZ (124 pairs)	rDZ (119 pairs)
20	.80	.42
48	.73	.44
57	.72	.35
63	.69	.35

Proportions of variance in BMI

Age (years)	Genetic	Environmental	
		Shared	Non-shared
20	.82	.00	.18
48	.78	.00	.22
57	.73	.00	.27
63	.73	.00	.27

Proportions of variance in BMI

Age (years)	Genetic		Environmental	
	Total	New	Total	New
20	.82		.18	
48	.78	.48	.22	.21
57	.73	.05	.27	.20
63	.73	.02	.27	.12

There are substantial genetic influences on BMI throughout adulthood, and some genetic influences in middle age that are independent of genetic influences in younger adults.

Individuals who are leaner for environmental reasons early in adult life are unlikely to sustain their leanness. Environmental influences need to be chronic to be influential over long periods.

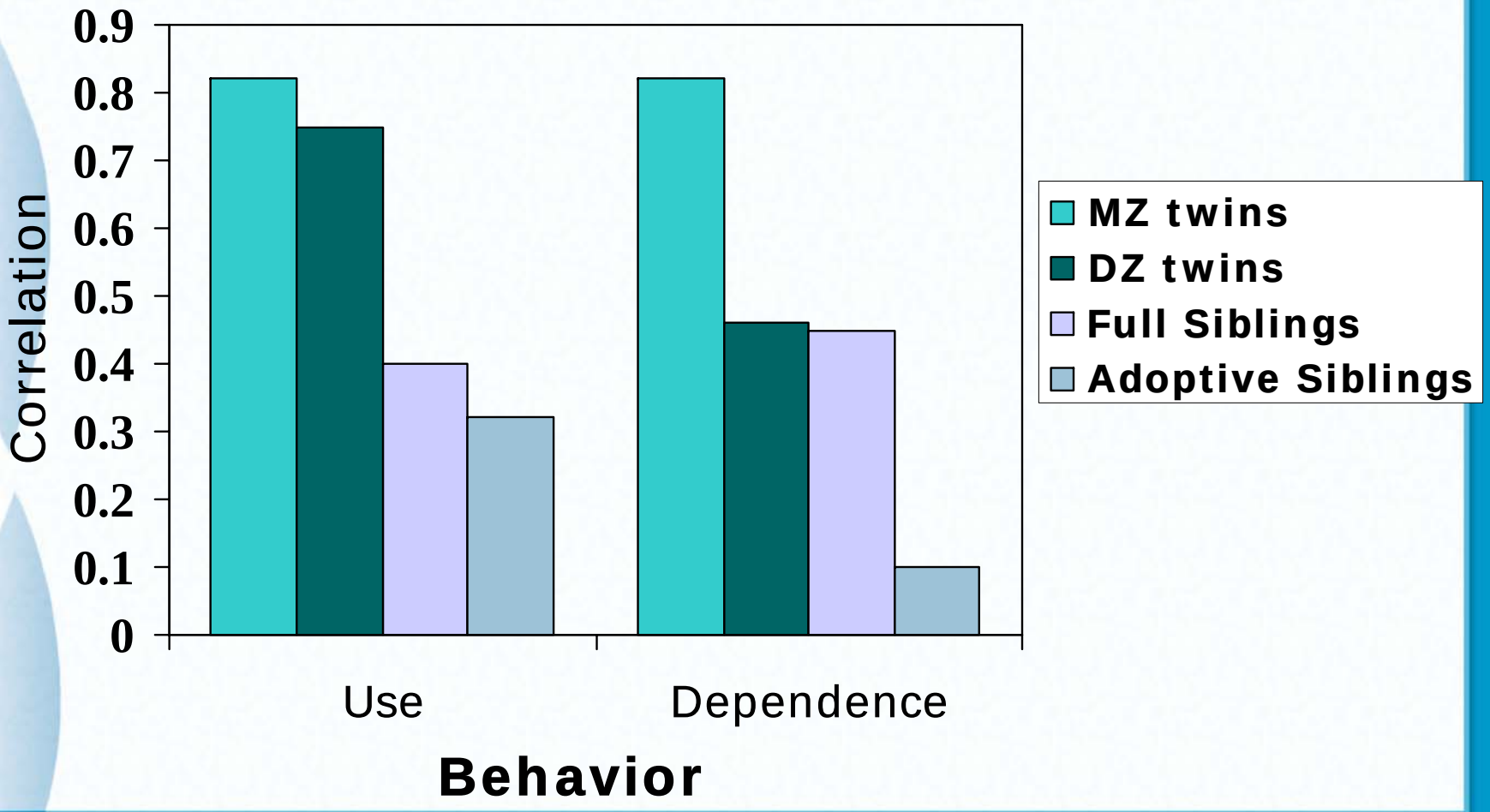
Human twin, family, and adoption studies of substance use/abuse/dependence

Rhee, Hewitt, Young, Corley, Crowley, & Stallings (2003) Genetic and environmental influences on substance initiation, use, and problem use in adolescents. *Arch Gen Psychiatry*. 60:1256-1264

Young, Corley, Stallings, Rhee, Crowley, Hewitt (2002) Substance use, abuse and dependence in adolescence: prevalence, symptom profiles and correlates. *Drug Alcohol Depend*. 68: 309-22.

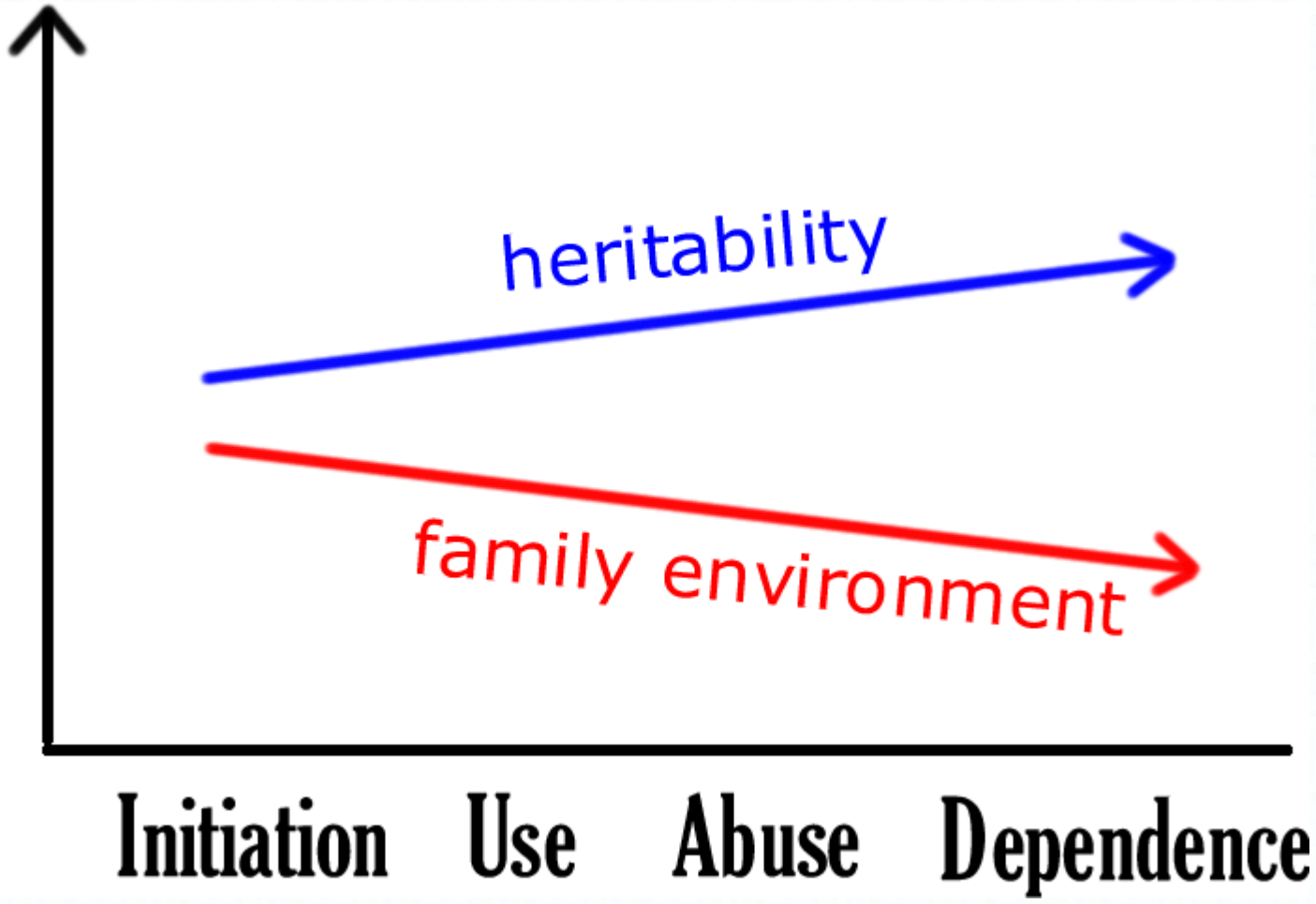
- Substance use and the development of dependence symptoms are common in adolescence.
- By age eighteen, 70% of adolescents are experimenting with alcohol, 1 in 3 with marijuana, 1 in 3 with tobacco, 1 in 10 with other illicit drugs. 1 in 5 show dependence on some substance (often nicotine).
- There are few marked sex differences in substance use or dependence.
- There is a marked, almost linear, increase in substance use and then dependence during the high school years.

Family resemblance for `any drug' in the Colorado Drug Research Center (Rhee et al, 2003)



- All aspects of substance use show family similarity.
- At least some of the family similarity appears to be genetic, especially for abuse and dependence.
- The shared environmental influences are more marked for close age siblings, underscoring the likely importance of peer influences.

Substance Use/Abuse



What kinds of environments do social scientists measure?

The National Longitudinal Study of Adolescent Health (AddHealth)

Kathleen Mullan Harris, Director
Carolina Population Center
University of North Carolina at Chapel Hill

UNC
CAROLINA
POPULATION
CENTER

Longitudinal View of Add Health

Adolescence		Young Adulthood	
Wave I	Wave II	Wave III	Wave IV
1994-95	1996	2001-02	2007-08
12-19	13-20	18-26	24-32
Social environmental data:			
school	school	college	college
family	family	family	family
romantic rel	romantic rel	romantic rel	romantic rel
neighborhd	neighborhd	neighborhd	neighborhd
community	community	community	community
peer			work

Illustrations of Environmental Data

- School and College: private/public, % students who smoke, % students live with two bio parents, school cohesion, race and ethnic composition, socioeconomic status, PTA participation….
- Family: parental educ, parental monitoring, parents' health, childhood maltreatment, household structure, closeness, shared activities.…
- Neighborhood and Community: crime, violence, poverty, residential segregation, unemployment, % foreign born, religious participation, social capital, food prices, access to parks and rec centers, STD prevalence, cigarette and alcohol taxes, welfare policies….
- Romantic relationships: intimacy, communication, commitment, progression of sexual activity.…
- Peer: risk behavior, achievement, attitudes….

Elaborations of the simplest view of genes and environments:

- g,e correlation;
- migration;
- g x e interaction;
- assortative mating;
- non-additive genetic variation;
- social interaction;
- observer effects;
- pleiotropy;
- patterns of development;
- sex-limitation

Lessons from the `Lanarkshire milk experiment'

The comments of W.S. Gosset, better known as `Student', famous as the developer of his t-test.

In his 1931 critique of an epidemiological nutrition study of 20,000 children in Scotland, `Student' proposed that instead of involving 20,000 children in an experiment fraught with possible artifacts, such as non-random assignment to experimental conditions, that a carefully controlled study of 50 pairs of MZ twins would yield more dependable results. He concluded that ``… identical twins are probably better experimental material than is available for feeding experiments carried out on any other mammals, and the error of comparison between them may be relied upon to be so small that 50 pairs of these would give more reliable results than the 20,000 with which we have been dealing'' (`Student', 1931, p.405).

- Gosset’s conclusion, on purely mathematical grounds, is somewhat overstated unless the MZ twin correlation for the dependent variable is very high. However, he was also drawing attention to the very considerable additional advantages of the experimental control that can be exerted when working with a small number of closely matched pairs whose only difference is the experimental

- In our case, different environments are not assigned to the members of the discordant MZ pairs by randomized experimental fiat, and so we still do not have a truly randomized experiment.
- However, members of MZ twin pairs reared together are perfectly matched for genotype, household, age, parents' characteristics, and siblings, among other things.
- As a result, a quasi-experiment comes as close to allowing us to draw causal inferences --- from environment to outcome --- as any possible epidemiological study of the effects of the environment.
- MZ twins also offer exquisite opportunities for the study of gene X environment interaction.
- A relatively small N (say 4000 pairs from 1,000,000) yields considerable power for environmental influences that differentiate individuals within familes (E).

Conclusions

1. Environmental influences differentiate members of a family as well as making them similar.

2. G-e correlations (family genetic variation, migration, environmental selection) complicate the interpretation of epidemiological studies of environmental influences.

3. The influence of the environment may be different at different stages of development. Transitory environments (compared to chronic) often have transitory effects. But our genes are a `chronic influence'.

4. Social scientists have long experience of the assessment of environmental influences on behavior and health ---

I recommend contacting the director of the Add Health study (Kathie Mullan Harris) for advice.

5. The incorporation of a deliberate sampling of MZ twins, with extended assessments of the environment, may provide a powerful, efficient, well controlled, design enhancement for the study of environmental influences and GxE interactions.

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