Smoking and caffeine consumption: A genetic analysis of their association

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Introduction

- Smoking and caffeine consumption are highly correlated
- The mechanism underlying this association is unknown
- Possibly explanation: shared genetic and/or environmental factors
- The *bivariate twin model* estimates genetic & environmental correlations
- Genome wide association (GWA) studies provide an additional method of estimating genetic overlap: *LD-Score regression*[1]

Methods

Bivariate twin models

Data: survey data in 10,620 participants from the Netherlands Twin Register (mean age 32.5 [SD 14.5], 68.1% female)

Measures: current smoking (0=never/former smoking, 1=current smoking) **|** coffee use (0=low, 1=high) **|** total caffeine use (0=low, 1=high)

Analyses: monozygotic (MZ) twins share 100% and dizygotic (DZ) twins ~50%, of their segregating genes; both may share their environment

- if *r*MZ > DZ → additive genetic influences (A)
- if *r*DZ > 0.5 *r*MZ → common environmental influences (C)
- If *r*MZ < 1 → unique environmental influences (E)

LD-Score regression[1]

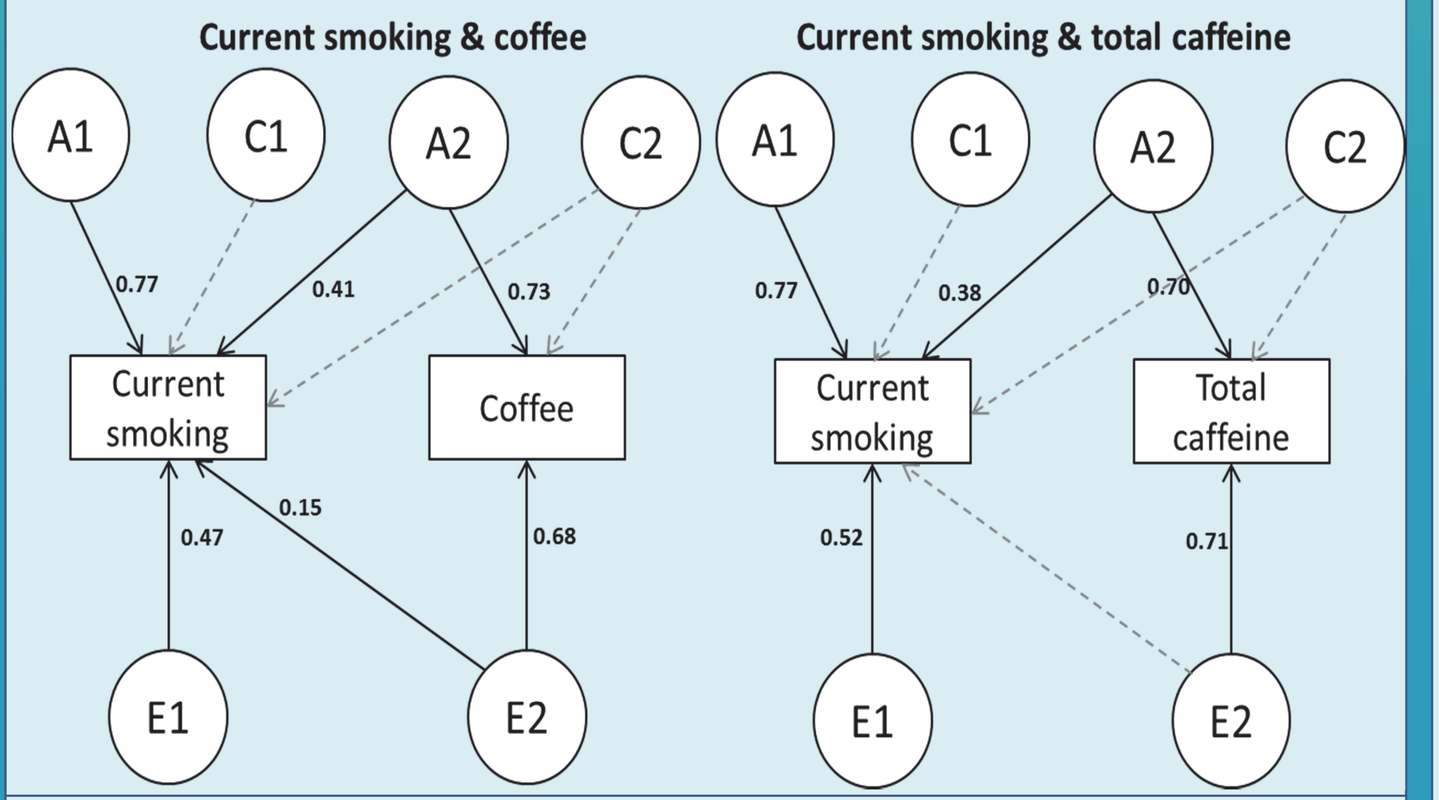
Data: summary statistics from GWA meta-analyses of smoking[2] & coffee[3]

Measures: number of cigarettes per day **|** smoking initiation (0=never smoking, 1=former/current smoking)**|** smoking persistence (0=former smoking, 1=current smoking) **|** cups of coffee per day

Analyses: the expected product for the Z scores of the association between a SNP and two phenotypes (smoking and coffee) is modelled as a function of LD-score (= degree of Linkage Disequilibrium a SNP has with all neighboring SNPs).

Results: bivariate twin models

ACE models (dotted lines were not significant)



Genetic correlation (A) = ***r*0.47**

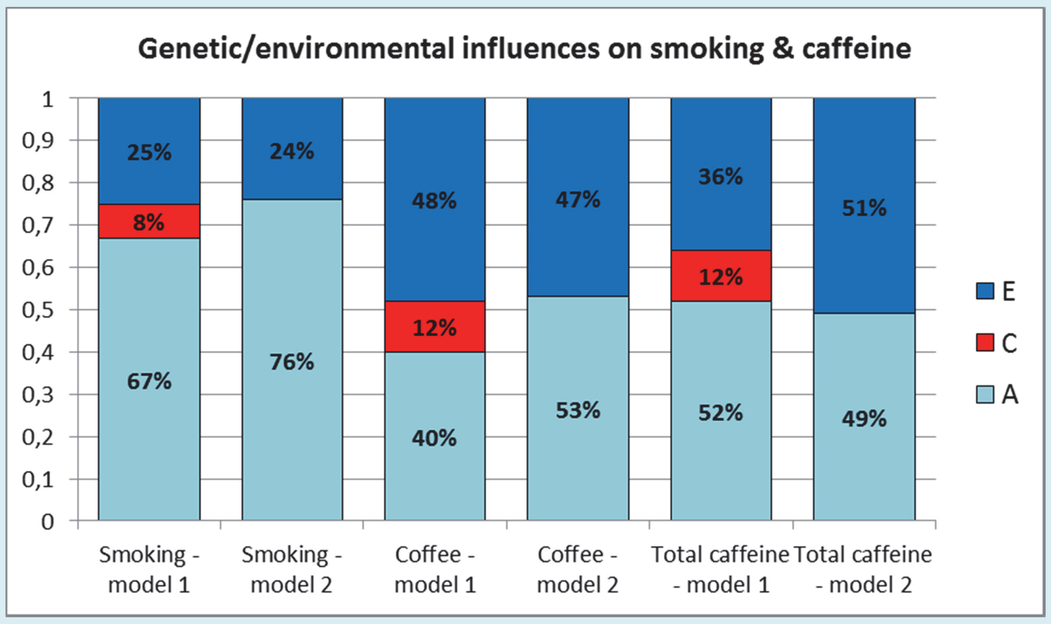
Unique environmental correlation (E) = ***r*0.30**

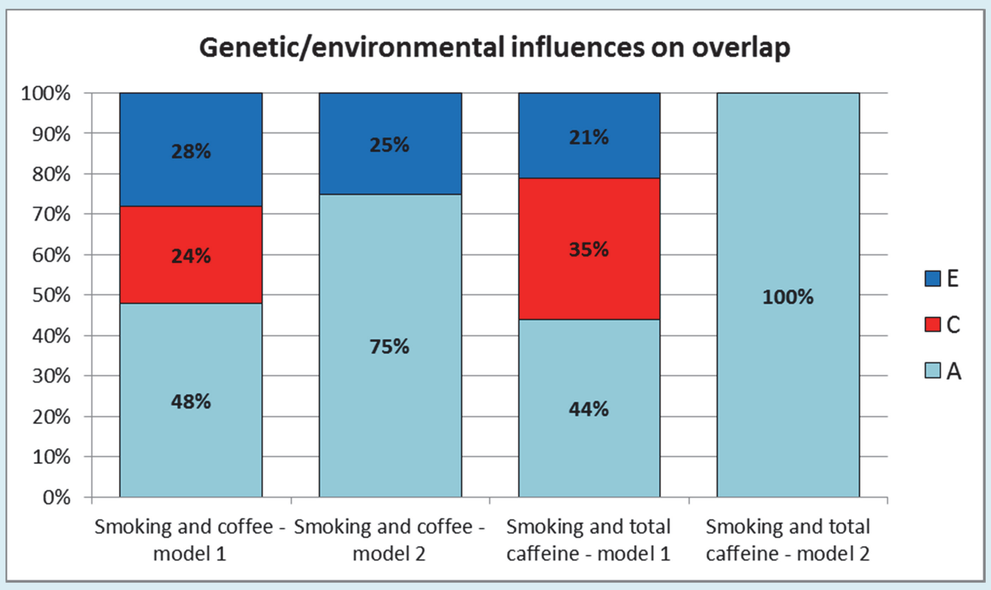
Genetic correlation (A) = ***r*0.44**

Results: LD Score regression (genetic correlations)

- Cigarettes per day & cups of coffee per day = ***r*0.44**
- Smoking initiation & cups of coffee per day = ***r*0.28**
- Smoking persistence & cups of coffee per day = ***r*0.25**

Results: bivariate twin models





Model 1 = initial model, **Model 2** = best-fitting model
A = additive genetic influences, **C** = common environmental influences, **E** = unique environmental influences

Conclusions

- Consistent, moderate genetic correlation between smoking and caffeine consumption
- Genetic factors explain most of the association between smoking & caffeine (similar to previous US-based twin studies)
- Initiating smoking may be especially undesirable for heavy caffeine consumers, given their genetic susceptibility

References:
1. Bulik-Sullivan *et al.* (2015)
2.Tobacco and Genetics Consortium (2010)
3. The Coffee and Caffeine Genetics Consortium (2014)

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