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 regression¹

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 rMZ > DZ → additive genetic influences (A)
- if rDZ > 0.5 rMZ → common environmental influences (C)
- if rMZ < 1 → unique environmental influences (E)

LD-Score regression¹

Data: summary statistics from GWA meta-analyses of smoking² & coffee³

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).

Bivariate twin models

ACE models (dotted lines were not significant)

Current smoking & coffee

Current smoking & total caffeine

Genetic correlation (A) = r0.47
Unique environmental correlation (E) = r0.30

Results: LD Score regression (genetic correlations)

- Cigarettes per day & cups of coffee per day = r0.44
- Smoking initiation & cups of coffee per day = r0.28
- Smoking persistence & cups of coffee per day = r0.25

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References:

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