Smoking and caffeine consumption: observational associations and causality

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Introduction

- Smoking behaviour and coffee consumption are positively associated.
  Little is known about the association between smoking and other types of caffeinated drinks
- Cultural context may affect associations between smoking and caffeine.
  United Kingdom (UK) example of a 'tea-drinking country', *the Netherlands* a 'coffee-drinking country'
- Cause and direction of association between smoking & caffeine unclear→shared genetic and/or environmental influences, or causal effects?

Subjects

Netherlands Twin Register (NTR)
N = 21,872 (*M* age 40.9, 62.6% female, ***Dutch***)
Population based study of twins and family members (started 1987)
Avon Longitudinal Study of Parents and Children (ALSPAC)
N = 9,242 (*M* age 33.1, 100% female, ***British***)
Birth cohort study, women recruited when pregnant (started 1991)
Follow up of the women, their children and partners

Survey data on smoking behaviour and caffeine consumption
Coffee (*75mg caff/cup*) | Tea (*40mg caff/cup*) | Cola (*33mg caff/can*) | Energy drink (*80mg caff/can,* only in NTR)

Methods – *Observational Regression Analyses*

Total group → $Y_{caffeine} = \beta_0 + \beta_1 x_{dummy1} + \beta_2 x_{dummy2} + \beta_3 x_{age} + \beta_4 x_{gender} + \beta_5 x_{education} + \varepsilon$

dummy1 = Former smokers versus Never smokers

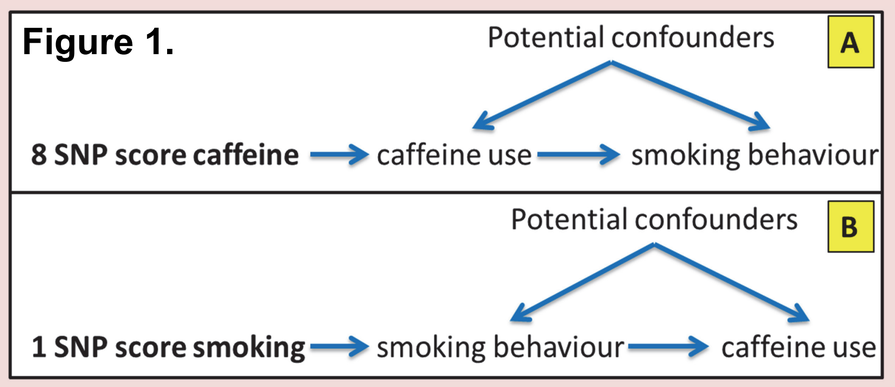
dummy2 = Current smokers versus Never smokers

Current smokers → $Y_{caffeine} = \beta_0 + \beta_1 x_{cigarettesperday} + \beta_2 x_{age} + \beta_3 x_{gender} + \beta_4 x_{education} + \varepsilon$

Methods - *Mendelian Randomization (MR)*

- Utilizes (a) genetic variant(s) associated with a trait as instrument / proxy for that same trait
- Prevents distorting effects of confounders
- Removes possibility of reverse causality

Figure 1.



Note: SNP = Single Nucleotide Polymorphism

- SNP score = risk of a trait based on sum score of 1 or more SNPs (0, 1 or 2 risk alleles per SNP)
- Top SNPs caffeine & smoking taken from previous meta-analyses[1,2]

➢ If **A** (*figure 1*) is significant and **B** is not → possible causal effect caffeine on smoking
➢ If **B** is significant and **A** is not → possible causal effect smoking on caffeine

Results

- Higher coffee intake in Dutch sample, higher tea intake in British sample (*table 1*)
- Smoking behaviour is strongly associated with total caffeine intake and individual caffeinated drinks. Difference in direction between countries for tea (*figures 2 & 3)*
- No significant associations between smoking and decaffeinated coffee

Mendelian Randomization	NTR (n=577/868)	ALSPAC (n=1,180/1,224)
β (p-value) 8 SNP score caffeine → caffeine	8.2 (p 0.39)	**82.9 (p 0.05)**
β (p-value) 8 SNP score caffeine→ smoking	0.03 (p 0.90)	-2.0 (p 0.15)
β (p-value) 1 SNP score smoking → smoking	0.06 (p 0.84)	**0.77 (p <0.01)**
β (p-value) 1 SNP score smoking → caffeine	19.9 (p 0.15)	-9.2 (p 0.34)

Table 1.	NTR ♂ (n=8,171)	NTR ♀(n=13,701)	ALSPAC ♀(n=9,242)
mg caffeine intake coffee (*M* [SD])	280.3 (222.7)	166.3 (174.3)	135.9 (166.3)
mg caffeine intake tea (*M* [SD])	46.2 (68.4)	65.9 (81.3)	121.2 (105.7)
mg caffeine intake cola (*M* [SD])	4.2 (9.9)	2.7 (8.1)	4.7 (7.6)
mg caffeine intake energy drink (*M* [SD])	2.1 (12.7)	1.8 (14.3)	-

Figure 2. Difference in caffeine intake (in mg per day) across smoking status

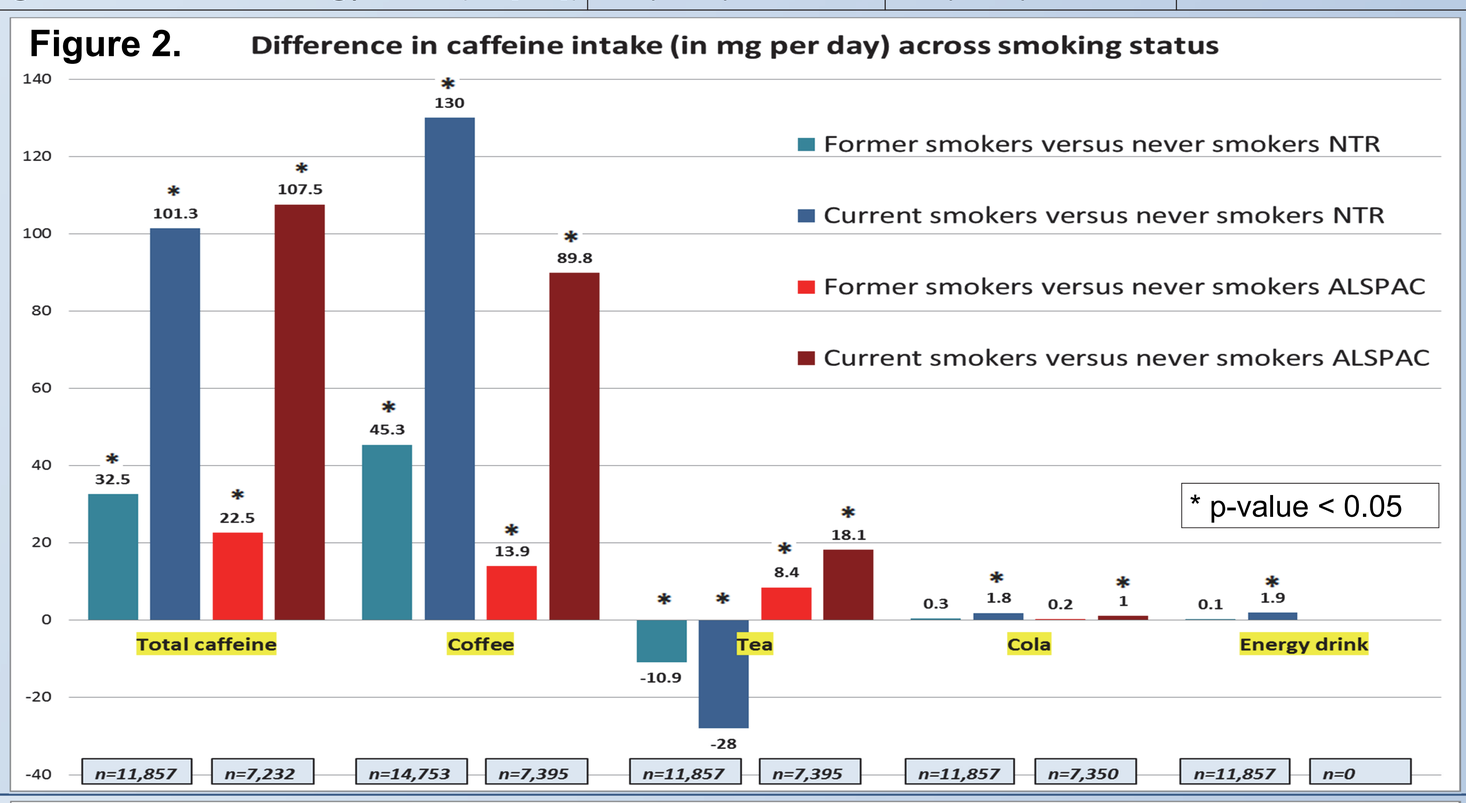
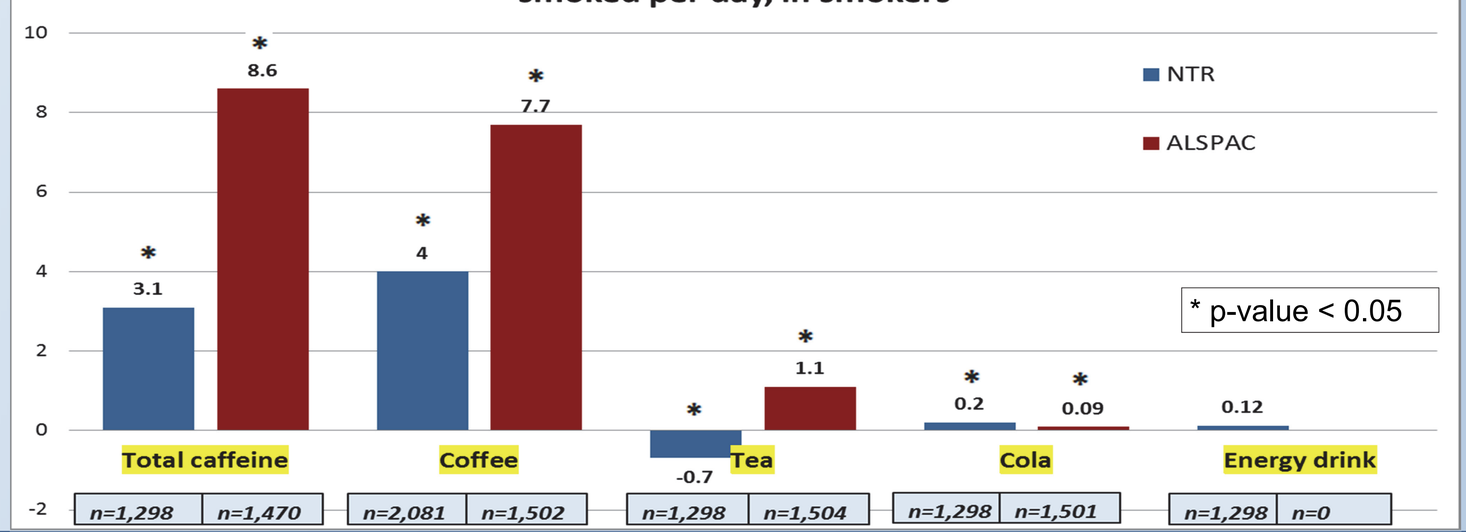


Figure 3. Increase in caffeine intake (in mg per day) per additional cigarette smoked per day, in smokers



Conclusions

- Smoking is associated with increased intake of caffeinated drinks (not explained by age, gender or education)
- Strong cultural difference for tea
- MR shows no evidence for causal effects, replication in larger sample necessary
- Investigation into shared genetic and / or environmental influences is ongoing

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References: 1.The Coffee and Caffeine Genetics Consortium (2014) 2.Tobacco and Genetics Consortium (2010)