Smoking and caffeine consumption: observational associations and causality

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Introduction
- Smoking behaviour and coffee consumption are positively associated.
- Cultural context may affect associations between smoking and caffeine.
- Little is known about the association between smoking and other types of caffeinated drinks.
- Life-style factors (e.g. socio-economic status, educational level) are confounders.
- Cause and direction of association between smoking & caffeine unclear
- Smoking behaviour and coffee consumption are positively associated.
- 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 → Ycoffee = β0 + β1xdummy1 + β2xda dummy2 + β3xage + β4xgender + β5xeducation + ε

dummy1 = Former smokers versus Never smokers
dummy2 = Current smokers versus Never smokers

Current smokers → Ycoffee = β0 + β1xsmokingspentday + β2xage + β3xgender + β4xeducation + ε

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

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

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

Table 1.

<table>
<thead>
<tr>
<th></th>
<th>NTR (n=8,171)</th>
<th>NTR (n=13,701)</th>
<th>ALSPAC (n=9,242)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg caffeine intake coffee (M [SD])</td>
<td>280.3 (222.7)</td>
<td>166.3 (174.3)</td>
<td>135.9 (166.3)</td>
</tr>
<tr>
<td>mg caffeine intake tea (M [SD])</td>
<td>46.2 (68.4)</td>
<td>65.9 (81.3)</td>
<td>121.2 (105.7)</td>
</tr>
<tr>
<td>mg caffeine intake cola (M [SD])</td>
<td>4.2 (9.9)</td>
<td>2.7 (8.1)</td>
<td>4.7 (7.6)</td>
</tr>
<tr>
<td>mg caffeine intake energy drink (M [SD])</td>
<td>2.1 (12.7)</td>
<td>1.8 (14.3)</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 2.

<table>
<thead>
<tr>
<th></th>
<th>NTR (n=577/868)</th>
<th>ALSPAC (n=1,180/1,224)</th>
</tr>
</thead>
<tbody>
<tr>
<td>β (p-value) 8 SNP score caffeine → caffeine</td>
<td>8.2 (p = 0.39)</td>
<td>82.9 (p = 0.05)</td>
</tr>
<tr>
<td>β (p-value) 8 SNP score caffeine → smoking</td>
<td>0.03 (p = 0.90)</td>
<td>-2.0 (p = 0.15)</td>
</tr>
<tr>
<td>β (p-value) 1 SNP score smoking → smoking</td>
<td>0.06 (p = 0.84)</td>
<td>0.77 (p &lt; 0.01)</td>
</tr>
<tr>
<td>β (p-value) 1 SNP score smoking → caffeine</td>
<td>19.9 (p = 0.15)</td>
<td>-9.2 (p = 0.34)</td>
</tr>
</tbody>
</table>

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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