Adverse effects of longer-term and habitual caffeine consumption on the central nervous system and the cardiovascular system

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OVERVIEW

CENTRAL NERVOUS SYSTEM

1. Sleep, anxiety and behavioural changes
   a. *Adults*
   b. *Children*

CARDIOVASCULAR SYSTEM

1. Blood pressure (BP)
2. Hypertension
3. Coronary heart disease (CHD)
4. Atrial fibrillation
5. Heart failure
6. Stroke
7. Cardiovascular disease (CVD)

CENTRAL NERVOUS SYSTEM

1. Sleep, anxiety and behavioural changes

Adults

- Tolerance to anxiogenic effect of caffeine develops with frequent consumption, even in genetically susceptible individuals

Children

- Four cross-over RCTs on effects of caffeine up to 2 weeks
- Caffeine up to ~ 3 mg/kg bw per day does not appear to induce behavioural changes. Studies are small and heterogeneous
- 10 mg/kg bw per day may increase anxiety and adversely affect behaviour and sleep in habitual low caffeine consumers
- Tolerance + withdrawal symptoms induced at > 300 mg/day
- No studies between 3 and 10 mg/kg bw per day

CARDIOVASCULAR SYSTEM

1. Blood pressure (BP)

Caffeine

Prospective cohort studies

- Association between habitual caffeine consumption and long-term changes in BP

  ⇒ mixed results (positive, negative and no association)

CARDIOVASCULAR SYSTEM

1. Blood pressure (BP)

Caffeine

RCT lasting ≥ 7 days

- 3 meta-analysis of RCT in unselected populations (17 studies)

Jee et al., 1999 ⇒ *sustained* BP-raising effect of coffee at ≥ 5 cups, but not at ≤ 4.5 cups

Noordzij et al., 2005 ⇒ sustained BP-raising effect at caffeine doses of ~ 400 mg per day, but not at lower doses

Steffen et al., 2012 ⇒ no significant sustained BP-raising effect of coffee between 3 and 6 cups per day

CARDIOVASCULAR SYSTEM

2. Hypertension

Meta-analysis

- Two meta-analysis including the same 6 prospective cohort studies
- Caffeinated coffee drinking was not significantly associated with an increased risk of hypertension at any category of coffee intake compared to the reference category

CARDIOVASCULAR SYSTEM

2. Hypertension

Prospective cohort studies

- Caffeinated coffee drinking is associated with higher risk of sustained hypertension in untreated stage 1 hypertensive carriers of the slow C/C or C/A allele (59 %) of the CYP1A2 gene ⇒ not the general population
- An increased risk for any level of caffeine intake, an inverse U-shape relationship and no relationship have been reported in unselected populations ⇒ **conflicting** evidence
- Two studies investigating caffeine from all sources ⇒ different (and **conflicting**) associations depending on the source

CARDIOVASCULAR SYSTEM

3. Coronary heart disease (CHD)

Meta-analyses

- Three (1 dose-response) meta-analyses of 56 prospective cohort studies
- Overall coffee not associated with an increased risk of CHD

Prospective cohort studies

- Only 8 (7 before 1995) associated coffee with risk of CHD

  ⇒ most did not control for confounders or used an inappropriate reference category

- Four studies on caffeine from various sources
- Overall no relationship or inverse association between caffeine intake and CHD risk

CARDIOVASCULAR SYSTEM

3. Coronary heart disease (CHD)

Case-control study

- suggests that polymorphisms of the CYP1A2 gene may affect the risk of MI in relation to caffeine consumption
- risk may be further affected by polymorphisms of the serotonin receptor gene HTR2A

but

- results have not yet been replicated or the hypothesis tested in prospective cohort studies

CARDIOVASCULAR SYSTEM

4. Atrial fibrillation

Meta-analyses of prospective cohort studies

- Two meta-analysis including the same 6 prospective cohort studies (+ 1 case-control)
- Three studies on coffee and 3 on caffeine from all sources
- Coffee/caffeine consumption not associated with an increased risk of atrial fibrillation in any meta-analysis or individual study

CARDIOVASCULAR SYSTEM

5. Heart failure

Meta-analysis of prospective cohort studies

- One dose-response meta-analysis including 5 prospective cohort studies
- Most studies on caffeinated coffee
- Caffeinated coffee consumption not associated with an increased risk of heart failure in the meta-analysis or any of the individual studies

CARDIOVASCULAR SYSTEM

6. Stroke

Meta-analyses of prospective cohort studies

- Three (one dose-response) meta-analyses including 20 prospective cohort studies
- Most studies on caffeinated coffee, 4 on caffeine from all sources
- Caffeinated coffee consumption was associated with an increased risk of stroke only in one study in hypertensive subjects which do not represent the general population

CARDIOVASCULAR SYSTEM

7. Cardiovascular Disease (CVD, all outcomes)

Meta-analysis of prospective cohort studies

- One dose-response meta-analysis including 36 prospective cohort studies
- Most studies on caffeinated coffee
- Overall, caffeinated coffee consumption not associated with an increased risk of CVD

CARDIOVASCULAR SYSTEM

Conclusions

- Caffeine intake (from coffee or supplements) of ≤ 400 mg/day does not raise fasting BP significantly after caffeine habituation
- Data on the association between habitual caffeine intake and the risk of hypertension is conflicting
- Hypertension is an established risk factor for CVD (stroke, CHD, heart failure)

BUT

- No increased risk of stroke, CHD and heart failure related to habitual caffeine intakes (mostly from caffeinated coffee), particular not at intakes up to ~ 400 mg/day

LONGER-TERM EFFECTS OF CAFFEINE: CNS AND CVS

OPEN FOR DISCUSSION