Coffee and caffeine consumption are associated with SHBG in the E3N cohort study

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La consommation de café et de caféine est associée à la sex hormone-binding globulin (SHBG) dans la cohorte E3N

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Résumé

Objectif : Une SHBG basse constitue un facteur de risque indépendant de diabète de type 2, en particulier chez la femme. La consommation de café est associée à une réduction du risque de diabète de type 2 mais ses effets sur la SHBG restent mal connus.

Matériel et méthodes : 2453 femmes saines de la cohorte E3N pour lesquelles la SHBG à l'inclusion a été mesurée (ECLA sur Elecsys, Hitachi 911), ont été incluses. Des informations sur leur alimentation (incluant leur consommation de café et de caféine), leur mode de vie et leur santé étaient recueillies. La relation entre la consommation de café et de caféine et la SHBG a été modélisée, avec ajustement sur les facteurs confondants et stratification selon l'IMC et le statut ménopausique.

Résultats : L'âge moyen des 2453 femmes était de 57,3 ± 6,4 ans et 61% d'entre elles étaient ménopausées. Des apports élevés de café (≥3 tasses/jour) ou de caféine (≥265 mg/jour) étaient associés à une diminution du risque de SHBG basse (OR=0,69[0,52-0,92] et OR=0,68[0,50-0,94] respectivement). Après stratification, ces associations n'étaient retrouvées que chez les femmes avec un IMC ≥25 kg/m^2 ou ménopausées. L'association avec la SHBG était observée pour la consommation de caféine, de café caféiné, mais pas avec celle de café décaféiné.

Discussion : Une consommation élevée de café et de caféine est associée à une réduction de 30% du risque de SHBG basse, ce qui peut expliquer leurs effets protecteurs pour le diabète de type 2.

Coffee and caffeine consumption are associated with sex hormone-binding globulin in the E3N cohort study

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Abstract

Objective: Low sex hormone-binding globulin (SHBG) is a consistent risk factor for type 2 diabetes, particularly in women. Coffee consumption is associated with a lower risk of type 2 diabetes but its effects on SHBG are less known.

Design and methods: 2,453 healthy pre- and post-menopausal women from the E3N cohort study whose baseline SHBG was measured, were included. Information on diet (including coffee and caffeine consumption), lifestyle and medical condition was collected through questionnaires. The relationship between coffee and caffeine consumption and SHBG was modeled, with adjustment for covariates and stratification by body mass index (BMI) categories (< or ≥25 kg/m^2) and menopausal status.

Results: Of 2,453 women, mean age was 57.3 ± 6.4 years. High coffee intake (≥3 cups/day) and high caffeine intake (≥265 mg/day) were associated with a reduced risk of low SHBG, defined as < 46.3 $nmol \cdot L^{-1}$, the 1^{st} quartile of the SHBG levels distribution in the population studied (OR: 0.69 [95% CI 0.52-0.92] and OR: 0.68 [95% CI 0.50-0.94] respectively). No association was found between tea consumption and SHBG levels. In multivariable models, after stratification by BMI categories and menopausal status, these associations were observed among women with a BMI ≥25 kg/m^2 or being postmenopausal. The association with SHBG was consistently noted with both consumption of caffeinated coffee and caffeine, but not for decaffeinated coffee.

Discussion: High coffee and caffeine consumptions are associated with an ~30% reduced risk of low SHBG, which might contribute to the protective effects of coffee for type 2 diabetes.

Introduction

Low sex hormone-binding globulin (SHBG) has been identified as a consistent risk factor for type 2 diabetes mellitus (T2DM), particularly in women and in the setting of a low metabolic risk at baseline[1,2]. In addition, Mendelian randomization studies showed that carriers of *SHBG* polymorphisms associated with low SHBG levels had an increased risk of T2DM, suggesting a causal relationship[3–5].

In parallel, coffee consumption is one of the few known dietary protective factors against T2DM. Indeed, coffee and caffeine have been associated with a lower risk of T2DM in several prospective studies, including the E3N/EPIC (Etude Epidémiologique auprès de Femmes de la Mutuelle Générale de l'Education Nationale/European Prospective Investigation into Cancer and Nutrition) cohort study[6]. Recent meta-analyses reviewed this relationship and showed a ~30% reduced risk of T2DM for the highest levels of coffee or caffeine intakes[7–9].

The mechanisms of this protective effect of coffee on the risk of type 2 diabetes have not been clearly identified. It has been suggested that SHBG may mediate the association between coffee and caffeine consumption and the risk of T2DM. Indeed, the inverse associations of caffeinated coffee and caffeine with T2DM risk was no longer significant after adjustment for plasma SHBG in a case-control study in postmenopausal women with or without T2DM[10].

An inverse relation between coffee and caffeine intake and SHBG has been observed in most studies conducted in postmenopausal women[10–13], but studies which investigated this relation in premenopausal women, showed in contrast conflicted and inconclusive results[13–17].

Therefore, the aim of that study was to investigate the relationship between both coffee and caffeine consumption and plasma SHBG concentration in a large population of pre- and postmenopausal women who had a detailed estimation of their diet habits but also of physical

activity, which could be a potential confounding factor in the relation between low SHBG concentration and the risk of diabetes[2,18].

Subjects and methods

Study population

The E3N cohort study is the French component of the European Prospective Investigation into Cancer and nutrition (EPIC)[19]. 98,995 French female aged 40-65 years were included in 1990 after returning mailed questionnaires about their lifestyle and medical condition. These information were updated every 2-3 years through self-administered questionnaires, with a loss of follow-up since 1990 < 3%. All women signed informed consent.

For the present study, we included healthy individuals enrolled as controls in existing case-control studies nested within the E3N cohort, whose SHBG had been measured on fasting serum samples by electrochemiluminescence (Elecsys, Hitachi 911). After excluding duplicates (n=148), women with no SHBG measurement (n=105), no dietary information (n=27) or with aberrant energy intake (n=35), the final study population was of 2,453 women.

Assessment of coffee and caffeine consumption and covariates

Usual diet over the previous year was assessed in 1993 by using a validated diet-history questionnaire[20]. Participants reported the frequency, usual serving size and type of coffee consumed (caffeinated or decaffeinated). Coffee consumption was converted into standardized cups (125 mL) per day. Participants also reported the frequency and usual serving size of tea consumed. Mean daily caffeine intake was calculated.

The following data were collected along with the blood samples: anthropometric measurements (waist circumference, hip circumference, body mass index), smoking, physical activity, menopausal status and former or current use of menopausal hormone therapy or oral contraceptives.

The date of menopause was defined as the date preceding 12 consecutive months of amenorrhea (excluding hysterectomy), the date of bilateral oophorectomy or, if not available, the self-reported date of menopause, the date when menopausal hormone therapy was started, or an imputed date corresponding to age 47 if menopause was due to oophorectomy and age 51 in other cases (respective median ages for surgical and natural menopause in the cohort).

Statistical analysis

SAS statistical software (version 9.4; SAS Institute Inc., Cary, NC) was used for all analyses. Statistical tests were two-sided with statistical significance defined as $P < 0.05$. Logistic regression models were performed to estimate the risk of low SHBG, defined as < 46.3 $nmol \cdot L^{-1}$, the 1st quartile of the SHBG levels distribution in the population. For logistic regression analyses, model 1 was unadjusted (model 2 adjusted for age, physical activity, BMI, model 3 further adjusted for smoking, and model 4 further adjusted for menopausal status and use of oral contraceptives or menopausal hormone therapy).

Stratification by BMI categories (<25 vs ≥25 kg/m^2) and menopausal status was also performed.

A spline regression model was computed to evaluate the shape of the continuous relationship between coffee and caffeine consumption and the risk of low SHBG (ie. SHBG within the lowest quartile). Three knots were used, corresponding to the quartiles of coffee and caffeine consumption. ORs and 95% confidence intervals (CI) were systematically estimated.

Results

Descriptive characteristics of the study population by quartiles of SHBG are summarized in Table 1. Of 2,453 women, the mean age was 57.3 ± 6.4 years and 61% were postmenopausal. The median SHBG value was 63.9 nmol·L^{-1}. Women with low SHBG had higher BMI and less frequent use of oral contraceptives than other women.

Odds ratios for low SHBG across categories of caffeine and coffee intakes, estimated by logistic regression, are shown in Table 2, Table 3 (after stratification by BMI categories) and Table 4 (after stratification by menopausal status). After adjusting for confounding factors, caffeine and total coffee consumption were inversely associated with the presence of low SHBG (*P* for trend=0.004 and *P* for trend=0.01 respectively in the fully adjusted model). Women with the highest levels of total coffee intake (≥3 cups/day) had a ~30% reduced risk of low SHBG (OR=0.69, 95% CI 0.52-0.92). Similar results were found in women with the highest levels of caffeine intake (≥265 mg/day) (OR=0.68, 95% CI 0.50-0.94) (Table 2).

Decaffeinated coffee intake was not significantly associated with the risk of low SHBG.

Spline models adjusted for all covariates also showed an association between caffeine, total coffee, caffeinated coffee and SHBG, but not between decaffeinated coffee and SHBG (Figure 1).

Stratifications by body mass index and menopausal status

After stratification by BMI categories, significant associations between caffeine (*P* for trend=0.005), total coffee (*P* for trend=0.005), caffeinated coffee intake (*P* for trend=0.04) and SHBG were observed in overweight women only (n=713) (Table 3).

After stratification by menopausal status, SHBG was associated with caffeine and total coffee intake (*P* for trend=0.002 and 0.03 respectively) in postmenopausal (n=1,485) but no significant association was observed in premenopausal women (n=968) (Table 4).

No relationship was found between tea consumption and SHBG levels (data not shown).

Discussion

The present study examined the effects of coffee and caffeine consumption on the risk of low SHBG, a strong predictor for type 2 diabetes independently of metabolic variables[5]. High coffee consumption and high caffeine intake were associated with a ~30% reduced risk of having low SHBG concentration in this large population of 2,453 healthy French women.

Previous studies addressing this issue suggested differential effects of caffeine and coffee on SHBG according to gender and menopausal status.

In the sole intervention randomized controlled study ever performed[16], 28 women and 14 men were assigned to consumption of 5 cups per day of caffeinated coffee, decaffeinated coffee or water. After 8 weeks of follow-up, there were no significant differences in SHBG levels between treatment groups. In parallel, no changes in glycaemia, insulin sensitivity or insulin secretion were observed[21]. The small sample size and the short duration of the study might account for these negative results. It has also been hypothesized that the acute effects of coffee consumption might be different from the effects of long-term habitual coffee consumption[22].

Previous observational studies included men[23–27], premenopausal women[13–15,17], postmenopausal women[10–13,27], or women without specified menopausal status[28]. In men, only the largest study of 1,563 Norwegian subjects showed a positive association between coffee consumption and SHBG[26]. In postmenopausal women, three observational studies found that caffeine intakes are positively correlated with SHBG[10,12,13]. Similar results were observed between coffee and SHBG in most studies among postmenopausal women[10–13], excepted in the smallest study, which also included women with type 2 diabetes, potentially explaining its different conclusions[27]. In premenopausal women, existing data are conflicting since two studies reported a positive association between coffee and caffeine consumption and SHBG levels[15,17], while two others reported no association[13,14]. It is worth to note that when different types of coffee were analyzed separately, a positive association with SHBG could be found

with caffeinated coffee but never with decaffeinated coffee[10,11,13,14]. In addition, no association was found between tea consumption and SHBG, although tea contains small amounts of caffeine[10,11,13,14,17]. This supports a cumulative threshold concentration for caffeine intake in order to modulate SHBG concentration.

The present study provides more evidence that coffee and caffeine have differential effects on SHBG according to menopausal status. After stratification, coffee and caffeine reduced the risk of low SHBG in postmenopausal, but not in premenopausal women, although this study has included the largest number of premenopausal women to date. The underlying mechanisms are not fully understood. SHBG levels are known to decrease at the time of the menopause, which is partially explained by a reduction in estradiol levels[29]. It is not clear if coffee and caffeine may limit the decline in estradiol related to menopause[13,14], and thus maintain higher levels of SHBG. Furthermore, a low SHBG concentration is more common in women after menopause and therefore, the impact of coffee would be more apparent in this setting.

Similarly, the present study also showed that the beneficial effects of coffee and caffeine on SHBG are particularly pronounced among women with a BMI above 25 kg/m^2. BMI is one of the strongest predictor of SHBG levels, with a reduction of about 30% in subjects with increased BMI compared to lean subjects[11,30,31].

Our findings suggest therefore that coffee and caffeine intake are associated with SHBG levels in women who are at higher risk of having low SHBG and ultimately type 2 diabetes. However, only an intervention study would allow to demonstrate a direct effect of coffee on SHBG concentration in this population at risk.

There are various mechanisms by which coffee and caffeine may affect SHBG. As no association was found between decaffeinated coffee consumption and SHBG levels neither in this nor in previous studies, caffeine is likely to be the component responsible for this effect.

Caffeine has been shown to lower liver fat accumulation, which is a strong predictor of serum SHBG levels[32–34].

The molecular mechanism underlying this relationship has been investigated in mice expressing a human *SHBG* transgene, which expression and blood levels were reduced by monosaccharide-induced hepatic lipogenesis[35].

However, the lack of association between decaffeinated coffee and SHBG might be due to a lack of power related to the low consumption of this beverage. Moreover, because caffeinated coffee is the main source of caffeine, the association between caffeine and SHBG may be confounded by other components of coffee. These other components include principally chlorogenic acid, lignans and magnesium. Neither chlorogenic acid, a polyphenol present in large amounts in coffee and in only small amounts in other foods and beverages, nor its metabolite, caffeic acid, have demonstrated any effect on SHBG levels. Magnesium sulfate, administered as a single intravenous dose, did not affect SHBG concentrations in a randomized placebo-controlled study in elderly male subjects[36]. By contrast, urinary excretion of lignans, which are found in coffee but also in fiber-rich food, showed a positive association with plasma SHBG in a small group of premenopausal women[37].

Still, some data have suggested that SHBG may only partly explain the inverse associations of coffee and caffeine with type 2 diabetes risk, and that other mechanisms may be involved[27]. Coffee has been shown to influence glucose absorption, glucose hepatic output through inhibition of glucose-6-phosphatase by chlorogenic acid, glucose storage, and to improve insulin sensitivity, potentially through increasing adiponectin levels[21,38]. A decrease in iron absorption, and thus in body iron stores, may also contribute to the beneficial effects of coffee on glucose metabolism[39,40].

The strengths of our study include the large sample size and the inclusion of both pre- and postmenopausal women. Furthermore, our study was conducted in Europe, whereas previous

studies were mainly conducted in North America[10–16,23,28]. European and North American populations notably differ by their BMI, diet and lifestyle. In particular, BMI is a major determinant of SHBG levels, which is likely to explain the wide range of SHBG across studies. As reproducibility of the investigated association in various populations is an important issue in epidemiology, our study makes the association between coffee and caffeine consumption and SHBG more consistent. In addition, another strength of the present study was to systematically take into account for the degree of physical activity of the women, which is able to influence the concentration of SHBG, independently of body weight[18].

Limitations of our study include the fact that the women studied were not representative of the French population and possibly were more health-conscious than the general population. This may affect the generalizability of our findings. Another limitation is the cross-sectional design of the study, which limits the assessment of causality. Moreover, SHBG was measured only on a single serum sample taken at any time of the menstrual cycle. However, though SHBG might vary slightly during menstrual cycle[41], this measure bias should be non-differential and is unlikely to substantially affect the results.

In conclusion, in this large study among 2,453 pre- and postmenopausal women, high coffee and caffeine intakes were associated with a ~30% reduced risk of low SHBG, a known risk factor for type 2 diabetes. This association was particularly marked among overweight and postmenopausal women, who are at higher risk of developing diabetes. Our results support the hypothesis that SHBG may partly explain the protective effect of coffee and caffeine against incident diabetes.

Declaration of interest

There is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Author contributions

Fabrice Bonnet, Guy Fagherazzi and Florence Pihan-Le Bars contributed to the study conception. Gaëlle Gusto carried out the data analysis. Florence Pihan-Le Bars drafted the first version of the article and all the other authors revised it critically for important intellectual content.

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Figure legends

Figure 1 : Spline relation between coffee and caffeine and risk of low sex hormone-binding globulin (SHBG)[1] (n= 2,453)[2]

A – Spline relation between total coffee and risk of low SHBG

B – Spline relation between caffeinated coffee and risk of low SHBG

C – Spline relation between decaffeinated coffee and risk of low SHBG

D – Spline relation between caffeine and risk of low SHBG

[1]i.e. within the lowest quartile <46.3 nmol·L^{-1} ; [2]Data are presented as odds ratios (solid curves) and 95% CI (dashed curves) and are adjusted for age, physical activity, BMI, smoking, menopausal status, use of oral contraceptives and use of menopausal hormone therapy.

Table 1 : Baseline characteristics of the E3N cohort study population by quartiles of sex hormone-binding globulin (n=2,453)[1]

	Total (n=2,453)	SHBG (nmol·L^{-1}) <46.3 (n=613)	[46.3-63.9[(n=613)	[63.9-86.9[(n=613)	≥86.9 (n=614)	*P*-value 1[4]	*P*-value 2[5]
Age (y)	57.3 ± 6.4	57.5 ± 6.4	57.5 ± 6.4	57.3 ± 6.4	56.8 ± 6.3	0.18	0.26
Body mass index (kg/m^2)	23.7 ± 3.6	25.9 ± 4.1	23.8 ± 3.3	22.9 ± 3.0	22.4 ± 3.0	**<0.0001**	**<0.0001**
Menopausal status						0.24	0.20
Premenopausal	958 ± 39.1	226 ± 36.9	238 ± 38.8	234 ± 38.2	260 ± 2.3		
Postmenopausal[2]	1495 ± 60.9	387 ± 63.1	375 ± 61.2	379 ± 61.8	354 ± 57.7		
Past or current use of oral contraceptives						**0.04**	**0.01**
No	965 ± 39.3	267 ± 43.6	239 ± 39.0	240 ± 39.2	219 ± 5.7		
Yes[2]	1488 ± 60.7	346 ± 56.4	374 ± 61.0	373 ± 60.8	395 ± 64.3		
Past or current use of menopausal hormone therapy						0.18	0.06
No	1562 ± 63.7	410 ± 66.9	393 ± 64.1	374 ± 61.0	385 ± 2.7		
Yes[2]	891 ± 36.3	203 ± 33.1	220 ± 35.9	239 ± 39.0	229 ± 37.3		
Tobacco use						0.75	0.32
Former smokers	839 ± 34.2	213 ± 34.7	216 ± 35.2	204 ± 33.3	206 ± 3.6		
Current regular smokers	186 ± 7.6	47 ± 7.7	45 ± 7.3	46 ± 7.5	48 ± 7.8		
Current occasional smokers	113 ± 4.6	36 ± 5.9	20 ± 3.3	27 ± 4.4	30 ± 4.9		
Never-smokers[2]	1315 ± 53.6	317 ± 51.7	332 ± 54.2	336 ± 54.8	330 ± 53.7		
Physical activity (MET/d)[3]	49.5 ± 51.6	47.5 ± 37.7	48.7 ± 49.9	49.8 ± 46.3	51.7 ± 67.9	0.57	0.20
Caffeine (mg/d)	198.6 ± 143.9	191.8 ± 144.9	201.6 ± 136.9	203.8 ± 148.8	197.1 ± 144.8	0.44	0.18
Coffee intake (mL/d)							
Total coffee	283.7 ± 259.6	273.7 ± 258.8	292.4 ± 245.9	289.8 ± 270.6	278.9 ± 262.7	0.36	0.27
Caffeinated coffee	195.2 ± 226.7	185.8 ± 212.2	204.8 ± 231.1	201.4 ± 240.4	188.7 ± 222.1	0.50	0.22
Decaffeinated coffee	20.5 ± 99.0	25.6 ± 124.4	17.9 ± 93.2	16.2 ± 67.9	22.5 ± 102.0	0.47	0.21

[1]Data are mean ± SD and statistically significant results are marked in bold ; [2]Reference categories ; [3]MET, Metabolic Equivalent Task ; [4]*P*-value 1 : comparison of all quartiles of SHBG ; [5]*P*-value 2 : comparison of quartile 1 (SHBG < 46.3 nmol·L^{-1}) with quartiles 2-4.

Table 2 : Risk of low sex hormone-binding globulin[1] according to coffee and caffeine consumption (n=2,453)

	SHBG ≥46.3 nmol·L^{-1} [n (%)]	SHBG <46.3 nmol·L^{-1} [n (%)]	OR (95% CI)[3]			
			M1[4]	M2[5]	M3[6]	M4[7]
Caffeine (mg/d)						
<94.23489	452 (24.57)	161 (26.26)	Ref	Ref	Ref	Ref
[94.23489-171.21073[	453 (24.62)	160 (26.10)	0.99 (0.77 -1.28)	1.03 (0.78 -1.35)	1.02 (0.78 -1.34)	1.03 (0.78 -1.35)
[171.21073-265.16084[	466 (25.33)	147 (23.98)	0.89 (0.68 -1.15)	0.84 (0.64 -1.11)	0.82 (0.62 -1.09)	0.84 (0.63 -1.10)
≥265.16084	469 (25.49)	145 (23.65)	0.87 (0.67 -1.12)	**0.70 (0.53 -0.93)**	**0.69 (0.52 -0.91)**	**0.69 (0.52 -0.92)**
P trend			0.21	**0.004**	**0.003**	**0.004**
Total coffee[2]						
0	256 (13.91)	89 (14.52)	Ref	Ref	Ref	Ref
]0-1 cup/d[	307 (16.68)	110 (17.94)	1.03 (0.74 -1.43)	0.92 (0.65 -1.31)	0.92 (0.65 -1.30)	0.93 (0.66 -1.32)
[1-2 cups/d[	360 (19.57)	118 (19.25)	0.94 (0.69 -1.30)	0.86 (0.61 -1.20)	0.85 (0.60 -1.19)	0.86 (0.61 -1.20)
[2-3 cups/d[	357 (19.40)	123 (20.07)	0.99 (0.72 -1.36)	0.88 (0.63 -1.23)	0.87 (0.62 -1.21)	0.87 (0.62 -1.23)
≥ 3 cups/d	560 (30.43)	173 (28.22)	0.89 (0.66 -1.19)	**0.69 (0.50 -0.95)**	**0.67 (0.49 -0.93)**	**0.68 (0.50 -0.94)**
P trend			0.31	**0.01**	**0.008**	**0.01**
Caffeinated coffee[2]						
0	563 (30.60)	203 (33.12)	Ref	Ref	Ref	Ref
]0-1 cup/d[	339 (18.42)	104 (16.97)	0.85 (0.65 -1.12)	0.80 (0.60 -1.08)	0.80 (0.60 -1.07)	0.80 (0.60 -1.08)
[1-2 cups/d[	296 (16.09)	105 (17.13)	0.98 (0.75 -1.29)	1.04 (0.77 -1.39)	1.02 (0.76 -1.37)	1.02 (0.76 -1.34)
[2-3 cups/d[	292 (15.87)	89 (14.52)	0.85 (0.63 -1.13)	0.92 (0.68 -1.24)	0.91 (0.67 -1.23)	0.91 (0.67 -1.23)
≥ 3 cups/d	350 (19.02)	112 (18.27)	0.89 (0.68 -1.16)	0.78 (0.58 -1.04)	0.77 (0.58 -1.03)	0.77 (0.58 -1.03)
P trend			0.42	0.18	0.16	0.17
Decaffeinated coffee[2]						
0	1,623 (88.21)	527 (85.97)	Ref	Ref	Ref	Ref
]0-1 cup/d[	124 (6.74)	46 (7.50)	1.14 (0.80 -1.63)	1.21 (0.83 -1.76)	1.22 (0.84 -1.78)	1.24 (0.85 -1.81)
[1-2 cups/d[	49 (2.66)	21 (3.43)	1.32 (0.78 -2.22)	1.26 (0.72 -2.21)	1.25 (0.71 -2.19)	1.26 (0.72 -2.22)
[2-3 cups/d[	19 (1.03)	9 (1.47)	1.46 (0.66 -3.24)	1.13 (0.48 -2.66)	1.13 (0.48 -2.65)	1.11 (0.47 -2.62)
≥ 3 cups/d	25 (1.36)	10 (1.63)	1.23 (0.59 -2.58)	1.07 (0.47 -2.42)	1.07 (0.47 -2.42)	1.06 (0.47 -2.40)
P trend			0.22	0.56	0.58	0.59

[1]i.e. within the lowest quartile <46.3 nmol·L^{-1} ; [2]1 cup = 125 mL ; [3]Logistic regression models were used, with Ref = reference, and statistically significant results are marked in bold ; [4]M1 unadjusted ; [5]M2 adjusted for age, physical activity, body mass index ; [6]M3 = M2+smoking ; [7]M4 = M3+ menopausal status, use of oral contraceptives, use of menopausal hormone therapy.

Table 3 : Risk of low sex hormone-binding globulin[1] according to coffee and caffeine consumption after stratification by body mass index categories (n=2,453)

	BMI <25 kg/m² (n=1,740)			BMI ≥25 kg/m² (n=713)		
	SHBG ≥46.3 nmol·L^{-1}[n(%)]	SHBG <46.3 nmol·L^{-1}[n(%)]	OR (95% CI)[3]	SHBG ≥46.3 nmol·L^{-1}[n(%)]	SHBG <46.3 nmol·L^{-1}[n(%)]	OR (95% CI)[3]
Caffeine (mg/d)						
<94.23489	367 (25.47)	81 (27.09)	Ref	85 (21.30)	80 (25.48)	Ref
[94.23489-171.21073[	377 (26.16)	83 (27.76)	1.00 (0.71 -1.40)	76 (19.05)	77 (24.52)	1.07 (0.69 -1.67)
[171.21073-265.16084[	367 (25.47)	72 (24.08)	0.90 (0.63 -1.28)	99 (24.81)	75 (23.89)	0.75 (0.49 -1.17)
≥265.16084	330 (22.90)	63 (21.07)	0.87 (0.60 -1.25)	139 (34.84)	82 (26.11)	**0.60 (0.40 -0.92)**
P trend			0.37			**0.005**
Total coffee[2]						
0	213 (14.78)	51 (17.06)	Ref	43 (10.78)	38 (12.10)	Ref
]0-1 cup/d[	252 (17.49)	53 (17.73)	0.89 (0.58 -1.37)	55 (13.78)	57 (18.15)	1.15 (0.64 -2.05)
[1-2 cups/d[	288 (19.99)	57 (19.06)	0.83 (0.55 -1.27)	72 (18.05)	61 (19.43)	0.92 (0.52 -1.60)
[2-3 cups/d[	286 (19.85)	58 (19.40)	0.87 (0.57 -1.32)	71 (17.79)	65 (20.70)	0.97 (0.55 -1.69)
≥ 3 cups/d	402 (27.90)	80 (26.76)	0.84 (0.57 -1.25)	158 (39.60)	93 (29.62)	0.62 (0.37 -1.03)
P trend			0.53			**0.005**
Caffeinated coffee[2]						
0	447 (31.02)	109 (36.45)	Ref	116 (29.07)	94 (29.94)	Ref
]0-1 cup/d[	271 (18.81)	37 (12.37)	0.56 (0.38 -0.85)	68 (17.04)	67 (21.34)	1.24 (0.80 -1.93)
[1-2 cups/d[	239 (16.59)	50 (16.72)	0.86 (0.59 -1.24)	57 (14.29)	55 (17.52)	1.16 (0.72 -1.84)
[2-3 cups/d[	236 (16.38)	50 (16.72)	0.87 (0.60 -1.26)	56 (14.04)	39 (12.42)	0.87 (0.53 -1.43)
≥ 3 cups/d	248 (17.21)	53 (17.73)	0.88 (0.61 -1.27)	102 (25.56)	59 (18.79)	0.71 (0.47 -1.10)
P trend			0.96			**0.04**
Decaffeinated coffee[2]						
0	1274 (88.41)	251 (83.95)	Ref	349 (87.47)	276 (87.90)	Ref
]0-1 cup/d[	95 (6.59)	30 (10.03)	**1.68 (1.08 -2.59)**	29 (7.27)	16 (5.10)	0.73 (0.39 -1.38)
[1-2 cups/d[	38 (2.64)	11 (3.68)	1.57 (0.79 -3.14)	11 (2.76)	10 (3.18)	1.01 (0.41 -2.47)
[2-3 cups/d[	14 (0.97)	4 (1.34)	1.44 (0.47 -4.44)	5 (1.25)	5 (1.59)	1.19 (0.34 -4.19)
≥ 3 cups/d	20 (1.39)	3 (1.00)	0.72 (0.21 -2.46)	5 (1.25)	7 (2.23)	1.83 (0.56 -5.96)
P trend			0.76			0.38

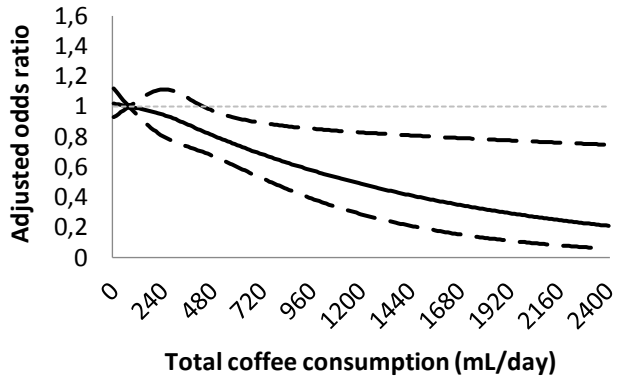
[1]i.e. within the lowest quartile <46.3 nmol·L^{-1} ; [2]1 cup = 125 mL ; [3]Logistic regression was used, with adjustment for age, physical activity, smoking, menopausal status, use of oral contraceptives and use of menopausal hormone therapy. Ref = reference. Statistically significant results are marked in bold.

Table 4 : Risk of low sex hormone-binding globulin[1] according to coffee and caffeine consumption after stratification by menopausal status (n=2,453)

	Postmenopausal (n=1,495)			Premenopausal (n=958)		
	SHBG ≥46.3 nmol·L^{-1}[n(%)]	SHBG <46.3 nmol·L^{-1}[n(%)]	OR (95% CI)[3]	SHBG ≥46.3 nmol·L^{-1}[n(%)]	SHBG <46.3 nmol·L^{-1}[n(%)]	OR (95% CI)[3]
Caffeine (mg/d)						
<94.23489	285 (25.72)	111 (28.68)	Ref	167 (22.81)	50 (22.12)	Ref
[94.23489-171.21073[	282 (25.45)	104 (26.87)	0.95 (0.68 -1.34)	171 (23.36)	56 (24.78)	1.21 (0.76 -1.93)
[171.21073-265.16084[	269 (24.28)	92 (23.77)	0.81 (0.57 -1.16)	197 (26.91)	55 (24.34)	0.91 (0.57 -1.46)
≥265.16084	272 (24.55)	80 (20.67)	**0.58 (0.40 -0.83)**	197 (26.91)	65 (28.76)	0.93 (0.58 -1.48)
P trend			**0.002**			0.47
Total coffee[2]						
0	158 (14.26)	54 (13.95)	Ref	98 (13.39)	35 (15.49)	Ref
]0-1 cup/d[	193 (17.42)	81 (20.93)	1.05 (0.68 -1.63)	114 (15.57)	29 (12.83)	0.72 (0.39 -1.31)
[1-2 cups/d[	225 (20.31)	72 (18.60)	0.86 (0.56 -1.33)	135 (18.44)	46 (20.35)	0.87 (0.51 -1.49)
[2-3 cups/d[	209 (18.86)	79 (20.41)	0.97 (0.63 -1.49)	148 (20.22)	44 (19.47)	0.76 (0.44 -1.31)
≥ 3 cups/d	323 (29.15)	101 (26.10)	0.69 (0.45 -1.04)	237 (32.38)	72 (31.86)	0.68 (0.41 -1.12)
P trend			**0.03**			0.19
Caffeinated coffee[2]						
0	335 (30.23)	133 (34.37)	Ref	228 (31.15)	70 (30.97)	Ref
]0-1 cup/d[	207 (18.68)	72 (18.60)	0.80 (0.55 -1.14)	132 (18.03)	32 (14.16)	0.79 (0.47 -1.31)
[1-2 cups/d[	196 (17.69)	63 (16.28)	0.81 (0.56 -1.18)	100 (13.66)	42 (18.58)	1.52 (0.94 -2.44)
[2-3 cups/d[	161 (14.53)	54 (13.95)	0.88 (0.59 -1.30)	131 (17.90)	35 (15.49)	0.98 (0.60 -1.59)
≥ 3 cups/d	209 (18.86)	65 (16.80)	**0.67 (0.46 -0.97)**	141 (19.26)	47 (20.80)	0.97 (0.61 -1.53)
P trend			0.07			0.99
Decaffeinated coffee[2]						
0	972 (87.73)	332 (85.79)	Ref	651 (88.93)	195 (86.28)	Ref
]0-1 cup/d[	69 (6.23)	33 (8.53)	1.34 (0.84 -2.15)	55 (7.51)	13 (5.75)	1.05 (0.55 -2.02)
[1-2 cups/d[	35 (3.16)	13 (3.36)	1.04 (0.52 -2.09)	14 (1.91)	8 (3.54)	2.01 (0.77 -5.28)
[2-3 cups/d[	15 (1.35)	4 (1.03)	0.67 (0.21 -2.15)	4 (0.55)	5 (2.21)	2.83 (0.69 -11.66)
≥ 3 cups/d	17 (1.53)	5 (1.29)	0.77 (0.25 -2.34)	8 (1.09)	5 (2.21)	1.60 (0.46-5.51)
P trend			0.56			0.10

[1]i.e. within the lowest quartile <46.3 nmol·L^{-1} ; [2]1 cup = 125 mL ; [3]Logistic regression was used, with adjustment for age, physical activity, body mass index, smoking, use of oral contraceptives and use of menopausal hormone therapy. Ref = reference. Statistically significant results are marked in bold.

A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0,8
0,6
0,4
0,2
0
0
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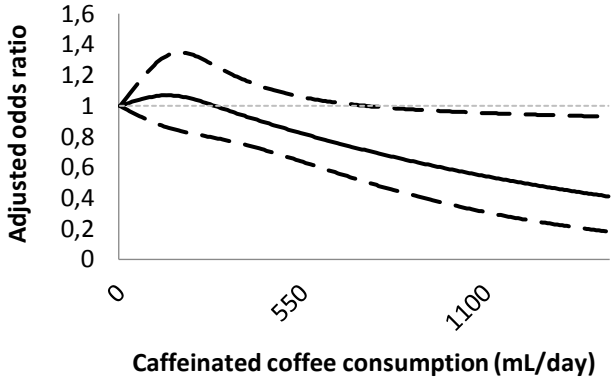
480
720
960
1200
1440
1680
1920
2160
2400
Total coffee consumption (mL/day)

B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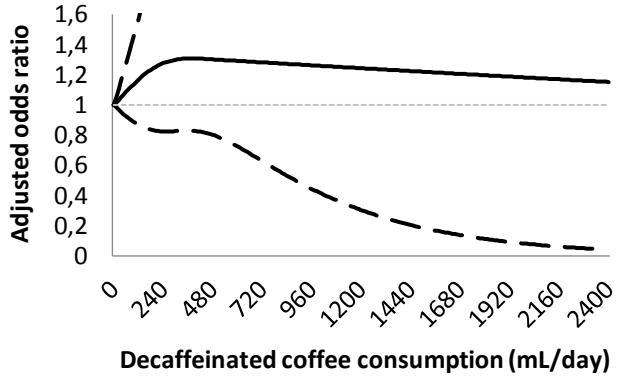
0,6
0,4
0,2
0
0
550
1100
Caffeinated coffee consumption (mL/day)

C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0,8
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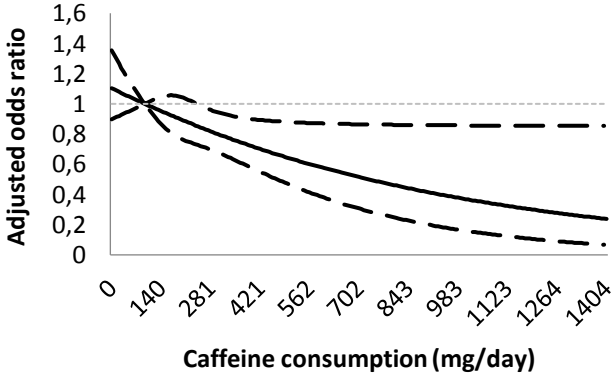
0,4
0,2
0
0
240
480
720
960
1200
1440
1680
1920
2160
2400
Decaffeinated coffee consumption (mL/day)

D


Adjusted odds ratio
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1,2
1
0,8
0,6
0,4
0,2
0
0
140
281
421
562
702
843
983
1123
1264
1404
Caffeine consumption (mg/day)

U.F.R. DE **MEDECINE** DE RENNES

N°

PIHAN-LE BARS, Florence - La consommation de café et de caféine est associée à la sex hormone-binding globulin (SHBG) dans la cohorte E3N

feuilles 43, illustrations 0, graphiques 1, tableaux 4, 30 cm.- Thèse : (Médecine) ; Rennes 1; 2016 ; N° .

Résumé

Objectif : Une SHBG basse constitue un facteur de risque indépendant de diabète de type 2, en particulier chez la femme. La consommation de café est associée à une réduction du risque de diabète de type 2 mais ses effets sur la SHBG restent mal connus.

Matériel et méthodes : 2453 femmes saines de la cohorte E3N pour lesquelles la SHBG à l'inclusion a été mesurée (ECLA sur Elecsys, Hitachi 911), ont été incluses. Des informations sur leur alimentation (incluant leur consommation de café et de caféine), leur mode de vie et leur santé étaient recueillies. La relation entre la consommation de café et de caféine et la SHBG a été modélisée, avec ajustement sur les facteurs confondants et stratification selon l'IMC et le statut ménopausique.

Résultats : L'âge moyen des 2453 femmes était de 57,3 ± 6,4 ans et 61% d'entre elles étaient ménopausées. Des apports élevés de café (≥3 tasses/jour) ou de caféine (≥265 mg/jour) étaient associés à une diminution du risque de SHBG basse (OR=0,69[0,52-0,92] et OR=0,68[0,50-0,94] respectivement). Après stratification, ces associations n'étaient retrouvées que chez les femmes avec un IMC ≥25 kg/m² ou ménopausées. L'association avec la SHBG était observée pour la consommation de caféine, de café caféiné, mais pas avec celle de café décaféiné.

Discussion : Une consommation élevée de café et de caféine est associée à une réduction de 30% du risque de SHBG basse, ce qui peut expliquer leurs effets protecteurs pour le diabète de type 2.

Rubrique de classement : ENDOCRINOLOGIE

Mots-clés : sex hormone-binding globulin, café, caféine, diabète, femmes, mode de vie

Mots-clés anglais MeSH : sex hormone-binding globulin, coffee, caffeine, diabetes, women, lifestyle

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