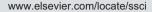


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# Caffeine intake has no effect on sleep quality in community dwellers living in a rural Ecuadorian village (The Atahualpa Project)



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## ABSTRACT

More information is needed to better understand the effect of caffeine on sleep quality at the community level. In a population-based, cross-sectional study design, we aimed to assess the effect of caffeine intake on sleep quality by the use of a multivariate exposure-effect model, adjusted for relevant confounders. All Atahualpa residents aged  $\geq$  40 years were identified during a door-to-door survey and interviewed with the Pittsburgh Sleep Quality Index (PSQI) and a structured instrument designed to estimate the daily amount of caffeine intake. An exposure-effect model was built using augmented inverse probability weighting taking into account variables that were associated with exposure (using a probit model) and variables that were associated with outcome (in a linear model). Out of 779 eligible individuals, 716 (92%) were included. Consumption of <100 mg/day of caffeine was recorded in 320 (45%) participants, from 100 to 200 mg/day in 299 (42%), and >200 mg/day in 97 (13%). Mean score in the PSQI was 4.5  $\pm$  2.2 points, with 203 (28%) individuals classified as poor sleepers (  $\geq$  6 points). The exposureeffect model, adjusted for variables associated with the exposure (symptoms of depression, total cholesterol blood levels and smoking) and the outcome (age, symptoms of depression, physical activity and fasting glucose levels), revealed no effect of caffeine intake in sleep quality (average exposure effect: 0.027, 95% C.I.: -0.284 to 0.338, p=0.866). This population-based study shows that caffeine intake has no effect on sleep quality in community-dwelling adults living in a rural village of Ecuador.

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#### 1. Introduction

Caffeine, an adenosine receptor antagonist, is the most commonly used legal stimulant in the world. Intake of this substance has long been associated with increased alertness as well as with improved motor and cognitive performance [1,2]. These beneficial effects might be counterbalanced by impairment of sleep quality. However, from the very first study attempting to demonstrate the effects of caffeine intake on sleep quality, it was noticed a widespread individual variability in this relationship [3]. Further studies have shown contradictory results, but most of them have been limited to small numbers of participants, to certain groups of individuals, or under artificial circumstances that might not be representative of the population at large [4–7].

Recent studies have shown that age, tolerance, differences in caffeine bioavailability (prolonged half-life), genetic predisposition and even external factors such as sleep deprivation, may account for the observed differences on the effects of caffeine intake on sleep quality [8–10]. More information is needed to better understand the effect of caffeine intake on sleep quality in different populations. In this study, we aimed to assess the naturalistic effect of caffeine intake on sleep quality at night in community-dwellers adults living in a quiet rural Ecuadorian village.

# 2. Methods

#### 2.1. Study population

Atahualpa is a village representative of rural coastal Ecuador. The weather is hot and dry, with 12 daily hours of sunlight all over the year. Inhabitants do not migrate, and a sizable proportion of them have never visited large urban centers. More than 95% of the population belongs to the Ecuadorian native/Mestizo ethnic group, and their living characteristics are homogeneous, as detailed elsewhere [11]. There are no fast-food restaurants or coffee shops in the village, and most people eat at home. Atahualpa has street lighting but there are no lighted or neon signs. Shift work is quite uncommon (less than 1% of the population work as security guards during nightly hours), and light or noise pollution are practically inexistent during nightly hours in the village.

# 2.2. Study design

Using a population-based, cross-sectional study design, all Atahualpa residents aged  $\geq$  40 years identified during doorto-door surveys and enrolled in the Atahualpa Project were interviewed with field instruments to assess the average amount of daily caffeine intake and the quality of sleep in the month before the survey. The effect of caffeine intake on sleep quality was assessed by the use of an exposure-effect model adjusted for relevant confounders. The Institutional Review Board of Hospital-Clínica Kennedy, Guayaquil, Ecuador (FWA 00006867) approved the protocol and the informed consent form.

#### 2.3. Caffeine consumption

Caffeine intake (during the month before the survey) was assessed by direct face-to-face interviews with the use of a structured questionnaire that inquired about the average number of cups/servings of coffee, tea, chocolate (beverages or bars), caffeine-containing soft drinks and energy drinks ingested per day, on the basis of the content of each of these products (http://www.energyfiend.com/the-caffeine-database); in addition, use of caffeine-containing pills (showing the participants a list of locally available medications) was specifically inquired and recorded.

#### 2.4. Sleep quality investigation

We used a validated Spanish version of the Pittsburg Sleep Quality Index (PSQI) [12]. This instrument consists of a combination of Likert-type and open ended questions assessing sleep duration (total amount of sleep obtained during the nocturnal sleep episode), sleep disturbances (symptoms that change sleeping habits), sleep latency (length of time that it takes to fall asleep), day dysfunction due to sleepiness (daytime somnolence), sleep efficiency (ratio of time spent asleep to the amount of time in bed), overall sleep quality (self-perceived satisfaction with sleep), and medications needed to sleep (use of sedatives, sleep inductors, etc.). The maximum score is 21 points, and the cutoff value for poor sleep quality is  $\geq 6$  points.

#### 2.5. Clinical covariates investigated

Demographics, level of education, alcohol intake, symptoms of depression and cardiovascular risk factors were assessed through direct interviews and procedures previously described in the Atahualpa Project [13,14]. In brief, alcohol intake was dichotomized in  $\leq$  50 or > 50 g/day; symptoms of depression were assessed by the depression axis of the depression–anxiety–stress-21 scale (a reliable field instrument that measures dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest/involvement, anhedonia, and inertia [15]), and cardiovascular risk factors were investigated by the use of the seven metrics proposed by the American Heart Association to assess the cardiovascular health status (smoking status, body mass index, physical activity, diet, blood pressure, fasting glucose, and total cholesterol blood levels) [16].

#### 2.6. Statistical analyses

Data analyses were carried out by using STATA version 14 (College Station, TX, USA). In the univariate analysis, we separately evaluated the association between the amount of caffeine intake and the quality of sleep with each of the confounding variables. For these comparisons, continuous variables used linear models and categorical variables either  $x^2$  or Fisher exact test as appropriate. Thereafter, we constructed separate exposure (caffeine intake) and effect (sleep quality) models to determine which variables were significantly associated with either the exposure or the effect. An exposure effect model, which takes into account the confounding effect

of some variables over exposure and over outcome, was built using augmented inverse probability weighting taking into account variables that were associated with exposure using a probit model and variables that were associated with outcome in a linear model. The association between exposure and outcome was then ascertained in the form of the average exposure effect of caffeine intake on sleep quality after adjusting for all confounders.

## 3. Results

Information on caffeine intake and sleep quality was available in 716 (92%) out of 779 eligible individuals. Mean age was  $61\pm13$  years, 405 (57%) were women, 450 (63%) had primary school education only, 130 (18%) admitted alcohol consumption of >50 g/day, and 84 (12%) had symptoms of depression. Regarding cardiovascular risk factors, 27 (4%) individuals were smokers, 49 (7%) had poor physical activity, 32 (4%) had a poor diet, 184 (26%) had a body mass index  $\geq$  30 kg/m<sup>2</sup>, 256 (36%) had blood pressure  $\geq$  140/90 mmHg, 209 (29%) had fasting glucose levels  $\geq$  126 mg/dL, and 83 (12%) had total cholesterol levels  $\geq$  240 mg/dL.

Consumption of <100 mg/day of caffeine was recorded in 320 (45%) participants, from 100 to 200 mg/day in 299 (42%), and >200 mg/day in the remaining 97 (13%). The main source of caffeine intake was coffee, which was most often consumed early in the morning and in the late afternoon. Overall, 115 (16%) individuals admitted daily ingestion of  $\geq$  2 cups of coffee, 267 (37%) between 1 and 2 cups, 147 (21%) less than one, and the remaining 187 (26%) reported no intake of coffee at all. Second in importance were caffeinecontaining soft-drinks (consumed by 67% of the population). Energy drinks were eventually consumed and only by men during working hours, while chocolate (often with milk) was a preferred beverage for women during or after dinner. Consumption of black tea was reported by less than 5% of the population and was irrelevant to the average amount of caffeine intake in most cases. The intake of caffeinecontaining pills (pain relievers) was also uncommon and irrelevant for the main findings.

Mean score in the PSQI was  $4.5\pm2.2$  points, with 203 (28%) individuals classified as poor sleepers ( $\geq 6$  points). Of interest, more than 90% of individuals admitted to be regularly awake before 8 am (even in weekends), and nobody acknowledged the use more than two sleeping pills per month. To confirm this, we visited local drug stores and inquired pharmacists who confirmed that prescription sleep medications are rarely sold.

Characteristics of participants across categories of caffeine intake and sleep quality are summarized in Table 1. In univariate analyses, depression was the single variable significantly associated with higher amounts of caffeine intake. On the other hand, individuals with poor sleep quality were older, less educated, reported worse physical activity and had more often symptoms of depression than those with good sleep quality.

An exposure logistic regression model showed significant association of the amount of caffeine intake with symptoms of depression (p=0.031) and total cholesterol blood levels

	Total series (n=716)	Daily caffeine intake				Sleep quality		
		<100 mg (n=320)	100–200 mg (n=299)	> 200 mg (n=97)	p Value	Good (n=513)	Poor (n=203)	p Value
Age, mean $\pm$ SD	$61 \pm 13$	$61 \pm 13$	$60\pm13$	$63\pm13$	0.187	$59\pm 12$	$66\pm15$	< 0.001
Women, n (%)	405 (57)	178 (56)	172 (58)	55 (57)	0.891	294 (57)	110 (54)	0.498
Primary education, n (%)	450 (63)	202 (63)	183 (61)	65 (67)	0.583	310 (60)	140 (69)	0.041
Alcohol intake $>50g/day$ , n (%)	130 (18)	66 (21)	50 (17)	14 (14)	0.269	98 (19)	32 (16)	0.348
Current or past smoker, n (%)	27 (4)	17 (5)	9 (3)	1 (1)	0.101	17 (3)	10 (5)	0.424
Body mass index $\geq 30 \text{ kg/m}^2$ , n (%)	184 (26)	78 (24)	81 (27)	25 (26)	0.741	139 (27)	45 (22)	0.206
Poor physical activity, n (%)	49 (7)	22 (7)	18 (6)	6) 6	0.543	121 (4)	28 (14)	< 0.001
Poor diet, n (%)	32 (4)	12 (4)	17 (6)	3 (3)	0.397	25 (5)	7 (3)	0.527
Blood pressure $\geq$ 140/90 mmHg, n (%)	256 (36)	115 (36)	111 (37)	30 (31)	0.541	177 (35)	79 (39)	0.306
Fasting glucose $\geq$ 126 mg/dL, n %)	209 (29)	100 (31)	83 (28)	26 (27)	0.543	136 (27)	73 (36)	0.016
Total cholesterol $\geq 240 \text{ mg/dL}, n (\%)$	83 (12)	28 (9)	40 (13)	15 (15)	0.088	63 (12)	20 (10)	0.431
Symptoms of depression, $n$ (%)	84 (12)	47 (15)	24 (8)	13 (13)	0.031	42 (8)	42 (21)	< 0.001
Caffeine intake >200 mg/day, n (%)	97 (14)	1	1	1	I	69 (13)	28 (14)	0.999
PSQI score, mean $\pm$ SD	$4.5\pm 2.2$	$4.6\pm2.2$	$4.5\pm2.2$	$4.6 \pm 2.1$	0.834	1	I	I
Poor sleep quality, n (%)	203 (28)	98 (31)	77 (26)	28 (29)	0.403	I	I	I

(p=0.042), and a marginal association with smoking status (p=0.061). A generalized lineal model showed significant association of sleep quality (continuous PSQI score) with age (p<0.001), symptoms of depression (p<0.001) and physical activity (p=0.009), and marginal association with fasting glucose levels (p=0.069). The exposure-effect model, adjusted for relevant confounders, revealed no effect of caffeine intake on sleep quality (average exposure effect: 0.027, 95% C.I.: -0.284 to 0.338, p=0.866).

## 4. Discussion

This population-based study shows that caffeine intake has no effect on sleep quality in community-dwelling adults living in a quiet rural village of Ecuador. As previously noted, the effect of caffeine intake on sleep quality at the population level has been scarcely investigated and, to our knowledge, there is only one study in 181 community-dwellers showing no relationship between these variables [17].

The assessment of the effect of caffeine intake on sleep quality at the population level may be complicated by personal experiences of given individuals, as it is possible that those who think are "sensitive to coffee" avoid this substance at night. In the present study, however, we quantified the total amount of caffeine intake from sources other than coffee. A 500 ml bottle of Pepsi<sup>®</sup> or Coca-Cola<sup>®</sup> (the most commonly consumed soft drinks in the village) contain more than 40 mg of caffeine, which if consumed at dinner, would be enough to keep plasma caffeine concentrations over the night. In Ecuador, labels of these soft drinks just mention their caffeine, but there is no additional information about the amounts of milligrams per serving.

Caffeine half-life has been estimated to be about six hours but wide variability exists among individuals, and it is known to be modified by age, alcohol intake, pregnancy, liver failure and several other conditions and diseases [18–20]. Moreover, it has been shown that residual caffeine in concentrations enough to be associated with poor sleep quality, may be detected in saliva up to 16 h after a single 200 mg dose of coffee [21]. Therefore, assessment of day-long consumption of caffeine should not be seen as a major limitation of the present study. Nevertheless, further studies should formally investigate differences between morning and late afternoon caffeine intake in sleep quality to confirm this assumption.

Another important aspect to be considered in the context of our findings is the milieu of Atahualpa residents, since light and noise pollution is virtually nonexistent during sleep hours. These factors, which are known to negatively influence sleep quality [22], might enhance potential detrimental effects of caffeine intake in some individuals. The absence of light and noise pollution is common to most rural villages of developing countries and is a different scenario to that seen in most of the developed world. Such differences must be taken into account when analyzing the results of the present study, which might not represent the reality of urban centers.

We did not investigated genetic variations in the Adenosine  $A_{2a}$  receptor gene or other candidates genes that may explain the "resistance" of caffeine intake [9,10]. This is a limitation of the present study, particularly in view of the ethnic homogeneity of our participants. It is also possible that relatively small amounts of caffeine intake by some Atahualpa residents accounted for the lack of effect in sleep quality in the entire cohort. On the contrary, the populationbased design with unbiased selection of participants and the field instruments used for obtaining information about total amount of caffeine intake and sleep quality, argue for the strengths of our findings. Further support for the validity of our results are the associations observed in the separate exposure and effect models. Caffeine intake was inversely associated with symptoms of depression and directly with total cholesterol blood levels, as reported by other investigators [23,24], and poor sleep quality was directly associated with age, symptoms of depression and poor physical activity, as previously described [25,26].

# **Conflicts of interest**

Nothing to disclose.

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