Effects of Alcohol, Coffee, and Tobacco, Alone or in Combination, on Physiological Parameters and Anxiety in a Young Population

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Objective: The objective was to evaluate the effects of a single dose of alcohol, caffeine, and nicotine, alone or in combination, on physiological parameters (systolic and diastolic blood pressure [SBP and DBP] and heart rate [HR]) and state-trait anxiety in healthy young volunteers.

Method: The procedure reproduces the conditions under which the subjects ($n=76$) usually ingest alcohol (through an alcoholic beverage), caffeine (through a cup of coffee), and nicotine (by smoking a cigarette), separately or in combination, according to their consumption habits of each individual. SBP and DBP, HR, and state anxiety (SA) were registered before (phase 1) and after (phase 2) treatment.

Results: Intake of alcohol or alcohol-nicotine reduced DBP. Comparisons between control and combined treatment (coffee-alcohol-nicotine) groups revealed a decrease in HR in the former group but not in the latter. The coffee consumers alone exhibited a tendency toward an increase in SA, while the control group showed a tendency toward a decrease in this measure. When Phase 1 and Phase 2 were compared, a decrease was observed in SBP (alcohol and coffee-alcohol groups), DBP (alcohol and alcohol-nicotine groups), HR (all groups, except coffee-alcohol and coffee-alcohol-nicotine groups), and SA (coffee-alcohol-nicotine group).

Conclusions: (i) A low dose of alcohol, either alone or in combination with a cigarette, decreases DBP but not SBP; (ii) the polyconsumption of coffee, alcohol, and nicotine blocks the adaptation response (the reduction in HR in control subjects in the second phase); (iii) an increase of SA is observed after consuming coffee, while the opposite occurs in control subjects (a decrease of SA).

Introduction

ALCOHOL, CAFFEINE in coffee, and nicotine in tobacco are the three most widely consumed psychoactive substances in the world. These drugs exert a considerable influence on the cardiovascular system¹⁻³ and behavioral mood state.^{1,4} Nicotine and caffeine tend to have the opposite effects to alcohol, with the former two substances producing stimulating effects and the latter generally producing sedating effects.⁵

The effects of alcohol, caffeine, and nicotine on the central nervous system (CNS) are multifaceted, with diverse actions in several neurotransmitter systems. When a low dose of alcohol is ingested, the dopaminergic, serotonergic, and noradrenergic systems are stimulated.⁶ On the one hand, the intake of a high dose of alcohol produces a reduction of dopaminergic and noradrenergic transmission. On the other hand, gamma-aminobutyric acid (GABA)'s general central depressant actions are potentiated through ethanol-induced enhancement of its binding to the GABA_A receptor complex.⁷

In the brain, caffeine is a nonselective adenosine receptor antagonist that mainly targets adenosine A₁ and A_{2A} receptors and has agonist effects on dopamine.^{8,9} Nicotine is a potent activator of the sympathetic nervous system and it also enhances acetylcholine neurotransmission in the basal forebrain and dopamine release in the mesolimbic dopamine system.¹⁰ In contrast to nicotine and caffeine, alcohol acts as a CNS depressant. In addition, alcohol and adenosine generally have sedative effects in the CNS. Animal studies have demonstrated that some of the effects of alcohol are mediated by adenosine; for example, animals that are tolerant to adenosine's effects are also tolerant to alcohol's effects, adenosine agonists exacerbate alcohol's effects on motor incoordination, and adenosine induces sedation.¹¹

Considering the social dimension of alcohol, coffee, and tobacco consumption and the fact that large numbers of the population consume them together, it is surprising that the possible interactive effects of combinations of these psychoactive drugs on anxiety and cardiovascular functioning and the relation between them have rarely been examined.

TABLE 1. SUMMARY OF ANALYSIS OF VARIANCES FOR SYSTOLIC BLOOD PRESSURE

Treatment group	Mean ($\pm$ SEM) phase 1	Mean ($\pm$ SEM) phase 2	Treatment	Phase	Treatment $\times$ phase	Phase 1 vs. phase 2
Co	10.91 ($\pm$ 0.36)	10.45 ($\pm$ 0.42)	—	—	—	—
A	11.16 ($\pm$ 0.32)	10.64 ($\pm$ 0.28)	n.s.	*	n.s.	—
C	11.03 ($\pm$ 0.64)	11.14 ($\pm$ 0.52)	n.s.	n.s.	n.s.	—
N	10.92 ($\pm$ 0.39)	10.6 ($\pm$ 0.4)	n.s.	n.s.	n.s.	—
C-N	11.39 ($\pm$ 0.58)	11.53 ($\pm$ 0.57)	n.s.	n.s.	n.s.	—
A-N	10.42 ($\pm$ 0.25)	9.95 ($\pm$ 0.31)	n.s.	n.s.	n.s.	—
C-A	10.67 ($\pm$ 0.44)	9.95 ($\pm$ 0.23)	n.s.	*	n.s.	—
C-A-N	11.42 ($\pm$ 0.28)	11.13 ($\pm$ 0.45)	n.s.	n.s.	n.s.	—

* $p < 0.05$.

Treatment groups (for this and the following tables): Co, control; A, alcohol; C, caffeine; N, nicotine; C-N, caffeine-nicotine; A-N, alcohol-nicotine; C-A, caffeine-alcohol; C-A-N, caffeine-alcohol-nicotine; n.s., not significant.

Nicotine and alcohol are often consumed concurrently.¹² When consumed alone they produce significant subjective and cardiovascular responses, but nicotine attenuates the sedating and intoxicating effects of alcohol and additive subjective and cardiovascular effects are generally observed when the two drugs are consumed together.¹³ For example, infusion of nicotine after ingestion of alcohol produces an additive increase in the heart rate (HR) and systolic blood pressure (SBP).¹⁴

Caffeine consumption is widespread among young students.¹⁵ Caffeine has been associated with increases in several cardiovascular disease risk factors,^{16,17} such as higher blood pressure (BP), an acute effect of coffee.¹⁸ In contrast, recent studies have reported health benefits associated with coffee consumption.^{19,20} At low doses, caffeine improves hedonic tone and reduces anxiety, while it produces an increase in tense arousal, including anxiety, nervousness, and jitteriness, at high doses.²¹ Several studies have found that caffeine can reverse many of the performance-impairing effects of ethanol²²; for example, a low dose of caffeine prevented the sleepiness and performance impairment associated with a moderate dose of ethanol.²³ Conversely, there are studies of the effects of caffeine on alcohol-induced impairment that have not shown the former drug to reverse the performance deficit produced by the latter.²⁴

A combination of nicotine and caffeine generally produces additive subjective and cardiovascular effects.^{25,26} A significant association between nicotine and caffeine has been detected in subjective measures and BP responses.²⁷ The results of some research endorse giving coffee rather than pure caffeine to subjects as a more appropriate method of evaluating its effects, as this reproduces the conditions

under which caffeine is normally ingested.²⁸ This reasoning can be translated to tobacco and alcohol; smoking a cigarette reproduces the conditions under which nicotine is normally consumed, and drinking an alcoholic beverage reproduces the conditions under which alcohol is normally consumed. As far as we know, to date no studies have investigated the combined effects of alcohol, coffee, and tobacco administered in these conditions.

The objective of the present research was to evaluate the effects of a single dose of alcohol, caffeine, and nicotine, alone or in combination, on several physiological measures (SBP and diastolic blood pressure [DBP] and HR) and on state-trait anxiety in healthy young volunteers by reproducing the manner in which they are normally consumed by these subjects.

Materials and Methods

Subjects

Participants were 76 healthy undergraduate students at the Faculty of Psychology, University of Valencia, Spain (12 men and 64 women; numbers were representative of the gender distribution of these students in the Psychology Faculty; mean age: 20.34 ± 2.34 years). The volunteers were recruited as experimental subjects for this study according to self-report of their consumption habits and general health. They were distributed as follows: 10 control subjects, 10 smokers (≥ 7 cigarettes per day), 10 habitual coffee consumers (≥ 1 cup of coffee per day), 10 social consumers of alcohol (≥ 3 standard drinks per week), 10 smokers and habitual coffee consumers, 8 smokers and social consumers of alcohol, 9 social consumers of alcohol and habitual coffee consumers, and 9 smokers, habitual coffee consumers, and social consumers of alcohol.

TABLE 2. SUMMARY OF ANALYSIS OF VARIANCES FOR DIASTOLIC BLOOD PRESSURE

Treatment group	Mean ($\pm$ SEM) phase 1	Mean ($\pm$ SEM) phase 2	Treatment	Phase	Treatment $\times$ phase	Phase 1 vs. phase 2
Co	6.67 ($\pm$ 0.21)	6.67 ($\pm$ 0.33)	—	—	—	n.s.
A	7.06 ($\pm$ 0.19)	6.37 ($\pm$ 0.18)	n.s.	**	**	**
C	6.97 ($\pm$ 0.32)	6.64 ($\pm$ 0.23)	n.s.	n.s.	n.s.	—
N	6.75 ($\pm$ 0.34)	6.67 ($\pm$ 0.3)	n.s.	n.s.	n.s.	—
C-N	6.84 ($\pm$ 0.46)	7.07 ($\pm$ 0.71)	n.s.	n.s.	n.s.	—
A-N	6.92 ($\pm$ 0.15)	6.31 ($\pm$ 0.13)	n.s.	*	*	**
C-A	6.87 ($\pm$ 0.13)	6.36 ($\pm$ 0.3)	n.s.	n.s.	n.s.	—
C-A-N	7.13 ($\pm$ 0.17)	6.78 ($\pm$ 0.26)	n.s.	n.s.	n.s.	—

* $p < 0.05$.** $p < 0.01$.

Informed consent was obtained from all participants and the study was conducted in accordance with the Declaration of Helsinki. The inclusion criteria were as follows: 18 years old or older, a body mass index of 18–27, and good health (reported by the subjects themselves). The exclusion criteria were as follows: being on medication, a history of mental disorders, an irregular sleep pattern during the night before the experiment, a history of substance abuse, and intake of caffeine, alcohol, or tobacco during the afternoon-night prior to the experiment, except in the case of the habitual consumers.

Tests and apparatus

- The State-Trait Anxiety Inventory (STAI)²⁹ is a questionnaire consisting of 20 items referring to self-reported state anxiety (SA) and 20 items referring to trait anxiety (TA). All subjects completed the standardized Spanish version of the STAI.
- The Alcohol Use Disorders Identification Test (AUDIT)³⁰ was employed to measure alcohol dependency among the subjects. AUDIT is composed of 10 questions examining the quantity and frequency of alcohol drinking and alcohol-related behaviors and consequences, with a range of 0–40 in which a score of 8 or more indicates a problematic use of alcohol. A higher score is related to greater severity of alcohol dependence.
- The Fagerström Test for Nicotine Dependence³¹ was used to measure nicotine dependency among subjects. The test is comprised of 6 items with a range of 0–10, with higher scores indicating greater dependence.
- An alcoholmeter (Alcoquant® 6020, Envitec, Germany) was used to measure the concentration of alcohol in air expired by the social consumers of alcohol, before and after a drink.
- A co-oximeter (micro-CO meter, Micro Medical Limited, England) was employed to measure the concentration of carbon monoxide (CO) in air expired by smokers before and after smoking a cigarette.
- A digital automatic blood pressure monitor (M10-IT, OMRON, Spain) was used to measure SBP, DBP, and HR in all the subjects.

Procedure

The experimental procedure was approved by the Human Research Committee of the University of Valencia. According to their consumption habits, subjects were assigned to one of eight experimental treatment groups: Alcohol (A) (15.8 g in women and 18.7 g in men through an alcoholic beverage; these alcohol doses were chosen for every gender following the Widmark formula³² to obtain similar expected blood alcohol contents); Caffeine (C) (intake of a cup of coffee containing 80.6–86.73 mg caffeine, determined using the high-performance liquid chromatography technique); Nicotine (N) (the smoking of a cigarette after a minimum period of abstinence of 30 minutes); Caffeine-Nicotine (C-N) (the smoking of a cigarette and intake of a cup of coffee); Alcohol-Nicotine (A-N) (intake of an alcoholic drink and the smoking of a cigarette); Caffeine-Alcohol (C-A) (intake of a cup of coffee and an alcoholic drink); Caffeine-Alcohol-Nicotine (C-A-N) (intake of a cup of coffee and an alcoholic drink and the smoking

FIG. 1. Mean (+SEM) systolic blood pressure. Treatment groups: Co, control; A, alcohol; C, caffeine; N, nicotine; C-N, caffeine-nicotine; A-N, alcohol-nicotine; C-A, caffeine-alcohol; C-A-N, caffeine-alcohol-nicotine.

of a cigarette); and Control group (Co) (no intake). Each subject participated in two phases separated by an interval of 25 minutes: treatment (10 minutes) and waiting time (15 minutes). In the first phase, the physiological parameters of BP and HR were registered in all the subjects. The concentration of CO in the smokers was measured using a co-oximeter and the concentration of alcohol in the social consumers was measured by an alcoholmeter. SA was assessed using the STAI. In the second phase, the same measures were registered, as were TA, the AUDIT for alcoholic dependence in social consumers of alcohol (mean score: 6.5 ± 1.08), and the Fagerström questionnaire for smokers (mean score: 2.51 ± 0.41). An increase of CO was observed in all smokers after smoking a cigarette. The index of the concentration of alcohol in air expired before and after taking an alcoholic drink was 0.00 mg/L and 0.10–0.19 mg/L, respectively. All the experimental tests were performed between 10:00 a.m. and 01:00 p.m.

Statistics

Separate analysis of variances (ANOVAs) were performed for each measure (SBP, DBP, HR, SA, and TA) in each treatment

FIG. 2. Mean (+SEM) diastolic blood pressure. Treatment groups: Co, control; A, alcohol; C, caffeine; N, nicotine; C-N, caffeine-nicotine; A-N, alcohol-nicotine; C-A, caffeine-alcohol; C-A-N, caffeine-alcohol-nicotine. ** $p < 0.01$ versus same group pretreatment.

TABLE 3. SUMMARY OF ANALYSIS OF VARIANCES FOR HEART RATE

Treatment group	Mean ($\pm$ SEM) phase 1	Mean ($\pm$ SEM) phase 2	Treatment	Phase	Treatment $\times$ phase	Phase 1 vs. phase 2
Co	79.4 ($\pm$ 4.01)	74.1 ($\pm$ 2.88)	—	—	—	*
A	79.4 ($\pm$ 3.82)	75.8 ($\pm$ 3.17)	n.s.	**	n.s.	—
C	79.5 ($\pm$ 3.38)	72.5 ($\pm$ 4.01)	n.s.	**	n.s.	—
N	85.1 ($\pm$ 3.86)	78.9 ($\pm$ 3.19)	n.s.	**	n.s.	—
C-N	84.5 ($\pm$ 4.69)	77.3 ($\pm$ 4.25)	n.s.	**	n.s.	—
A-N	80.8 ($\pm$ 3.0)	76.7 ($\pm$ 3.07)	n.s.	*	n.s.	—
C-A	76.7 ($\pm$ 3.57)	77.8 ($\pm$ 4.33)	n.s.	n.s.	+	n.s.
C-A-N	75.3 ($\pm$ 3.22)	76.4 ($\pm$ 3.27)	n.s.	n.s.	*	n.s.

* $p < 0.05$.** $p < 0.01$.+ $p = 0.06$.

group (A, C, N, C-N, A-N, C-A, and C-A-N) with respect to Co, with two factors: the between-subjects factor "Treatment" and the intra-subjects factor "Phase." When their interaction was statistically significant, *post hoc* analyses were carried out by means of Student's *t*-tests for dependent and independent samples. Correlations between SA and the rest of the physiological parameters were calculated. All analyses were performed using the "Statistica" software package, version 5.5 for windows.³³

Results

Blood pressure

A summary of the BP results is provided in Tables 1 and 2.

The ANOVAs revealed that the factor "Treatment" was not significant for SBP or DBP in any of the treatment groups. When the factor "Phase" was significant, a decrease of SBP and DBP was observed in the A group [$F(1,18)=4.5$; $p < 0.05$ and $F(1,18)=8.66$; $p < 0.01$, respectively] and a decrease of DBP was observed in the A-N group [$F(1,16)=5.78$; $p < 0.05$]. No significant interaction was found for SBP (see Fig. 1).

Significant interactions were observed in the treatment group A [$F(1,18)=8.65$; $p < 0.01$] and in the treatment group A-N [$F(1,16)=5.78$; $p < 0.05$] for DBP. The comparisons of dependent samples revealed no changes in DBP in the control group [$t(9)=0$; *n.s.*] and a decrease in the A [$t(9)=5.67$; $p < 0.005$] and A-N [$t(7)=4.60$; $p < 0.005$] treatment groups (see Fig. 2). The comparisons of independent samples showed no significant differences ($ps > 0.05$).

Heart rate

A summary of HR results is provided in Table 3.

The factor "Treatment" was not significant for HR in any of the treatment groups. When the factor "Phase" was significant, a decrease of HR was observed in the following treatment groups: A [$F(1,18)=9.20$; $p < 0.01$], C [$F(1,18)=25.30$; $p < 0.01$], N [$F(1,18)=10.22$; $p < 0.01$], C-N [$F(1,18)=16.78$; $p < 0.01$], and A-N [$F(1,16)=7.30$; $p < 0.01$]. A significant interaction was detected for the C-A-N treatment group [$F(1,17)=6.05$; $p < 0.05$] and a tendency toward a significant interaction was observed in the C-A group [$F(1,17)=3.84$; $p = 0.06$]. The comparisons of dependent samples showed a significant decrease in the control group [$t(9)=3.15$; $p < 0.05$] and no differences in the C-A-N group [$t(8)=0.55$; *n.s.*] and the C-A group [$t(8)=0.38$; *n.s.*] (see Fig. 3). The comparisons of independent samples showed no significant differences ($ps > 0.05$).

State-trait anxiety

A summary of the SA results is provided in Table 4.

The factor "Treatment" was significant in the A treatment group, in which there was an increase of SA. The factor "Phase" was significant in C-A-N treatment group, which showed a decrease in SA. A significant interaction with SA was observed only in the C treatment group [$F(1,18)=7.49$; $p < 0.05$]. The comparisons of dependent samples showed a tendency toward a decrease in the control group [$t(9)=1.99$; $p = 0.07$] and an increase of SA in the C treatment group [$t(9)=2.02$; $p = 0.07$] (see Fig. 4). The comparisons of independent samples showed no significant differences ($ps > 0.05$).

No significant effects on TA were observed for any of the treatment groups in any of the ANOVAs performed.

Posttreatment correlations between SA and BP (systolic and diastolic) and SA and HR are indicated in Table 5. Statistically significant positive correlations were observed between SA and DBP ($p < 0.05$) in the C group, and between SA and HR ($p < 0.05$) in the N group.

Discussion

Alcohol, coffee, and tobacco are the most widely consumed psychoactive substances in the world, and the effects of each one have been widely studied. However, the effects of their

FIG. 3. Mean ($\pm$ SEM) heart rate. Treatment groups: Co, control; A, alcohol; C, caffeine; N, nicotine; C-N, caffeine-nicotine; A-N, alcohol-nicotine; C-A, caffeine-alcohol; C-A-N, caffeine-alcohol-nicotine. * $p < 0.05$ versus same group pre-treatment.

TABLE 4. SUMMARY OF ANALYSIS OF VARIANCES FOR STATE ANXIETY

Treatment group	Mean ($\pm$ SEM) phase 1	Mean ($\pm$ SEM) phase 2	Treatment	Phase	Treatment $\times$ phase	Phase 1 vs. phase 2
Co	22.3 ($\pm$ 5.53)	13.7 ($\pm$ 4.08)	—	—	—	+
A	28.0 ($\pm$ 4.05)	35.0 ($\pm$ 6.04)	*	n.s.	n.s.	—
C	16.0 ($\pm$ 3.98)	21.0 ($\pm$ 3.64)	n.s.	n.s.	*	+
N	17.3 ($\pm$ 6.54)	13.3 ($\pm$ 4.9)	n.s.	n.s.	n.s.	—
C-N	25.3 ($\pm$ 9.52)	23.6 ($\pm$ 9.93)	n.s.	n.s.	n.s.	—
A-N	18.87 ($\pm$ 6.16)	21.87 ($\pm$ 5.88)	n.s.	n.s.	n.s.	—
C-A	15.77 ($\pm$ 4.39)	12.88 ($\pm$ 1.93)	n.s.	n.s.	n.s.	—
C-A-N	18.88 ($\pm$ 2.31)	13.0 ($\pm$ 3.03)	n.s.	*	n.s.	—

* $p < 0.05$.+ $p = 0.07$.

polyconsumption at low doses on physiological parameters and anxiety in young populations have rarely been examined.

We have observed in our student population that DBP decreases after intake of alcohol, either alone or in combination with a cigarette, while no significant effects on SBP are produced. This finding challenges previously published data suggesting that alcohol consumption increases BP³⁴ and that the infusion of nicotine after ingestion of alcohol produces an additive increase in HR and SBP.¹⁴ An almost significant negative correlation between anxiety and SBP—the lower the SBP, the higher the SA—was detected in the alcohol-nicotine group. However, no changes in SBP and SA were observed in this treatment group.

HR decreased, independently of the factor "Treatment," in all our subjects, with the exception of the C-A and C-A-N polyconsumers. We believe that this effect could be due to a process of adaptation to the experimental situation, reflecting a physiological relaxation characterized by a decrease in HR. The interaction of "Treatment" and "Phase" was statistically significant only in the polyconsumption (C-A-N) group, while there was a tendency toward significance in the C-A group. A reduction of HR was observed in the control group, as previously reported,³⁵ while the combined intake of coffee, alcohol, and nicotine blocked an adaptation of this physiological response. The novelty of these results lies in that the strongest effects were observed with a combination

of the three substances, which suggests a synergic effect that is not present when any one drug is consumed alone or paired with one of the other two.

With respect to SA, alcohol consumers showed higher levels of SA than control subjects when the factor "Phase" was not considered. However, under the acute effects of alcohol, SA did not vary in these consumers. The literature shows that during acute alcohol intake caffeine antagonizes the unwanted effects of alcohol by blocking the adenosine A₁ receptor that mediates alcohol's somnogenic and ataxic effects.³⁶ We did not observe this antagonism of the two drugs with respect to SA. Caffeine alone had anxiogenic effects, in contrast to the anxiolytic observed by Nehlig²¹ with low doses of caffeine, and no effects were observed with alcohol. Our coffee consumers showed a different pattern of SA response when compared with control subjects; after coffee consumption SA increased in the former group and decreased in the latter group. The dose of caffeine employed (80.6–86.73 mg) is within the range of those commonly administered in studies examining the effects of this substance.^{37–39} Our results are similar to those of other studies reporting an alteration of SA³⁸ and studies in which neither HR nor BP was altered by doses of 75 and 150 mg of caffeine, alone^{38,40} or in combination with nicotine.⁴⁰ We think that the dose administered in the present study was too low to modify the pattern of cardiovascular response or to produce the additive cardiovascular effects (when combined with nicotine) previously described by Perkins *et al.*²⁵ Nevertheless, we can report that caffeine disrupts the process of adaptation to an experimental situation without disrupting cardiovascular parameters.

In contrast to our results, other studies have found that nicotine affects anxiety.^{41,42} However, the route of administration, dose, and time course could result in a differential activation of the pathways involved in emotionality, so that, depending on the behavioral study in question, nicotine may have either an anxiolytic or anxiogenic effect.⁴²

As expected, all our subjects exhibited similar TA independently of the treatment received. In accordance with this finding, it is reasonable to suppose that differences in SA observed in the treatment groups were due to the experimental treatment in question rather than to stable individual differences of personality.

Although a positive correlation was observed between anxiety and DBP in the caffeine group (the higher the SA, the higher the DBP), only SA (and not BP) was affected in the caffeine consumers. The scarcity of correlations between anxiety and cardiovascular parameters (see Table 5) is in

FIG. 4. Mean ($\pm$ SEM) state anxiety. Treatment groups: Co, control; A, alcohol; C, caffeine; N, nicotine; C-N, caffeine-nicotine; A-N, alcohol-nicotine; C-A, caffeine-alcohol; C-A-N, caffeine-alcohol-nicotine. + $p = 0.07$ versus same group pre-treatment.

TABLE 5. POSTTREATMENT CORRELATIONS BETWEEN STATE ANXIETY AND SYSTOLIC BLOOD PRESSURE, DIASTOLIC BLOOD PRESSURE, AND HEART RATE

Treatment group	SBP	DBP	HR
Co	0.07 ($p=0.84$)	-0.12 ($p=0.75$)	-0.03 ($p=0.94$)
A	0.01 ($p=0.98$)	0.49 ($p=0.15$)	-0.42 ($p=0.23$)
C	-0.02 ($p=0.96$)	0.63 ($p=0.05$)*	-0.19 ($p=0.59$)
N	0.22 ($p=0.54$)	0.61 ($p=0.06$)	0.70 ($p=0.02$)*
C-N	-0.43 ($p=0.21$)	-0.26 ($p=0.47$)	-0.13 ($p=0.72$)
A-N	-0.68 ($p=0.06$)	-0.52 ($p=0.19$)	0.41 ($p=0.31$)
C-A	0.41 ($p=0.28$)	0.26 ($p=0.49$)	-0.22 ($p=0.57$)
C-A-N	0.18 ($p=0.64$)	0.57 ($p=0.11$)	0.56 ($p=0.17$)

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

* $p \leq 0.05$.

agreement with literature, in which anxiety appears not manifested by elevated HR and BP in healthy population.⁴³

Nicotine normally elicits a potent cardiovascular activity.⁴⁴ However, our results demonstrate that its administration in the form of a cigarette after a minimum abstinence period induces tolerance to cardiovascular responses to this drug in young normotensives. A positive correlation between anxiety and HR was observed in this group of smokers—the higher the SA, the higher HR—but neither SA nor HR was affected in this treatment group. A positive close-to-significant correlation between anxiety and DBP was also detected in this group, although these measures (BP and SA) were not affected by nicotine.

In summary, taking into account that the present results have been obtained in a sample of young people according to their consumption habits and reproducing the conditions under which they normally consume these substances, we can affirm that

- (1) a low dose of alcohol, either alone or in combination with a cigarette, decreases DBP but not SBP.
- (2) HR is unaffected with respect to controls, with the exception of combined consumption of coffee, alcohol, and nicotine, in which there is a blockage of the normal adaptation response.
- (3) an increase of SA occurs after consumption of coffee, while control subjects show an opposite pattern (a decrease of SA).

Future research is required to better understand the interrelationships between alcohol, caffeine, and tobacco in young people with consumption habits established since adolescence. Importantly, the conditions under which subjects normally consume these substances should be reproduced as closely as possible when carrying out such studies. Knowledge of these factors should be of great assistance in the development and improvement of drug addiction prevention programs.

Acknowledgments

The authors wish to thank Mr. Brian Normanly for his editorial assistance. This study is supported by a grant GV2007-083 from "Generalitat Valenciana," Spain (PI: C.V.-C.).

Author Disclosure Statement

All authors declare that they have no conflicts of interest.

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