



Full length article

Hostility predicts alcohol consumption over a 21-year follow-up in the Gazel cohort



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ARTICLE INFO

Keywords:

Hostility

Hostile behaviors

Alcohol

Risk factor

Longitudinal analysis

Survey

ABSTRACT

Background: Hostility has been found to be positively associated with alcohol intake in cross-sectional studies. Our aim was to examine prospectively the long-lasting association of hostility with alcohol consumption.

Methods: We included 10,612 men and 3834 women from the French Gazel cohort with mean ages in 1993 of 48.6 (SD = 2.9) and 45.7 (SD = 4.2), respectively. Hostility (i.e., total, cognitive and behavioral) was assessed in 1993 with the Buss and Durkee Hostility Inventory. Alcohol consumption was self-reported annually from 1994 to 2014. Hostility scores were introduced successively in general linear mixed models with annual alcohol consumption in drinks per week as dependent variable. Multivariable analyses were adjusted for age, occupational status, marital status, retirement status and depression score. All the analyses were stratified by sex.

Results: Among men (women), 83.0% (76.2%) completed at least 75% of all annual assessment of alcohol consumption over a 21-year follow-up. In univariate analysis, alcohol consumption was associated with total and behavioral hostility in both sex (all $p < 0.001$). In multivariable analyses, these associations remained significant with a greater size effect for behavioral hostility. Estimated means of alcohol consumptions ranged from 10.50 [95%CI: 10.01–10.92] drinks per week to 13.32 [95%CI: 12.90–13.74] in men and from 4.09 [95%CI: 3.71–4.46] to 5.78 [95%CI: 5.39–6.17] in women, for the first and last quartiles respectively (p trends < 0.001 and all pairwise comparisons < 0.01). Similar effects were observed among participants with at-risk alcohol consumption at baseline.

Conclusions: In both men and women, behavioral hostility predicted alcohol consumption over a 21-year follow-up. Interventions aiming at modulating behavioral hostility may help reducing its long-lasting influence on alcohol consumption.

1. Introduction

Harmful use of alcohol is one of the world's leading risk factors for morbidity, disability, and mortality (Nutt et al., 2010; Rehm et al., 2003; World Health Organization, 2014). Even if alcohol consumption tends to decrease with aging (Eastwood, 2013; Hoertel et al., 2015b; Whiteman et al., 1997), its damages are often underestimated in the elderly, despite being possibly more severe in older adults than in younger ones (Caputo et al., 2012). Among strategies aiming at reducing these damages, identifying risk factors of excessive alcohol consumption has been a critical issue (Iparraguirre, 2015; Leamy et al.,

2016). Prior research has identified multiple contributing factors to alcohol consumption, most of them being non-modifiable. For example, sex (Erol and Karpyak, 2015), age (Whiteman et al., 1997), and exposure to adversity during childhood (Keyes et al., 2011; Pilowsky et al., 2009) have an enduring influence on alcohol consumption over the lifespan. Some life events, such as retirement, bereavement, or marriage or separation (Keyes et al., 2011; Perreira and Sloan, 2001; Tamers et al., 2014; Zins et al., 2011) may have a transient effect on alcohol consumption (Tamers et al., 2014; Zins et al., 2011). Among other factors, socioeconomic status may also influence alcohol consumption (Heckley et al., 2016). Although this knowledge can be useful

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to clinicians in order to increase prevention and early interventions in these contexts (Sandler et al., 2016), the identification of modifiable predictors of alcohol consumption over time that can be targeted by specific interventions constitutes a major public health challenge. Among the identified long-lasting and partially modifiable risk factors, personality traits have been put forward (Hakulinen et al., 2015; Sher et al., 2000). Nevertheless, although the link between personality and alcohol consumption is often observed by clinicians or in cross-sectional studies, there is still a lack of prospective data to objectify such a link, its strength, and its reliability in both men and women (Littlefield and Sher, 2010; Nolen-Hoeksema, 2004).

Among personality traits, hostility has been found to be positively associated with alcohol intake (Barthelme et al., 2010; Lee et al., 1988; Schonwetter and Janisse, 1991; Whiteman et al., 1997) and with negative consequences of alcohol use (Butryn and Zeichner, 1997) in cross-sectional studies. Hostility is a multidimensional construct that encompasses both cognitive hostility (i.e., hostile thoughts such as resentment and suspicion) and behavioral hostility (e.g., aggressiveness) (Airagnes et al., 2015; Lemogne et al., 2010). Among 3326 men current drinkers, Boyle et al. found an association between hostility and total monthly intake of alcohol (Boyle et al., 2008). There was also a 15.1% reduced impact of hostility on mortality when adjusted on drinks per drinking day, suggesting a partial mediation effect of alcohol consumption on the relationship between hostility and all-cause mortality (Klabbers et al., 2013). A previous study conducted among 1592 participants found that cognitive hostility was associated with higher levels of alcohol consumption in both men and women after adjusting for age and occupational status whereas this association did not reach statistical significance regarding behavioral hostility (Whiteman et al., 1997). Indeed cognitive hostility has been found to be associated with other types of risk behaviors such as suicide attempts (Lemogne et al., 2011). Nevertheless, earlier studies tend to show stronger associations with the behavioral component of hostility (Butryn and Zeichner, 1997). Moreover, hostile behaviors are associated with impulsivity (Garcia-Forero et al., 2009), which is known to be related to excessive alcohol consumption (Leamy et al., 2016; Verdejo-Garcia et al., 2008). It is noteworthy that interventions aiming at reducing hostility exist. Pharmacological strategies, such as antidepressant, could be useful (Kamarck et al., 2009). Non-pharmacological strategies aimed at diminishing hostility have been developed for patients with coronary heart disease, with evidence for their ability to improve outcomes (Gidron et al., 1999; Gulliksson et al., 2011; Whalley et al., 2011). However, cross-sectional studies may not be able to rule out reverse causality and longitudinal studies are needed to provide compelling evidence that hostility might be a risk factor of alcohol consumption, and thus a potentially useful target in both preventive and therapeutic interventions. To our knowledge, no study examined the potential long-lasting association of both behavioral and cognitive hostility on alcohol consumption.

Since 1989, the Gazel cohort has followed up employees of the French National Gas and Electricity Company who typically stayed in the same company during their entire career and continued to be followed after retirement (Goldberg et al., 2015). Hostility has been assessed in 1993 and participants reported annually their alcohol consumption over a 21-year follow-up. Our aim was therefore to take advantage of the opportunity offered by the Gazel cohort to examine the long-lasting association of hostility with alcohol consumption with a prospective design. We hypothesized that more hostile subjects will present higher levels of alcohol consumption over time. Due to the lack of reliability in previous findings regarding the differential impact

between behavioral and cognitive hostility components, we had no a priori hypothesis. However, determining whether one component is more strongly linked to alcohol consumption may help to further refine strategies targeting hostility and more generally interventions aiming at reducing alcohol consumption. Even if men-women convergence arises in younger birth cohorts (Slade et al., 2016), differences between men and women remain noteworthy regarding their pattern of alcohol use (i.e., abstinence, alcohol use and at-risk consumption) and their vulnerability for alcohol disorders, especially in middle-age and older subjects (Chan et al., 2007; Erol and Karpyak, 2015; French et al., 2014; Nuevo et al., 2015). Consequently, associations were examined in men and women, separately.

2. Material and methods

2.1. Participants

Details of the GAZEL cohort study are available elsewhere (Goldberg et al., 2015). In summary, the target population consisted of 44,922 employees of the French national gas and electricity company (Electricité de France-Gaz de France): 31,411 men aged 40–50 and 13,511 women aged 35–50. In January 1989, after an information campaign, these employees were invited to participate in the cohort on a voluntary basis. The invitation did not mention diseases or specific risk factors, but simply proposed participation in a long-term health study to help medical research. Data collection was anonymous and no data had been reported to the company. Refusal to participate in the survey had no impact on working life. Since beginning, the GAZEL cohort study has been managed by the same independent research team of the Institut National de la Santé et de la Recherche Médicale (INSERM), without any interference from the company in relation to the scientific work or publication of results (Goldberg et al., 2007). The study protocol was approved by the French authority for data confidentiality (Commission Nationale Informatique et Liberté) and by the Ethics Evaluation Committee of the Institut National de la Santé et de la Recherche Médicale, or INSERM (IRB0000388 and FWA00005831). In 1989, 20,625 employees (45.8%) (15,011 men and 5614 women) agreed to participate in the GAZEL cohort study. Since 1989, participants have been followed by means of an annual mailed questionnaire as well as through administrative databases. In 1993 a specific questionnaire, which was mailed to the 20,480 still-living cohort members, included measures of hostility with the Buss and Durkee Hostility Inventory (BDHI) and an assessment of depressive symptoms with the Center of Epidemiologic Studies Depression scale (CESD) (Buss and Durkee, 1957; Consoli et al., 1993; Fuhrer and Rouillon, 1989; Radloff, 1977). Alcohol consumption was self-reported in the annual questionnaire from 1993 to 2014. Among the 20,480 GAZEL volunteers still in the cohort in 1993, we identified as responders the 14,674 who completed the BDHI in 1993. Among the responders, 14,456 had reported at least once their alcohol consumption between 1994 and 2014. Among the responders who fulfilled this inclusion criterion, 10 had missing data for occupational status, thus 14,446 have finally been included (Supplemental Fig. 1).

2.2. Hostility assessment

Hostility was assessed thanks to the Buss and Durkee Hostility Inventory (BDHI) (Buss and Durkee, 1957; Lemogne et al., 2011). This scale is a measure of general aggression and hostility, composed of 75 items with ‘true-false’ answers. It has eight subscales, seven of which

are designed to measure different components of hostility: assault, verbal aggression, indirect hostility (i.e., devious hostility like gossip), irritability, negativism (i.e., usually oppositional behavior against authority, refusing to cooperate), resentment and suspicion (Nabi et al., 2006). The sum of these subscales leads to a ‘total hostility’ score. Several factor analyses identified two overarching factors, namely ‘behavioral’ (i.e., hostile behaviors) and ‘cognitive’ hostility (i.e., hostile thoughts), formed by the first three subscales and the last two subscales, respectively. The behavioral component of hostility includes items such as “There are people who pushed me so far that we came to blows” and “I can’t help getting into arguments when people disagree with me”. The cognitive component of hostility includes items such as “I wonder why sometimes I feel so bitter about things” and “When people are especially nice, I wonder what they want”. Regarding internal consistency of the BDHI, Cronbach’s alpha were 0.87; 0.78 and 0.77 in Lemogne et al. (Lemogne et al., 2011), and they are 0.88; 0.80 and 0.78 in the present study, for total, behavioral and cognitive scales, respectively. A pilot study in 1991 among a random sample of 408 male G-AZEL cohort members examined the 3-month retest reliability of the French version of the BDHI, ranging from $r = 0.63$ to $r = 0.80$ for these five subscale (Consoli et al., 1993).

2.3. Alcohol consumption assessment

According to the prospective design of the study, since hostility (i.e., our exposure) was assessed in 1993, alcohol consumption (i.e., our outcome) was assessed every year from 1994 to 2014. This assessment was based on a questionnaire already used in the literature (Zins et al., 2011) that comprised the following questions: “Have you consumed any wine (beer, cider, spirits) over the past week? If yes, what was the maximum quantity per day (number of glasses)? On how many days during the past week did you drink wine (beer, cider, spirits)?”. For each type of beverage, the volunteers checked a box under a drawing representing a standard drink. From these responses, we computed the number of drinks consumed weekly to define our continuous variable (Zins et al., 2011). We used this variable to categorize alcohol consumption in four classes according to the World Health Organization (WHO) levels of risk classification (World Health Organization, 2000). Thus we used the following cut-offs in men (women): $< 28(14)$; $< 43(29)$; $< 71(43)$ and $\geq 71(43)$ to define low, medium, high or very high risk categories, respectively.

2.4. Covariates

Age, sex, and occupational status (i.e., blue-collar workers or clerks, first-line supervisors or sales representatives and management or training) in 1993 were obtained from the employer’s human resources files as well as the date of retirement, which was used to compute the annual binary variable: retired or not. Marital status was asked annually in mailed questionnaire and used as a binary variable: living in couple or other (i.e., single, separated, divorced, widowed). Since depression has been found to influence the assessment of personality traits (Corruble et al., 2002), we also adjust our models for this covariate at the time of hostility assessment (i.e., in 1993). Depressive symptoms were assessed as a continuous variable in 1993 with the Center of Epidemiologic Studies Depression scale (CESD), which is a 20-item questionnaire designed for use in community studies. The CESD is known to have a high internal consistency (Fuhrer and Rouillon, 1989; Radloff, 1977), which is 0.77 in the present study. The CESD asks participants how often they have experienced specific symptoms during the previous week (e.g., ‘I felt depressed’, ‘I felt everything I did was an

effort’, ‘My sleep was restless’). Responses range from 0 (‘hardly ever’) to 3 (‘most of the time’).

2.5. Statistical analysis

To compute meaningful indicators, we recoded hostility scores for the total and both of the subscales (i.e., total, cognitive and behavioral) in dividing the crude scores by their sex-specific interquartile ranges (Burgess et al., 2009). To examine the longitudinal associations between hostility scores in 1993 and alcohol consumption measured from 1994 to 2014, we used general linear mixed models. We took as the dependent variable the annual alcohol consumption in drinks per week and we performed descriptive analyses of missing data for this variable, as displayed in the results section. All of the models included the year of assessment (i.e., from 1994 to 2014) as fixed effect, and a random effect on subjects for both slope and intercept (Jacqmin-Gadda et al., 2007). Hostility scores (i.e., total, cognitive and behavioral) were not introduced in the same model, but in three separate models, as fixed effects. In multivariable analysis, all the covariates were added simultaneously in the models as fixed effects. Since marital status and CESD score were missing for respectively 38.2% and 26.9% observations among included participants, we performed stochastic regression imputation to adjust the results of the entire sample for these covariates (Airagnes et al., 2016; Haukoos and Newgard, 2007). There were no missing data for other covariates. All analyses were stratified by sex.

When the association between hostility and alcohol consumption was significant, we examined the sex*hostility interactions. Furthermore, a dose-response relationship was searched for dividing the hostility score into quartiles. The impact of hostility on alcohol consumption was also examined in the sub-sample of at-risk consumers in 1993, defined as a belonging to medium, high or very high risk categories according to the World Health Organization (WHO) levels of risk classification, i.e., having reported an alcohol consumption higher than 28(14) drinks per week in men (women) (World Health Organization, 2000).

As sensitivity analysis, we searched for an interaction between each hostility component and the year of assessment. If significant, analyses have been redone within the three following periods: 1994–2000; 2001–2007 and 2008–2014, to examine whether the associations remained significant at different times of follow-up and that a cohort effect was not at work in our study. Since abstainers may differ from general population (Rodgers et al., 2000), we also planned to repeat the analysis when excluding the participants who reported zero drink per week in 1993. The remaining sample included 9625(90.7%) men and 2875(75.0%) women. Finally, we searched for similar results after dealing with missing data regarding alcohol consumption measures thanks to multiple imputations (Lee and Simpson, 2014).

As specificity analysis, in order to test whether the association between hostility and alcohol consumption may reflect of a general vulnerability to addictive behaviors, we repeated the main analysis with the annual smoking status (categorized as non-smoker, less than 10 cigarettes per day, between 11 and 20, and more than 21) as dependent variable. This variable has been computed annually from 1994 to 2014 following participants’ answers in the mailed questionnaire.

Statistical significance was determined using a two-sided alpha a priori set at 0.05 and analyses were performed with RStudio, Version 0.99.484 (RStudio, 2015) and IBM SPSS 22.0 (IBMCorp, 2013).

Table 1
Characteristics of men (n = 10,612) and women (n = 3834) at baseline (i.e. in 1993).

SEX	MEN		WOMEN	
N (%)	10,612 (73.5)		3,834 (26.5)	
CONTINUOUS VARIABLES	Mean	SD	Mean	SD
Age (years)	48.55	2.89	45.74	4.19
Depression score (CESD) ¹	13.21	9.19	13.30	9.21
Alcohol consumption (drinks per week) ²	13.00	12.30	4.60	6.77
Hostility scores (BDHI)³				
Total	2.02	0.72	2.27	0.74
Cognitive	1.16	0.74	1.06	0.62
Behavioral	2.09	0.76	2.05	0.73
CATEGORICAL VARIABLES	N	%	N	%
Occupational status				
Blue-collar workers, clerks	1144	10.8	828	21.6
First-line supervisors, sales representatives	5496	51.8	2588	67.5
Management	3972	37.4	418	10.9
Marital status¹				
Living in couple	9334	88.0	3336	87.0
Other	1278	12.0	498	13.0

SD: Standard Deviation; CESD: Center of Epidemiologic Studies Depression scale; BDHI: Buss and Durkee Hostility Inventory.

¹ Results are presented after imputation for missing data.

² From a subsample of 9,908 men and 3,571 women due to missing data.

³ Presented values are crude scores divided by their related interquartile ranges.

3. Results

3.1. Participants' characteristics

Compared to non-responders, responders were older at baseline ($p = 0.003$), more likely to be men ($p = 0.001$) and with a higher occupational status ($p < 0.001$) (Table S1). The study population included 10,612 men and 3834 women; their characteristics at baseline are presented in Table 1. The median number of available data points regarding alcohol consumption across the 21-year follow-up was 20 in both sexes. Among men(women) who survived throughout the entire follow-up, 83.0%(76.2%) completed at least 75% of all annual assessments. Overall, across sexes and periods, 87–97% of participants completed at least 75% of all annual assessments (Tables S2a and S2b). Descriptions of the changes for annually assessed variables (i.e., alcohol consumption in drinks per week, marital status and retired or not) over the three periods are presented in Table S3.

3.2. Predictors of alcohol consumption over the 21-year follow-up

In men, the univariate analysis revealed that alcohol consumption decreased over time and was higher among older men at baseline as well as after retirement (Table 2a). Depression at baseline, as well as occupational status and marital status were not associated with alcohol consumption. Total and behavioral hostility were significantly associated with alcohol consumption, showing estimated parameters of 1.1 and 1.2 drinks per week for each increase of 7-points (i.e., the interquartile range in men) in the total and behavioral hostility scale, respectively (both $p < 0.001$). In multivariable analysis, all these associations remained significant (all $p < 0.01$).

In women, the univariate analysis in the same way that alcohol

consumption decreased over time and was higher among women older at baseline as well as after retirement (Table 2b). Furthermore, alcohol consumption was greater among women with a higher occupational status and living in couple (both $p < 0.001$). Depression at baseline was not associated with alcohol consumption. Total and behavioral hostility were significantly associated with alcohol consumption, showing estimated parameters of 0.5 and 0.7 drinks per week for each increase of 7-points (i.e., the interquartile range in women) in the total and behavioral hostility scales, respectively (both $p < 0.001$). In multivariable analysis, all these associations remained significant (all $p < 0.001$).

In univariate analysis, the interactions with sex and both total ($F = 9.065$; $p = 0.003$) and behavioral ($F = 5.214$; $p = 0.022$) hostility components were significant, as well as in multivariable analysis. Since greater effect sizes were observed for behavioral hostility in both men and women, a graphical description of alcohol consumption in drinks per week according to behavioral hostility quartiles is presented in Fig. 1. Considering behavioral hostility quartiles in multivariable analysis, estimated means of alcohol consumptions ranged from 10.50[95%CI:10.01–10.92] drinks per week to 13.32[95%CI:12.90–13.74] in men and from 4.09[95%CI:3.71–4.46] to 5.78[95%CI:5.39–6.17] in women, for the first and last quartiles respectively (p trends < 0.001 and all pairwise comparisons < 0.01) (Fig. 2). Among the 1.375(13.0%) men and 298(7.8%) women who were at-risk consumers at baseline (i.e., medium risk category or above in 1993, defined as an alcohol consumption higher than 28(14) drinks per week in men (women)), estimated means of alcohol consumptions ranged from 24.73[95%CI:23.47–26.00] drinks per week to 25.89[95%CI:24.84–26.94] in men ($p = 0.524$) and from 12.88[95%CI:10.66–15.11] to 15.23[95%CI:13.47–16.98] in women ($p = 0.365$), for the first and last quartiles, respectively.

3.3. Sensitivity analysis

Since we found significant interactions between the year of assessment and total ($F = 33.714$; $p < 0.001$), cognitive ($F = 101.784$; $p < 0.001$) and behavioral hostility ($F = 61.197$; $p < 0.001$), we repeated the main analyses separately for each period of follow-up (i.e., 1994–2000; 2001–2007; 2008–2014) (Table 3). Regarding total and behavioral hostility, associations in multivariable analysis with alcohol consumption remained significant for the three periods although estimated parameters tend to slightly decrease throughout the follow-up. Consistent with the prevailing effect of behavioral hostility, cognitive hostility was associated with alcohol consumption only in men in the first period (i.e., 1994–2000) ($p = 0.002$).

When excluding abstainers at baseline (i.e., 1993), as well as after multiple imputations for missing data for alcohol consumption measures, significant associations between hostility and alcohol consumption remained significant in multivariable analysis, in both men and women.

3.4. Specificity analysis

When we took as dependent variable the annual smoking status in multivariable analysis, we found significant associations in both sex with total hostility (RR:1.17[95%CI:1.08–1.26] in men and RR:1.423[95%CI:1.254–1.614] in women) and with behavioral hostility (RR:1.194[95%CI:1.120–1.273] in men and RR:1.496[95%CI:1.331–1.682] in women) (all $p < 0.001$). No significant associations were found for the cognitive component of hostility. However, when including the annual smoking status as covariate in multivariable models

Table 2a
Univariate and multivariate longitudinal associations between hostility in 1993 and alcohol consumption from 1994 to 2014 in men (n = 10,612 at baseline).

TYPES OF VARIABLES	MODELS													
	UNIVARIATE ¹							MULTIVARIATE ²						
	Total hostility							Cognitive hostility						
CONTINUOUS VARIABLES	Estimated parameter ³	CI95%	t	p	Estimated parameter ³	CI95%	t	p	Estimated parameter ³	CI95%	t	p	Estimated parameter ³	p
Date of assessment (year)	-0.129	-0.134	-0.123	< 0.001	-0.222	-0.223	-0.214	< 0.001	-0.222	-0.230	-0.214	< 0.001	-0.222	< 0.001
Age in 1993 (years)	0.183	0.118	0.248	< 0.001	0.092	0.026	0.157	0.006	0.093	0.027	0.159	0.005	0.091	0.006
Depression score in 1993⁴	0.009	-0.012	0.029	0.394	-0.027	-0.049	-0.005	0.015	0.001	-0.022	0.024	0.074	-0.006	0.558
(Center and Epidemiological Scale for Depression)														
Hostility score in 1993⁵														
Total	1.125	0.863	1.388	< 0.001	1.294	1.008	1.579	8.882	< 0.001	0.264	-0.032	0.559	1.748	0.080
Cognitive	0.219	-0.037	0.475	0.094										
Behavioral	1.216	0.970	1.462	< 0.001									1.241	< 0.001
CATEGORICAL VARIABLES	Estimated mean ³	CI95%	F	p	Estimated mean ³	CI95%	F	p	Estimated mean ³	CI95%	F	p	Estimated mean ³	p
Occupational status in 1993			2.748	0.064			4.495	0.011			3.052	0.047		3.869
Blue-collar workers, clerks	11.759	11.182	12.336		11.305	10.723	11.886		11.402	10.816	11.988		11.330	
First-line supervisors, sales representatives	12.471	12.210	12.733		11.995	11.723	12.267		12.041	11.767	12.315		12.026	
Management	12.508	12.201	12.815		12.299	11.982	12.615		12.239	11.919	12.560		12.257	
Retirement status			1055.991	< 0.001			1033.614	< 0.001			1034.475	< 0.001		103.960
Yes	12.975	12.783	13.166		12.751	12.503	12.998		12.779	12.530	13.028		12.755	
No	11.192	10.991	11.394		10.982	10.726	11.238		11.009	10.752	11.266		10.986	
Marital status⁴			0.942	0.332			0.735	0.391			0.809	0.369		0.402
Living in couple	12.418	12.229	12.608		11.907	11.671	12.142		11.937	11.700	12.173		11.910	
Other	12.326	12.074	12.578		11.826	11.538	12.113		11.851	11.563	12.140		11.831	

CI: Confidence interval.

¹ Univariate analyses include the date of assessment as fixed effect and the subjects as random effect (slope and intercept).² Multivariate analyses include all the covariates as fixed effects and the subjects as random effect (slope and intercept).³ Alcohol consumption is assessed annually in drinks per week from 1994 to 2014.⁴ Results are presented after imputation for missing data.⁵ Crude scores of hostility were divided by their related interquartile ranges before being entered into the models.

Table 2b
Univariate and multivariate associations between hostility in 1993 and alcohol consumption from 1994 to 2014 in women (n = 3834).

TYPES OF VARIABLES	MODELS									
	UNIVARIATE ¹					MULTIVARIATE ²				
	Total hostility					Cognitive hostility				
CONTINUOUS VARIABLES	Estimated parameter ³	CI95%	t	p	Estimated parameter ³	CI95%	t	p	Estimated parameter ³	p
Date of assessment (year)	-0.038	-0.043	-0.033	< 0.001	-0.075	-0.083	-0.068	< 0.001	-0.075	< 0.001
Age in 1993 (years)	0.106	0.656	0.146	< 0.001	0.086	0.046	0.126	< 0.001	0.089	< 0.001
Depression score in 1993 ³	-0.012	-0.027	0.003	0.105	-0.025	-0.041	-0.009	0.002	-0.014	0.058
(Center and Epidemiological Scale for Depression)										
Hostility score in 1993 ³										
(Buss and Durkee Hostility Inventory)										
Total	0.482	0.256	0.709	< 0.001	0.733	0.489	0.978	< 0.001		
Cognitive	-0.196	-0.469	0.077	0.160						
Behavioral	0.724	0.493	0.955	< 0.001					0.820	< 0.001
CATEGORICAL VARIABLES	Estimated mean ³	CI95%	F	p	Estimated mean ³	CI95%	F	p	Estimated mean ³	p
Occupational status in 1993			15.723	< 0.001			17.938	< 0.001		< 0.001
Blue-collar workers, clerks	4.414	4.050	4.777		4.292	3.929	4.655		4.323	
First-line supervisors, sales representatives	4.561	4.356	4.765		4.366	4.161	4.571		4.366	
Management	6.056	5.547	6.564		5.983	5.478	6.489		5.927	
Retirement status			241.331	< 0.001			216.092	< 0.001		< 0.001
Yes	5.079	4.904	5.254		5.275	5.050	5.500		5.267	
No	4.250	4.073	4.428		4.486	4.260	4.711		4.477	
Marital status ⁴			91.781	< 0.001			81.929	< 0.001		< 0.001
Living in couple	4.884	4.711	5.057		5.201	4.980	5.421		5.192	
Other	4.206	4.010	4.401		4.560	4.322	4.798		4.552	

CI: Confidence interval.

¹ Univariate analyses include the date of assessment as fixed effect and the subjects as random effect (slope and intercept).

² Multivariate analyses include all the covariates as fixed effects and the subjects as random effect (slope and intercept).

³ Alcohol consumption is assessed annually in drinks per week from 1994 to 2014.

⁴ Results are presented after imputation for missing data.

⁵ Crude scores of hostility were divided by their related interquartile ranges before being entered into the models.

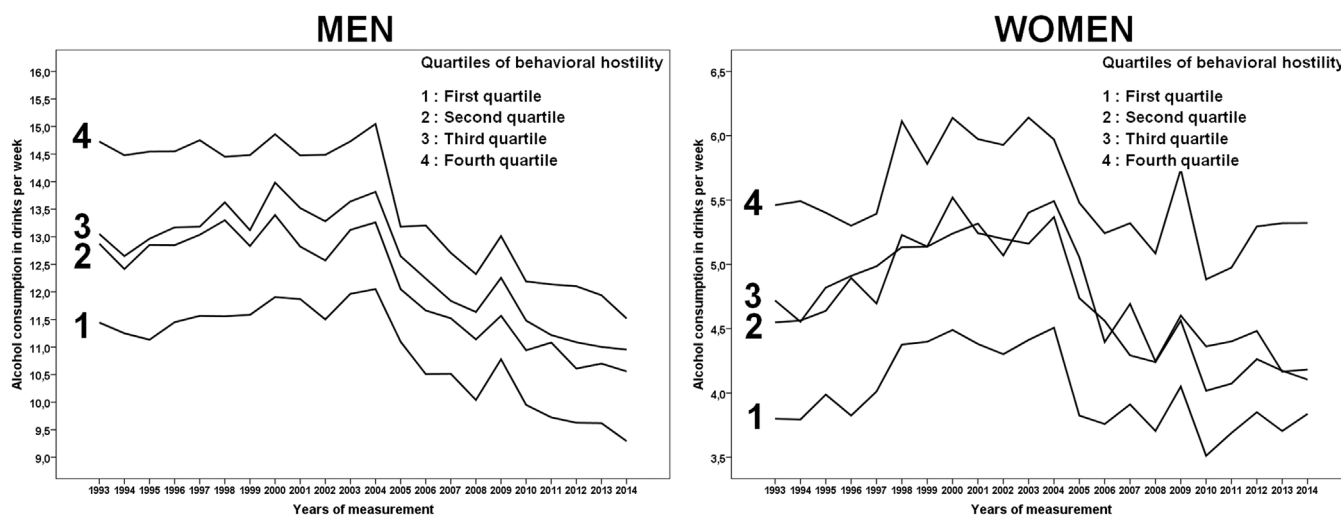


Fig. 1. Alcohol consumption trajectories following quartiles of hostility for both men ($n = 10,612$ at baseline) and women ($n = 3834$ at baseline).

The figure displays changes in annual alcohol consumption in drinks per week from 1993 to 2014 following each quartile of behavioral hostility, assessed with the Buss and Durkee Hostility Inventory, for men (left panel) and women (right panel), separately.

and taking alcohol consumption as dependent variable, statistical significance of results remained unchanged (data not shown).

4. Discussion

4.1. Summary of results

Our aim was to examine whether hostility (i.e., total, cognitive and behavioral) may predict alcohol consumption over a 21-year follow-up. In both men and women, total hostility was significantly associated with alcohol consumption in both univariate and multivariable analyses. These associations were mainly driven by the behavioral

component of hostility. A 7-point increase in behavioral hostility (i.e., the interquartile range) was associated with an estimated increase of 1.2 drinks per week and of 0.8 drinks per week, in men and women, respectively. These sex discrepancies have been found to be statistically significant in interactions tests. Moreover, similar effects were observed in participants belonging to at-risk categories of alcohol consumption

4.2. Strength and limitations

A major strength of this study is that it is based on alcohol measurements repeated yearly over an extended period of time. As

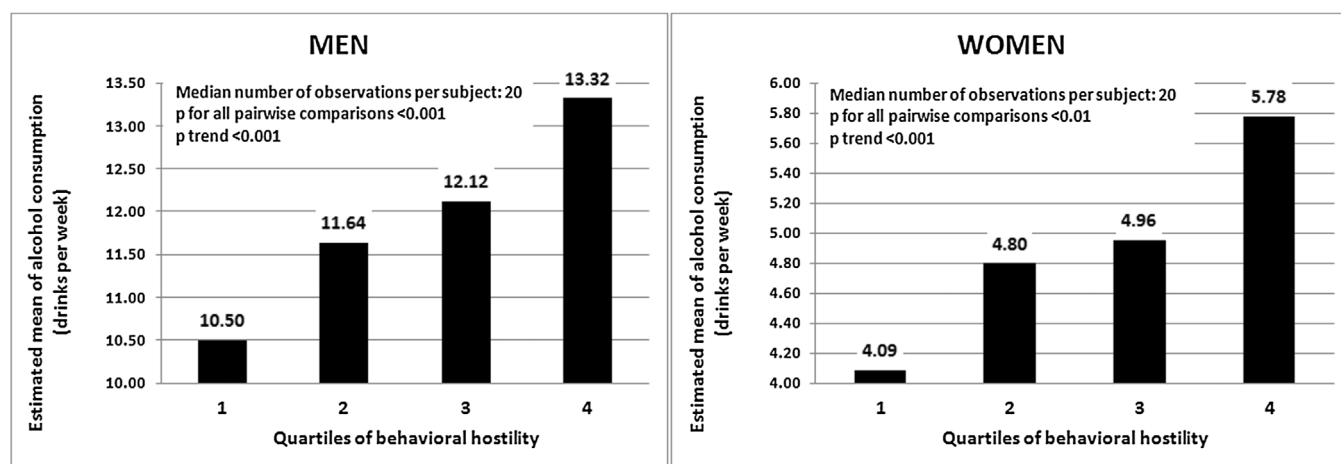


Fig. 2. Estimated means of alcohol consumption between 1994 and 2014 following quartiles of behavioral hostility, measured in 1993, in men ($n = 10,612$ at baseline) and women ($n = 3834$ at baseline), separately.

The figure displays estimated means of alcohol consumption in drinks per week across the entire follow-up (i.e., from 1994 to 2014) following quartiles of behavioral hostility, assessed with the Buss and Durkee Hostility Inventory, for men (left panel) and women (right panel), separately. Results derived from general mixed models, with alcohol consumption as dependent variable, and including the date of assessment as fixed effect, the subjects as random effect (slope and intercept) and adjustments for age, depression, occupational status, annually retirement status and annually marital status.

Table 3

Multivariate longitudinal analysis of the associations between hostility in 1993 and alcohol consumption from 1994 to 2014, divided into three successive periods, in men and women, separately.

Hostility score in 1993 (Buss and Durkee Hostility Inventory)	PERIODS											
	1994–2000				2001–2007				2008–2014			
	Estimated parameter	CI95%	t	p	Estimated parameter	CI95%	t	p	Estimated parameter	CI95%	t	p
MEN												
Total	1.567	1.249 1.885	9.667	< 0.001	1.186	0.871 1.501	7.382	< 0.001	1.054	0.746 1.361	6.715	< 0.001
Cognitive	0.516	0.184 0.847	3.051	0.002	0.047	−0.282 0.375	0.279	0.780	0.070	−0.251 0.391	0.428	0.669
Behavioral	1.410	1.135 1.685	10.059	< 0.001	1.176	0.905 1.448	8.490	< 0.001	1.012	0.746 1.277	7.469	< 0.001
WOMEN												
Total	0.752	0.489 1.015	5.597	< 0.001	0.773	0.491 1.056	5.367	< 0.001	0.649	0.379 0.918	4.713	< 0.001
Cognitive	0.132	−0.211 0.474	0.754	0.451	−0.012	−0.380 0.356	−0.065	0.948	−0.091	−0.443 0.261	−0.505	0.613
Behavioral	0.798	0.549 1.046	6.303	< 0.001	0.878	0.613 1.143	6.502	< 0.001	0.756	0.503 1.010	5.843	< 0.001

CI: Confidence interval. Alcohol consumption is assessed annually in drinks per week. These multivariate analyses include as fixed effects: date of assessment, age in 1993, depression score in 1993, occupational status in 1993, retirement status and marital status and the subjects as random effect (slope and intercept).

displayed in Fig. 1, the association between behavioral hostility and alcohol consumption remained virtually unchanged year after year over a 21-year follow-up. In addition, the overall pattern of alcohol consumption over the 21-year follow-up was consistent, especially in men, with both the effect of aging in alcohol consumption (Adams and Cox, 1995) and the decrease of consumption in the French general population during the two last decades (World Health Organization, 2014), thus strengthening the external validity of our results. The large sample size and the elevated response rate regarding our dependent variable are additional strengths. In addition, we were able to take into account several potential confounders including age (capturing both cohort effects and the effects of aging), occupational status, marital status, retirement status and depressive symptoms. The associations between covariates and alcohol consumption, as well as sex differences, were consistent with the literature (Reczek et al., 2016; Zins et al., 2011). Finally, as recommended in such cases, we used general linear mixed models including a random effect on subjects for both slope and intercept (Jacqmin-Gadda et al., 2007).

Since differences in estimated means of alcohol consumption between the first and the last quartiles of behavioral hostility were 2.8 drinks per week in men and 1.7 drinks per week in women, one may argue that the effect sizes may be too weak to be clinically meaningful. However, in the at-risk category of consumers, these differences continue to reach 1.16 and 2.35 drinks per week, in men and women, respectively. Since the burden of alcohol increases exponentially with the level of consumption (Rehm et al., 2011), the persistence of this gap in the at-risk category of consumers between the most hostile and less hostile subjects, and even a greater difference in women, should be taken into consideration in order to reduce alcohol-related harms.

There are some limitations. Firstly, subjects from the GAZEL cohort are not representative of the general population (Goldberg et al., 2007). Thus, our findings may not apply to others settings such as

younger subjects, lower job security, or other alcohol consumption patterns. Moreover, one might wonder about the reasons for such low attrition in our cohort and their potential consequences on our results. Although we cannot exclude that some participants might have felt compelled to participate to the study because the sample of Gazel participants is company-based, the company was not informed of who accepted to enter into the study. Moreover there was no obligation to participate to the cohort nor to answer the yearly questionnaires. All the data were collected anonymously, with a total independence of the company. The only incentives were the reception of a newspaper intended to the cohort's volunteers, the invitation at the annual conference and the satisfaction of being useful in participating in a medical research. Furthermore, at the time of inclusion in the study, participants were already in the cohort since four years and typically worked in the company for over twenty years with a great job security (Goldberg et al., 2007), limiting the risk of feeling his/her professional future threatened by the refusal to participate in a company-independent medical research. Secondly, the list-wise deletion of individuals who did not answer the 1993 questionnaire led to a decrease in statistical power and potentially a selection of the most motivated participants. Although responders did not differ from non-responders regarding sociodemographic data and alcohol consumption at baseline, we cannot exclude that hostility traits may increase the likelihood of being a non-responder. Therefore our results might have underestimated the weight of hostility in predicting alcohol consumption. Moreover, self-reported measures of behavioral hostility may reflect one's subjective representation of his (or her) own personality rather than objective aggressive behaviors. Thirdly, more than a quarter of participants did not fulfill the depression scale at baseline. Since hostility is influenced by depression and has been measured in a given point at baseline, adjustment for depressive symptoms aimed to avoid a biased assessment of hostility. We chose to deal with these missing data with imputation by stochastic regression on the other covariates (Graham et al., 2003). Nevertheless,

we cannot exclude that imputation fails to capture some depressed subjects. However, except for marital status, we had no missing data for the other covariates which may ensure the precision of the estimation of the depression score. Moreover, data were not missing in 73.1% of the cases and associations between hostility and alcohol consumption persist over two decades whereas depressive episodes are usually more circumscribed in time (Spijker et al., 2002). Fourthly, even a prospective design cannot rule out reverse causality, since hostility measured at baseline may partially result from past alcohol exposure (Heinz et al., 2011). Indeed, other potential confounding factors, such as impulsivity, were not measured. However, even if impulsivity may be a risk factor of alcohol consumption (Birkley and Smith, 2011), impulsivity and aggressiveness remain nonetheless two different constructs (García-Forero et al., 2009). Especially, even if aggressiveness may result from lack of self-control, which is related to impulsivity, it includes also thoughts and/or behaviors destined for doing harms to others or to oneself. Fifthly, hostility traits were measured at baseline only. Therefore, we cannot exclude subsequent changes in hostility levels that may explain the interaction between hostility and period. Even if associations between hostility and alcohol consumption slightly decreased over time, they remained significant while considering specifically the last period of follow-up (i.e., from 2008 to 2014). One may also argue that a putative decrease in hostility with aging, at least regarding its behavioral component (Barefoot et al., 1993), may contribute to the decrease in alcohol consumption. However, our analyses were based on a general mixed model taking age into account. Therefore, even if hostility traits may change with aging, the predictive value of the assessment of behavioral hostility on regarding alcohol consumption 21 years later remains clinically relevant. Finally, alcohol consumption was self-reported. Although the assessment of alcohol consumption may be less biased when the patient is alone through a decrease in social desirability bias (Del Boca and Darkes, 2003), self-report might have led to an underestimation of alcohol consumption. On the other hand, we estimated the weekly number of drinks from the number of days during the past week subjects reported that they drank alcohol and the maximum quantity consumed per day. This could have yielded an overestimation of alcohol consumption if levels of drinking vary to a great extent from one day to another (Zins et al., 2011). Nevertheless, the drinking pattern in middle-aged individuals over the last decades in France is globally stable, as in other South European countries like Italy where the questionnaire used in our study was developed (Corrao et al., 1991). Moreover, our aim was to examine the relationships between alcohol consumption and hostility rather than alcohol consumption per se.

4.3. Explanatory hypotheses

Our results were in accordance with previous cross-sectional findings regarding the associations between alcohol consumption and hostility. Since the behavioral component of hostility was primarily concerned in our study, our findings were also in agreement with previous findings on the role of impulsivity in alcohol use disorder (Fleury et al., 2014) given the strong association between impulsivity and hostile behaviors (Birkley and Smith, 2011; Leamy et al., 2016; Tikkanen et al., 2015; Verdejo-García et al., 2008). Moreover, programs aiming at reducing impulsivity among subjects who experience addictive behaviors may lead to a decrease in their substance consumption (Newton et al., 2016).

Although observational studies do not allow drawing causal conclusions, our results might nonetheless be consistent with direct causal

relationships to some extent. Firstly, there is evidence that hostility may predate alcohol use disorder. For instance, conduct disorders including hostile behaviors in the early adolescence has been found to be associated with subsequent alcohol use disorder (Cohen et al., 2007). These conduct disorders, which may occur in adolescents and young adults along with increasing impulsivity at this age, may thus explain why alcohol use disorders appear most often during this period (Littlefield and Sher, 2010). Secondly, hostility may contribute to reduced social support, which is associated with vulnerability to addictive behaviors in general (Boyle et al., 2008). Then, both hostility and poor social support could lead to depressive symptoms, which in turn are strongly associated with alcohol use disorder (Grant et al., 2004). Thirdly, alcohol intake may be used in the hope of controlling hostile behaviors (Schonwetter and Janisse, 1991). Some previous findings highlighted that hostile men may experience a better stress-response-dampening after alcohol intake than non-hostiles (Zeichner et al., 1995). These hypotheses are thus in agreement with alcohol expectancies theory which links alcohol damages to individual beliefs regarding the benefits of alcohol intake (Jones et al., 2001). Indeed, subsequent effects of acute alcohol intake may be highly dependent of individual differences in their a priori expectancies (Bjork, 2014). Therefore, acute alcohol intake is all the more likely to promote hostile behaviors that it has been driven by a wish to control hostility (Bartholow and Heinz, 2006) due to reduced behavioral inhibition (Pihl et al., 1993). Moreover, one could also suppose that hostile behaviors may be more socially accepted if they are attributed to alcohol consumption. Finally, as mentioned above, we cannot exclude that hostility measured at baseline may partially result from the long-standing effects of past alcohol exposure (Heinz et al., 2011). Chronic alcohol consumption has been associated with several changes in brain regions involved in cognitive control and behavioral inhibition (Makris et al., 2008) so that bidirectional causality may account for the strong association between behavioral hostility and alcohol consumption.

However, these strong associations between behavioral hostility and alcohol consumption might also be explained by common vulnerability factors. On a biological level, interactions between early life stress and genetic variations such as serotonin-related genes could lead to neurofunctional deregulations (e.g., increase in amygdala activity, impaired prefrontal function) that are related to an increased vulnerability to both alcohol consumption and aggressive behaviors (Heinz et al., 2011). More generally, several twin studies have suggested a shared genetic liability for a pattern of disorders that are characterized by impulsivity, including addictions and aggressive behaviors (Kendler et al., 2003). Since impulsivity (i.e., an impaired decision-making in the favor of an overemphasis on immediate rewards) has been repeatedly considered as an underlying mechanism of addictive behaviors (Gifford and Humphreys, 2007), this common vulnerability might explain, at least partially, the lack of specificity of the association between hostility and alcohol consumption, and thus the association with tobacco consumption as well. At a more general level, our findings are consistent with dimensional models of psychiatric comorbidity suggesting that an externalizing dimension, captured by behavioral hostility, might underlie the vulnerability for all substance use disorders (Blanco et al., 2013; Hoertel et al., 2015a).

4.4. Future research

The burden of alcohol intake is due to alcohol-related disorders but also to their behavioral consequences, including aggressive behaviors (Nutt et al., 2010). Our prospective study extend evidence

that behavioral hostility may be a risk factor of alcohol use disorder (Coccaro et al., 2016). Regarding hostility as a facilitator of alcohol-related damages (i.e., a moderator of the impact of alcohol), further prospective studies are needed to explore whether hostility may be a pathway between alcohol use disorder and violence (Tharp et al., 2012). Otherwise, since our results suggest that hostility might be a common predictor of alcohol and tobacco consumption during the lifespan, such associations might be explored in other addictions. For instance, cross-sectional findings among a sample of students suggest an association of hostility with alcohol use disorder as well as with marijuana consumption (Barthelmes et al., 2010). Further studies are needed to examine whether the increase in alcohol consumption following hostility is a mean increase over all the population or a greater increase among a specifically at-risk subsample. Future studies with repeated measures of hostility during lifespan may contribute to describe more precisely direction and potential changes in the strength of the associations between hostility and alcohol consumption considering current hostility assessment. Finally, future research may also focus on assessing the interventions aiming at reducing hostility, and especially its behavioral component, in order to reduce its long-lasting impact on alcohol consumption. These interventions, which have shown efficiency in other settings such as coronary heart disease (Gidron et al., 1999; Gulliksson et al., 2011; Whalley et al., 2011), might be implemented with two goals: as a preventive intervention, to prevent the development of an alcohol use disorder, or as a therapeutic intervention, to reduce alcohol intake in individuals with alcohol use disorders. These strategies suppose advances in standardizing the assessment of behavioral hostility in clinical practice, as well as specific communication tools since hostile subjects may challenge counseling interventions aiming at changing alcohol-related behaviors due to their unwillingness to trust others. In these situations, confrontational or impersonal educational approaches might be especially avoided, whereas motivational interviewing should be promoted (Barthelmes et al., 2010).

Conflicts of interest

Alice Gueguen, Nicolas Hoertel, Marcel Goldberg and Marie Zins have nothing to declare. Guillaume Airagnes has received speaker fees from Lundbeck. Cédric Lemogne has received speaker and consulting fees from Astra Zeneca, Daiichi-Sankyo, Lundbeck and Servier. Frédéric Limosin has received speaker and consulting fees from Astra Zeneca, Euthérapie-Servier, Janssen, Lundbeck, Otsuka Pharmaceutical France and Roche.

Contributors

Guillaume Airagnes and Cédric Lemogne designed the study and wrote the first draft of the manuscript. Marcel Goldberg and Marie Zins collected the data. Guillaume Airagnes managed the literature searches. Guillaume Airagnes and Alice Gueguen undertook the statistical analysis. All authors participated in the interpretation of results, revised the draft critically for important intellectual content and have approved the final manuscript.

Role of funding source

The GAZEL Cohort Study was supported by “Caisse d’Assurance Maladie des Industries Electriques et Gazières” (CAMIEG), the French Institute of Health and Medical Research (INSERM), the French “Cohortes Santé TGIR Programme”, Agence nationale de la recherche

(ANR) and Agence française de sécurité sanitaire de l’environnement et du travail (AFSSET). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Acknowledgement

Nothing to declare.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.drugalcdep.2017.03.034>.

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