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SCIENTIFIC INVESTIGATIONS

Circadian Sleep Propensity and Alcohol Interaction at the Wheel

Sergio Garbarino, PhD[1]; Lino Nobili, PhD[2]; Pierre Philip, PhD[3]; Giuseppe Plazzi, PhD[4]; Claudio Campus, PhD[5]; Elisa Morrone, PhD[6]; Fabrizio De Carli, MSc[7]; on behalf of the SALT group

[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal-Child Health, University of Genoa, Italy; [2]Center of Sleep Medicine, Niguarda Hospital, Milan, Italy; [3]University de Bordeaux, Sommeil, Attention et Neuropsychiatrie, Bordeaux, France; [4]Department of Biomedical and Neuromotor Sciences, University of Bologna and IRCCS Institute of Neurological Sciences, Bologna, Italy; [5]Italian Institute of Technology (IIT), Department of Robotics, Brain and Cognitive Sciences; [6]Sleep Center, Fondazione Salvatore Maugeri, IRCCS, Scientific Institute of Pavia, Italy; [7]Institute of Bioimaging and Molecular Physiology, National Research Council (CNR), Genoa, Italy

Study Objectives: The study was aimed at estimating the effect of alcohol consumption, time of day, and their interaction on traffic crashes in a real regional context.

Methods: Blood alcohol concentration (BAC) data were collected from drivers involved in traffic accidents during one year in an Italian region and in a control group of drivers over the same road network. Mean circadian sleep propensity was estimated from a previous study as function of time of day. Accident risk was analyzed by logistic regression as function of BAC and circadian sleep propensity.

Results: BAC values greater than zero were found in 72.0% of the drivers involved in crashes and in 40.4% of the controls. Among the former 23.6% of the drivers exceeded the BAC legal threshold of 0.05 g/dL, while illegal values were found in 10.4% of the controls. The relative risk showed a significant increase with both BAC and circadian sleep propensity (as estimated from time of day) and their interaction was significant.

Conclusions: Due to the significant interaction, even low BAC levels strongly increased accident risk when associated with high sleep propensity.

Keywords: crash risk, sleepiness, alcohol consumption, driving

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INTRODUCTION

Both alcohol consumption and sleepiness are primary risk factors for motor vehicle crashes.[1–3] Experimental studies showed that increasing levels of sleep deprivation, fatigue, and alcohol consumption progressively impair cognitive psychomotor performance with a comparable linear trend.[4] When associated with sleepiness, even low levels of alcohol intake can severely impair driving performance and risk perception.[5–8] Consistently, field studies suggested that serious road crashes more likely occur when sleepiness or fatigue are combined with alcohol intake.[9,10] The effect of sleepiness on car crashes in field studies was also evaluated by applying mathematical models considering the circadian and homeostatic processes of sleep-wake regulation[11,12]: estimated sleepiness proved to be an effective predictor of road crashes with a significant interaction with alcohol consumption.[11] In order to estimate the actual influence of circadian sleep propensity (as estimated from time of day), alcohol intake, and their interaction on the risk of car crashes, we prospectively investigated the distribution of accidents and alcohol consumption at the wheel in a Northern Italian region.

METHODS

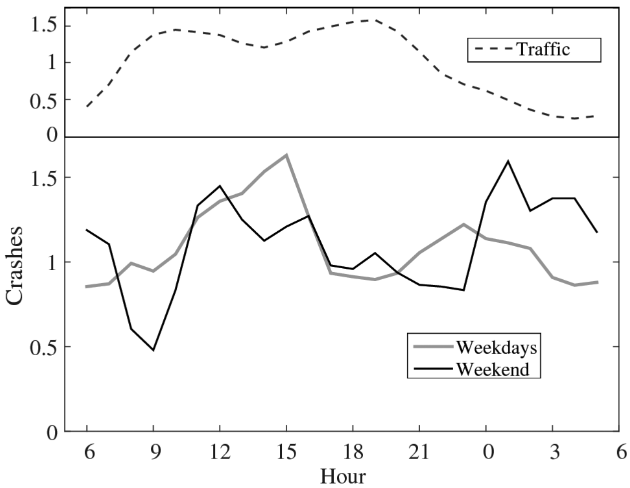
Drivers involved in car crashes occurred on highways, urban and suburban roads in Liguria (IT) during one year (2009–2010) underwent on-the-spot (breath-analyzer) or in-hospital (blood analysis) blood alcohol concentration (BAC). The sample involved almost all cases in which police assistance was requested and excluded a small number (75) of accidents in which the presence of psychoactive drugs was established, few cases in which emergency problems prevented data recording, and a number of minor crashes in which assistance was not requested. To estimate the 24-h alcohol exposure among car drivers over the same road network, Italian Highways and Metropolitan Police randomly collected on-the-spot BAC from control car drivers not involved in car accidents. The study involved police patrols controlling Ligurian highways, urban and suburban roads (about 5,350 km), and shift-working with 24-h coverage and 14 emergency units of Liguria Region, involved in data recording for road crashes. The recording of control

BRIEF SUMMARY

Current Knowledge/Study Rationale: Both alcohol consumption and sleepiness are known risk factors for motor vehicle crashes. Fields studies can provide an estimation of their actual impact and support prevention policies.

Study Impact: This study highlights the high impact of sleep propensity and alcohol consumption on crashes in a real context, showing that even low levels of alcohol concentration seriously increase their effect when associated with sleep propensity. Educational campaign and accurate reconsideration of legal limits for alcohol concentration are needed to definitely discourage driving in risky condition.

Figure 1—Distribution of crashes recorded for one year over the 24 hours of a day (bottom) and mean traffic over the road network involved in the study (top).



The crashes are divided as function of their occurrence during weekdays (from Monday to Friday–gray line) or weekend (Saturday and Sunday–black line) and are expressed as number of crashes per hour (over the whole year). Traffic-density data were supplied both by the Italian Highways Authority and by Genoa Municipal Police for urban traffic: data are displayed in normalized units with reference to their mean value. The arrangement of x-axis from 6 o'clock to 5 o'clock of the next day is aimed at setting a fair cutoff to seize the shift between a period characterized by drivers extending their activities through evening and night hours and drivers beginning their daytime activities.

data was planned to cover the 24-h cycle and to be distributed over the week and over the year. Policemen and physicians involved in the study were informed about the aims of the investigation, they were sensitized of sleep- and alcohol-related risks and carefully instructed in the modalities of collecting data. The study was supported and approved by Ligurian Region Health Department and all subjects gave written informed consent. Liguria is a coastal region, by Mediterranean Sea, in northern Italy (44°25' N, 08°54' E) where sunrise time ranges from 5h 40' (according to summertime, operating from April to October) to 8h 0' (end of December).

In order to evaluate the effect of alcohol intake, circadian sleep propensity and their interaction on the risk of car accidents, the distribution of accidents and controls were separately arranged as function of the time of the day (24 h) and BAC level (6 classes: BAC = 0, < 0.025, < 0.05, < 0.1, < 0.15, > 0.15 g/dL). Control drivers data were adjusted for the hourly distribution of traffic density: data regarding traffic density throughout the 24 h were supplied both by the Italian Highways Authority and by Genoa Municipal Police for urban traffic (unpublished data) and integrated with national statistics on moving vehicles (http://www.aci.it/laci/studi-e-ricerche/dati-e-statistiche/veicoli-e-mobilita.html). The number of drivers for each hour (i) and BAC level (j) was then estimated as:

$$n_{i,j} = N_i \frac{m_{i,j}}{M_i}$$

where N_i is the number of drivers moving in the i^{th} hour, as estimated from previously mentioned sources, M_i is the number of controls recorded in the i^{th} hour and $m_{i,j}$ is the number of controls in the i^{th} hour with BAC level j.

The effect of alcohol consumption and time of the day on the distribution of accidents in comparison with controls was first explored by evaluating the odds ratios (OR), that is the ratio between the share of accidents in the BAC > 0 group and the share of accidents in the zero-BAC group. OR with relevant confidence intervals (CI) were computed for each day period (night [0–6], morning [6–12], afternoon [12–18], and evening [18–0]). The same computation was repeated focusing on subjects with low BAC level (0 < BAC < 0.05 g/dL, below the legal threshold for Europe and many other countries) as compared with the zero-BAC group.

Logistic regression was then applied to fit accident rate as a quadratic function of circadian sleep propensity and BAC, together with their interaction according to the following formula:

$$\log\left(\frac{p}{1-p}\right) = c_1 \cdot CSP^2 + c_2 \cdot BAC^2 + c_3 \cdot CSP \cdot BAC$$

where p represents the crash probability, CSP the circadian sleep propensity, BAC the blood alcohol concentration, and c_1, c_2, c_3 are the regression coefficients.

Data on circadian sleep propensity (CSP) have been obtained from a previous published study,[13] where it was measured in a group of 9 healthy controls (for comparison with a matched group of narcoleptic patients). In that study the subjects were maintained on 16 h of diurnal sleep deprivation (from 7 to 23). Thereafter they spent 32 h in bedrest condition in a sound and light attenuated room, without stimuli or time cues. Their sleep-wake cycles were controlled by polysomnographic recording and sleep propensity was evaluated as the hourly distribution of sleep time: this distribution showed a main peak during night hours (1–3) and a secondary peak in the early afternoon (around 14). The circadian pattern drawn from this experiment was previously correlated to the frequency of road crashes.[2,12] To estimate the relative risk of car accidents, values estimated from the logistic regression model were normalized to the value estimated for the reference condition of zero BAC and minimum of sleep propensity.

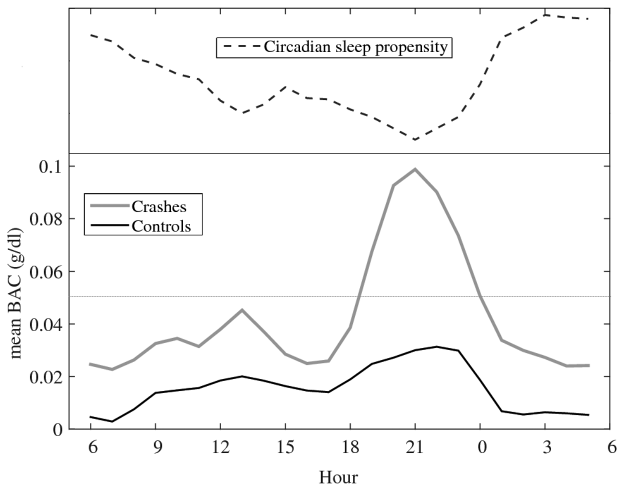
RESULTS

We collected BAC from 4,420 car drivers involved in vehicle accidents and from 3,363 controls. BAC values greater than zero were found in 3,180 (72.0%) drivers in the accident group and in 1,357 (40.4%) controls. Among the former, 1,044 (23.6%) drivers exceeded the BAC legal threshold of 0.05 g/dL, while illegal values were found in 348 controls (10.4%).

The distribution of recorded crashes through the daytime is reported in **Figure 1**, in which two separate lines represent crashes occurred during weekdays and during weekend, respectively. High values can be observed during the early afternoon (13–16) and during late evening (on weekdays) or night hours (on the weekend), the latter being particularly remarkable as associated with lower traffic density. The pattern of mean BAC during the same time span is reported in **Figure 2** for both drivers involved in car accidents and control drivers. Mean BAC values are clearly higher in the accident group with respect to controls and a remarkable increase of BAC during evening hours (around 21) was sharpened in the accident group: in this period the number of crashes involving drivers with BAC over legal threshold was 337 (40.5% of all crashes in the same time span) while 108 crashes (13.0% of the total) involved drivers with zero BAC. In the same period illegal BAC values were found in 165 controls (23.5% of the total) and zero BAC in 321 controls (45.8% of the total). This period was characterized by the minimum number of crashes involving zero-BAC drivers, that is a mean of 21.6 crashes per hour (through the whole year) versus a mean value for the whole day of 51.67 crashes per hour. As shown in **Figure 2** (top) this period is also characterized by the minimum level of the circadian sleep propensity (CSP) as estimated according to the previously mentioned study.[13]

The (log-transformed) ratio between the number of accidents and controls (adjusted for traffic density) as function of BAC level and time of day is reported in **Figure 3** and shows the higher accident risk during night hours with a sharp increase starting from the very low BAC level while the lowest risk is associated to evening hours and zero BAC and progressively increases with alcohol consumption. The odds ratios between the rate of accidents in alcohol exposed and not-exposed subjects is reported in **Figure 4A** and represents a measure of the rate of growth of accident frequency associated with alcohol consumption. We found about seven-fold increase of accident risk in the alcohol-exposed group with respect to non-exposed during the night (OR: 6.92, CI: 5.73–8.37) and five-fold increase during the evening (OR: 5.15, CI: 4.16–6.38). When the same analysis was focused on subjects with relatively low BAC level (**Figure 4B**), the OR relevant to the night period (5.68, CI: 4.59–7.03) was significantly higher than values found for morning, afternoon, and evening periods, which did not significantly differ from each other.

Figure 2—Time course of mean BAC (bottom) and estimated circadian sleep propensity (top) over the 24 hours of a day.



Mean BAC values (g/dL) are evaluated for the group of drivers involved in traffic crashes (gray line) and for controls (black line). The horizontal dotted gray line indicates the 0.05 g/dL level which is the legal limit in Italy. Time course of circadian sleep propensity was drawn from a previous study[13] involving a group of healthy controls following a bed rest protocol. The arrangement of x-axis from 6 o'clock to 5 o'clock of the next day is aimed at setting a fair cutoff to seize the shift between a period characterized by drivers extending their activities through evening and night hours and drivers beginning their daytime activities.

Figure 3—Distribution of the (log-transformed) rate between number of accidents and number of controls (adjusted for traffic density) as function of BAC level and time of day (night: 0–6; morning: 6–12; afternoon: 12–18; evening: 18–0).

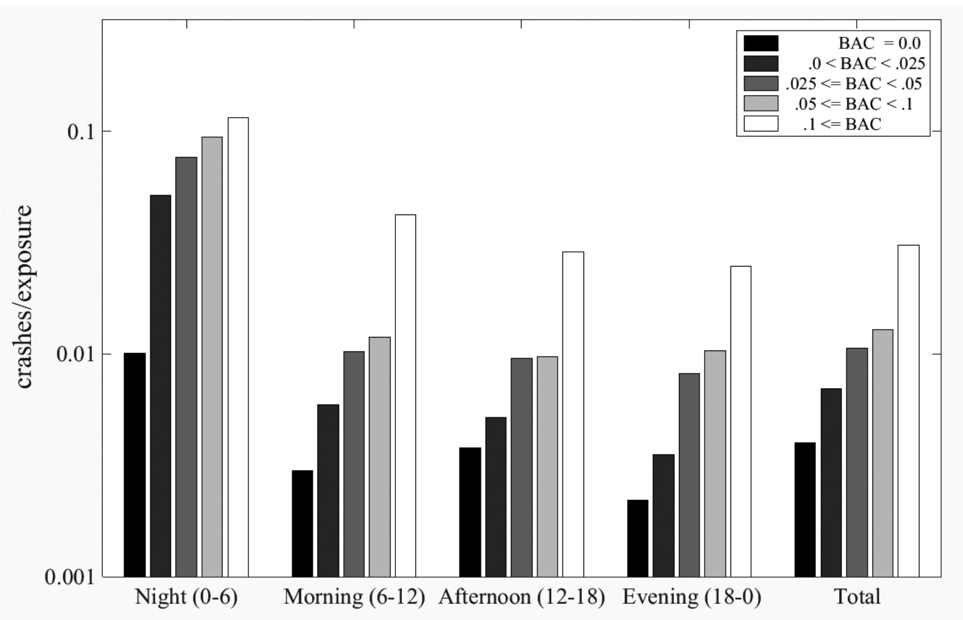
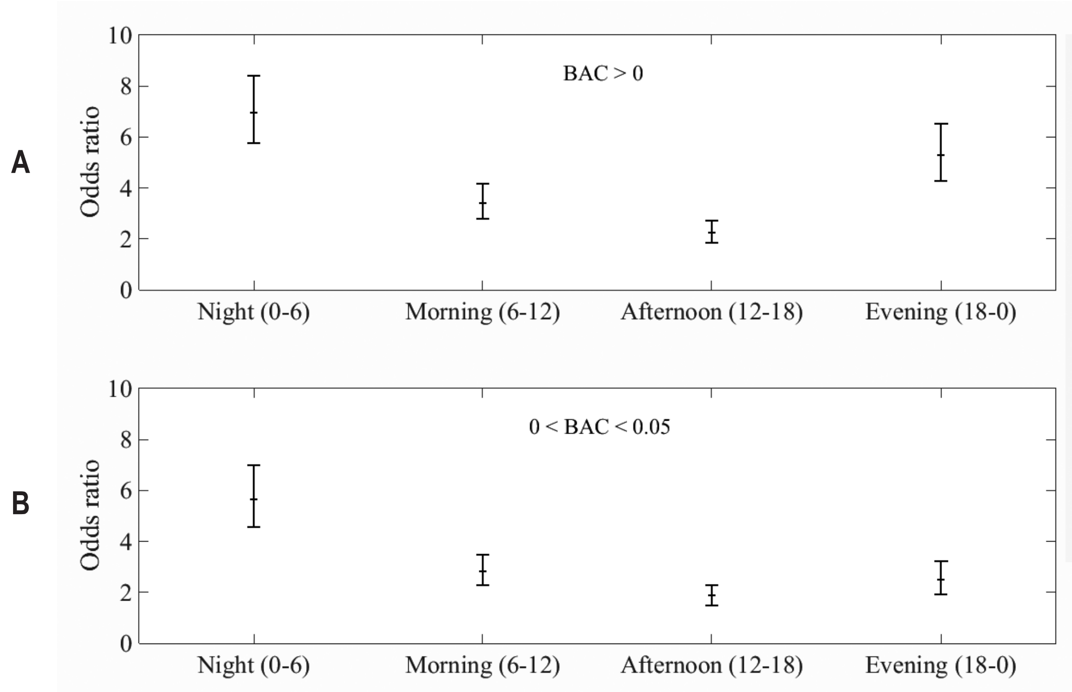
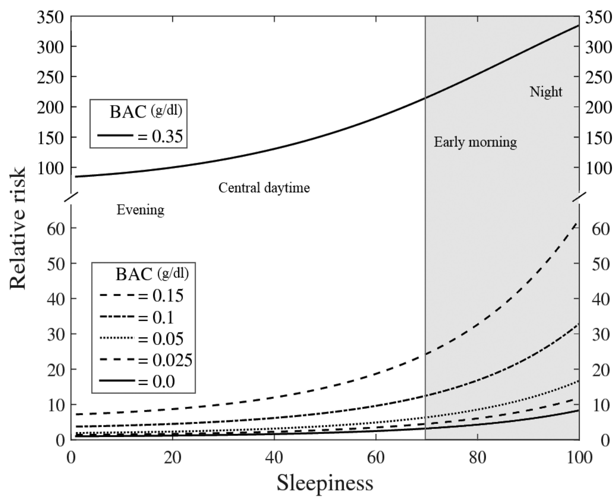


Figure 4—Odds ratios, computed as the ratio between the share of accidents in alcohol-exposed group and the share of accidents in the zero-BAC group and indicating the rate of growth of the risk associated to alcohol consumption with respect to non-exposed subject as function of the daytime period.



(A) odds ratios associated to any level of alcohol consumption; **(B)** odds ratios associated to low level of alcohol consumption (still referenced to zero BAC).

Figure 5—Relative risk of road accidents as function of expected sleepiness (estimated from experimental pattern of circadian sleep propensity) and Blood Alcohol Concentration (BAC level, g/dL, associated with different lines).



The relative risk is normalized to the reference condition of zero BAC and minimum sleep propensity while sleepiness is normalized between its minimum and maximum values. The lowest estimated sleepiness values are associated with evening hours (18–22), intermediate values characterize central daytime (8–18) and late evening (22–0) while the highest values (the area identified by gray background) are associated with early morning (6–8) and night hours (0–6).

The logistic regression model was highly significant as compared to the null (constant) model by the likelihood ratio test ($\chi^2_{(3)}$ = 4,820, $p < 0.001$), and all predictors were highly significant (CSP: t = 32.3, BAC: t = 24.2, interaction: t = 20.1, all $p < 0.0001$). Both CSP and BAC and their interaction heavily increased accident rate. The patterns of relative risk predicted by logistic regression as function of CSP for a set of BAC values throughout the range of recorded data are reported in **Figure 5**. The relative risk associated with the period of minimum CSP increased by factors 1.4 and 2.0 at legal BAC (0.025 and 0.05 g/dL respectively) and by factors 4.0 and 7.3 at illegal BAC (0.1 and 0.15 g/dL), showing a dramatic increase for higher BAC values (up to 85 for BAC = 0.35 g/dL). Relative risk strongly increased with CSP, with an increasing rate depending on BAC level. Only at the highest BAC level (≥ 0.15) the predominant effect of alcohol seemed to saturate the effect of CSP while the latter was already considerable at zero BAC with an increase of the relative risk up to 8.5 times during night hours. The relative risk maximum (for night hours) increased to 16.5 times for legal BAC and much more for BAC > 0.05 (**Figure 5**).

DISCUSSION

Circadian sleep propensity (as estimated from time of day) and BAC strongly increase the risk of car crashes at the wheel, with CSP exerting the major negative impact (at least with BAC < 0.15 g/dL). It is noteworthy that even low levels of alcohol concentration (BAC < 0.05 g/dL) significantly increase the risk of traffic accidents during time periods associated with high levels of sleep propensity.

The high odds ratio we found for night hours confirms the strong increase of accident risk when alcohol consumption is associated with increased circadian sleep propensity. The slightly lower odds ratio we found for the evening hours seems to be the result of the combination of the protective effect of the high circadian level of vigilance (relatively few accidents at zero BAC were found in this time span, as highlighted by **Figure 3**) and the favoring effect of high alcohol exposure due to social habits. When the evaluation was focused on moderate alcohol consumption (under the common 0.05 g/dL legal threshold) the highest effect involved only night hours, highlighting the combined effect of sleepiness and alcohol consumption. The application of the logistic model enabled the evaluation of both effects and their interaction. Interestingly, we can observe a considerable increase of the relative risk of crashes with the increase of BAC also in the range 0.05–0.10 g/dL (see **Figure 5**). This suggests that the 0.05 g/dL legal limit adopted by most European countries, and even more the 0.08 g/dL limit adopted in other countries including United States and Canada, may be associated with a significant increase of crash risk, particularly evident at higher level of sleepiness during the nocturnal hours. Previous studies[14] have reported that lowering the legal BAC limit to 0.05 g/dL could reduce the incidence of fatal crashes in the USA. Our study seems to suggest that even the 0.05 g/dL limit could be too high when driving under a condition of increased sleep pressure such as during the night hours. Educational campaigns have to make drivers aware of the problem and informed about the relationship between drinking, BAC, and sleepiness. Blood alcohol concentration depends upon many factors,[15,16] but a rough estimation may be provided as function of weight and gender. It is estimated that a 70-kg man can approach the 0.05 g/dL limit when drinking about 400 mL of wine or 1 L of beer during meal but the quantities are substantially lower if drinking without food (250 mL of wine or 580 mL of beer). The corresponding quantities for a 55-kg woman are 260 mL of wine or 630 mL of beer during meal and 150 mL of wine or 360 mL of beer without food (data estimated from reference tables provided with Italian traffic rules (see Note 1 in notes section at end of paper). Similar tables can be obtained from U.S Department of Transportation (see Note 2 in notes section at end of paper). Estimated BAC is proportional to alcohol intake; therefore, 60% more quantities rise BAC to the 0.08 g/dL limit. Of course the quantities are lower for spirits and other beverages with high alcohol content and the association of different drinks produces a cumulative effect.

A critical point of this study was the composition of the crash sample and of the control group with relation to the estimation of relative risk of road crashes: the two samples were representative of the relevant populations as a whole and not directly matched (as for specific location, age, sex, etc.) in the way adopted by other international surveys.[17] The sample of drivers involved in road crashes included almost all crashes occurred in Liguria through one year, only excluding the drivers possibly affected by psychoactive drugs and probably missing a number of minor crashes in which assistance was not requested. Control data were recorded on highways, urban, and suburban roads extensively covering the main traffic routes through Ligurian region (in particular the ones characterized by a significant rate of car crashes) and recording was distributed through the 24-h cycle and through the week for a period of one year. Extensive information about control drivers could not be collected but in our opinion it was representative of the general population of drivers in Liguria as for alcohol consumption, while time distribution of exposure was corrected using data on traffic density in the same region. In fact, the share of drivers with positive BAC was high in this study for both drivers involved in car crashes and controls. This high share can be placed in the context of alcohol consumption in Europe, which is estimated as the highest one in the world[18,19]: alcohol consumption is generally higher in high-income countries but is clearly higher in Europe than in United States. In the cited reports Italy is placed in the inferior portion of the European range (which is perhaps an underestimation) and is characterized by the widespread (but decreasing) traditional consumption of wine at meal while drinking beer or spirits out of meals and heavy episodic drinking are less frequent but increasing, particularly among young people. The high level of alcohol consumption recorded in the present study may be influenced by the fact that the collection of the control data was oriented to cover the roads and times mainly involved in car crashes, which could be a bias for a general estimation of alcohol consumption (as car crashes are more probable where alcohol consumption is higher) but a reliable estimation of exposure of drivers involved in car crashes (which is the main point to support the present analysis on the effect of alcohol on driving).

Many factors may affect crash risk and among them, along with sleepiness, also fatigue associated with night and shift working. Specific information about reason for moving were not available in this study and would be rather complex to be collected and analyzed; however, a certain portion of the recorded crashes presumably involved people during their job or driving to or from workplace. Night working is estimated to involve about 11% of Ligurian workers (4.4% of the whole population) and a study from the National Institute for Work Related Injuries Insurance (INAIL)[20] reports about one hundred accidents occurred in 2010 to night workers while driving to or from workplaces. This suggests that about 10% of night crashes analyzed in the present study could have involved night workers. On the other hand, night accidents increase during the weekend, which is likely related to leisure time activities involving both alcohol consumption and sleep deprivation.

A second critical point concerns the estimation of sleep propensity: we adopted a curve representing the 24-h cycle of sleep propensity drawn from a previous study[13] in which the hourly distribution of sleep time during the 24 h of a bed rest protocol was measured in healthy controls. The same curve was adopted in other studies[2,12] and showed significant correlation with crash risk. Individual data concerning previous sleep and possible sleep disorders could not be recorded in controls; therefore, sleepiness could not be estimated on individual basis: the circadian/circa-semidian curve can then represent a mean propensity to sleepiness and can also incorporate the effect of sleep deprivation which has higher probability to occur during night hours, in association with the main peak of the curve. This curve also presents a secondary peak in the early afternoon, a time interval in which an increase of crashes has been observed and was already associated to a circadian increase of sleepiness.[21,22] Hourly sleep propensity data inserted in the model were drawn from a single experimental study, but the main characteristics of the curve, that is the highest values during the night (1–5), a secondary maximum in the afternoon (15–16), and a marked minimum during the evening (19–22) are common findings in studies of the circadian oscillations of sleepiness and performance.[23–25]

In conclusion, our findings highlight the high impact of circadian sleep propensity and alcohol consumption on crashes in a real context. These findings should be taken into account for future educational campaign planning. The considerable increase of crash risk, when even legal BAC values are associated with sleep propensity, suggests a revision of legal BAC limits, particularly during night hours, in order to definitely discourage driving after alcohol consumption.

NOTES

Note 1: http://www.salute.gov.it/imgs/c_17_newsaree_463_listafile_itemname_3_file.pdf

Note 2: www.nhtsa.gov/staticfiles/numbers/Safety_In_Numbers_Drive_Sober_811871.pdf

ABBREVIATIONS

BAC, Blood alcohol concentration (measured in grams per deciliter, g/dl)
CI, confidence intervals
CSP, circadian sleep propensity
OR, odds ratios

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Author contributions: Dr. Garbarino had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data

analysis. Study concept and design: Garbarino, Nobili and De Carli. Acquisition of data: Garbarino, Nobili, Campus, Morrone and De Carli. Analysis and interpretation of data: Garbarino, Nobili, Philip, Plazzi,Campus, Morrone and De Carli. Drafting of the manuscript: Garbarino, Nobili and De Carli. Critical revision of the manuscript for important intellectual content: Philip and Plazzi. Statistical analysis: Campus, De Carli. Administrative, technical and material support: Garbarino. Study supervision: Garbarino and Nobili. Final approval of the version to be published: Garbarino, Nobili, Philip, Plazzi, Campus, Morrone and De Carli.

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Address correspondence to: Fabrizio De Carli, Institute of Bioimaging and Molecular Physiology, National Research Council (CNR), Largo P. Daneo, 3, 16132, Genoa, Italy; Tel: +39 0103537466; Email: f.decarli@ibfm.cnr.it

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