Original research

Effects of moderate alcohol consumption and hypobaric hypoxia: implications for passengers' sleep, oxygen saturation and heart rate on long-haul flights

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ABSTRACT

Background Passengers on long-haul flights frequently consume alcohol. Inflight sleep exacerbates the fall in blood oxygen saturation (SpO_2) caused by the decreased oxygen partial pressure in the cabin. We investigated the combined influence of alcohol and hypobaric hypoxia on sleep, SpO_2 and heart rate.

Methods Two groups of healthy individuals spent either two nights with a 4-hour sleep opportunity (00:00–04:00 hours) in the sleep laboratory (n=23; 53 m above sea level) or in the altitude chamber (n=17; 753 hPa corresponding to 2438 m above sea level, hypobaric condition). Participants consumed alcohol before one of the nights (mean±SE blood alcohol concentration 0.043±0.003%). The order of the nights was counterbalanced. Two 8-hour recovery nights (23:00–07:00 hours) were scheduled between conditions. Polysomnography, SpO_2 and heart rate were recorded.

Results The combined exposure to alcohol and hypobaric condition decreased SpO_2 to a median (25th/75th percentile) of 85.32% (82.86/85.93) and increased heart rate to a median (25th/75th percentile) of 87.73 bpm (85.89/93.86) during sleep compared with 88.07% (86.50/88.49) and 72.90 bpm (70.90/78.17), respectively, in the non-alcohol hypobaric condition, 94.97% (94.59/95.33) and 76.97 bpm (65.17/79.52), respectively, in the alcohol condition and 95.88% (95.72/96.36) and 63.74 bpm (55.55/70.98), respectively, in the non-alcohol condition of the sleep laboratory group (all p<0.0001). Under the combined exposure SpO_2 was 201.18 min (188.08/214.42) below the clinical hypoxia threshold of 90% SpO_2 compared with 173.28 min (133.25/199.03) in the hypobaric condition and 0 min (0/0) in both sleep laboratory conditions. Deep sleep (N3) was reduced to 46.50 min (39.00/57.00) under the combined exposure compared with both sleep laboratory conditions (alcohol: 84.00 min (62.25/92.75); non-alcohol: 67.50 min (58.50/87.75); both p<0.003).

Conclusions The combination of alcohol and inflight hypobaric hypoxia reduced sleep quality, challenged the cardiovascular system and led to extended duration of hypoxaemia (SpO_2 <90%).

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ To stay in a hypobaric environment is known to decrease oxygen saturation and increase heart rate. Aeroplane passengers with cardiopulmonary diseases have an increased risk of aggravation of symptoms due to the decreased cabin pressure at cruising altitude, which is amplified during sleep. Alcohol, which is often consumed on board, has similar effects, but hypobaric hypoxia-induced changes are usually more pronounced.

WHAT THIS STUDY ADDS

⇒ This study is the first to investigate the combined impact of hypobaric hypoxia and alcohol during sleep. Effects on oxygen saturation and heart rate were supra-additive. Young and healthy individuals experienced prolonged and clinically relevant desaturations.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ We show that the on-board consumption of alcohol is an underestimated health risk that could be easily avoided. Practitioners, passengers and crew should be informed about the potential risks, and it may be beneficial to consider altering regulations to restrict the access to alcoholic beverages on board aeroplanes.

INTRODUCTION

The number of long-haul flights has been increasing for many years. While in 2002 about one billion air travellers per year were estimated,[1] in 2018 the number had quadrupled.[2] The environmental conditions during flight might pose health risks for passengers, especially those with respiratory diseases.[3] To increase passenger safety, the minimal cabin pressure on commercial flights is equivalent to 2438 m (753 hPa) as prescribed by international regulations,[1] which is defined as the lower limit of moderate altitude.[4–7] Atmospheric pressure decreases exponentially with altitude due to the diminishing mass of the overlying air column and decreasing gravitational force. This leads to a decline in arterial oxygen partial pressure (PaO_2), which falls to approximately 73 hPa at 2438 m, a level that corresponds to a blood oxygen saturation (SpO_2 = proportion of oxygen-saturated haemoglobin) of approximately 90% in healthy persons.[5 6] Due to the sigmoid shape of the oxygen binding curve, a further reduction of PaO_2 below 73 hPa results in a more pronounced drop in SpO_2 per

linear drop in PaO_2[8] and is defined as hypobaric hypoxia.[9] Acclimatisation in the mountains can reduce the negative effects of the reduced atmospheric pressure on SpO_2.[10–12] However, such an acclimatisation cannot be achieved during a long-haul flight.

Offering free alcoholic beverages to passengers during long-haul flights is so common that surveys were conducted to see whether passengers would prefer to book non-alcoholic flights.[13] It is therefore important to understand the implications of a combination of alcohol consumption and sleep during long-haul flights.

Alcohol acts as a potent somnogen which leads to a reduced sleep onset latency and rapid eye movement (REM) sleep duration[14–18] and may result in cognitive impairment, difficulties in concentration and memory disorder.[19] The alcohol-induced systemic vasodilatation increases heart rate during sleep.[20] Hypobaric hypoxia leads to a shortened N3 and REM sleep duration and decreased SpO_2 during sleep while the heart rate is increased.[21] We hypothesised that the combination of alcohol and hypobaric conditions would exacerbate the changes in sleep observed under single exposure conditions.

METHODS

Participants

Forty-eight participants aged 18–40 years were randomly assigned to two groups stratified by age, gender and body mass index (for further details see online supplemental method). Applicants with physical, psychological, intrinsic sleep or circadian disorders were excluded from participation in this study based on the results of questionnaires, medical history, physical examination, blood and urine tests and electrocardiography.

Laboratory procedures

The study was performed at the Institute of Aerospace Medicine of the German Aerospace Centre in Cologne. The protocol described in this paper was a segment of a larger research project that investigated a range of related research goals (see online supplemental method).[22] This paper presents data of two experimental nights in which sleep opportunities lasted 4 hours (00:00–04:00 hours). One of the experimental nights was preceded by alcohol exposure in the evening.

The Control Group slept under conditions of normobaric normoxia in the sleep laboratory (53 m altitude) whereas the InFlight Group slept in a simulated crew-rest compartment in the altitude chamber where the pressure was decreased to 753 hPa, simulating the minimal pressure inside an aeroplane cabin at cruising altitude. In addition, realistic noise as inside a plane (70 dB(A) recorded during a flight from Cologne to Kairo) was generated.

The following two groups and conditions were compared:

Control Group: (a) one night without alcohol consumption in normobaric conditions at sea level (Control NonAlc) and (b) one night with previous alcohol consumption in normobaric conditions at sea level (Control Alc).

InFlight Group: (a) one night without alcohol consumption in hypobaric conditions (InFlight NonAlc) and (b) one night with previous alcohol consumption in hypobaric conditions (InFlight Alc).

The flowchart in figure 1 provides details of study flow.

Alcohol administration

The individual amount of alcohol needed to achieve the target value of 0.06% blood alcohol concentration (BAC) was selected with reference to the usual BAC limits for driving in Western Europe (0.05%) and the USA (0.08%) and was calculated according to the modified Widmark formula of Watson *et al*.[23] This is equivalent to drinking two cans of beer (5%) or two glasses of wine (175 mL, 12%). At 23:15 hours the participants drank the calculated amount of pure vodka (on average 114.5 mL). Due to individual variability in resorption and absorption rates, the average BAC of the subjects measured at 23:45 hours was 0.043±0.003%. The next morning at 06:00 hours the BAC was 0.0±0.0% in both groups. All mentioned BACs were calculated from the measured breath alcohol concentrations (with Dräger Alcotest 6810) according to Pavlic *et al*.[24]

During the nights polysomnography, SpO_2 and heart rate were monitored continuously.

Polysomnography

Polysomnography was recorded according to the international 10–20 system (electroencephalography (EEG): C3, F3, O1, and C4, F4, O2, referenced to A2 and A1, respectively, electrooculography, submental electromyography) as previously described.[7] One trained technician scored sleep stages and EEG

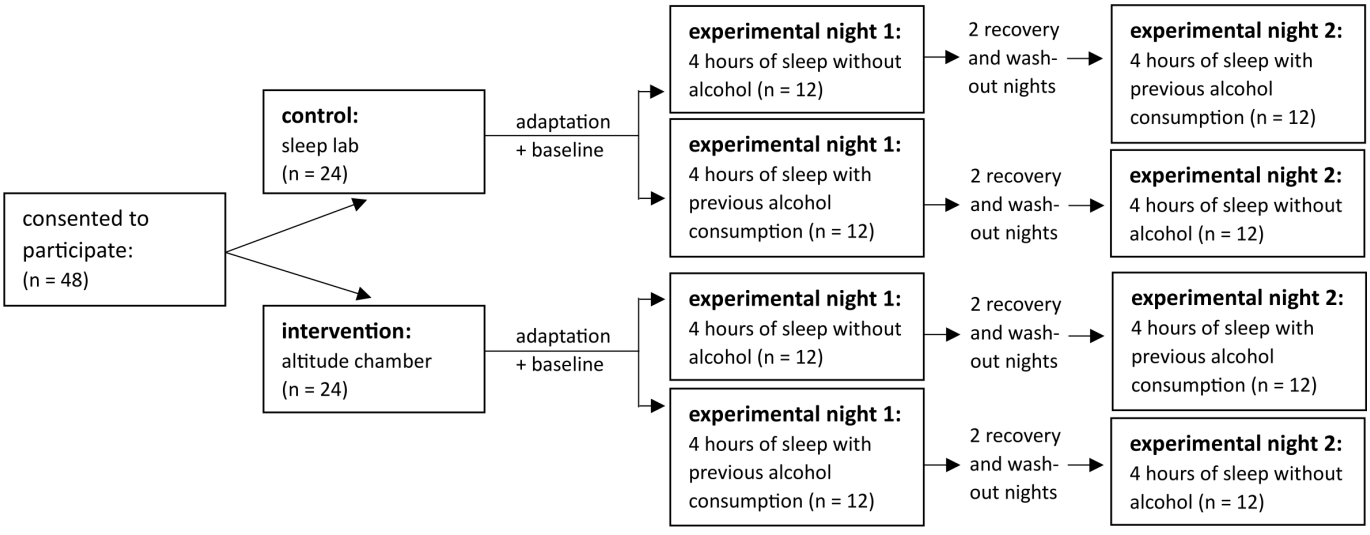

Figure 1 Study flow.

arousals according to conventional criteria.[25] Heart rate was recorded with one-lead electrocardiography.

We derived the following dependent variables: total sleep time (TST), sleep efficiency (SE; TST/time in bed×100), sleep onset latency (SOL) defined as the first occurrence of any sleep stage deeper than N1 (ie, N2, N3, or REM), duration spent in sleep stages N1–3 and REM, wake after sleep onset (WASO; ie, wake duration between sleep onset and end of time in bed), number of sleep stage changes (per hour TST) and number of arousals (per hour TST). Mean heart rates were calculated per TST, N1–3 and REM.

Blood oxygen saturation (SpO_2)

A finger tip sensor was part of the sleep recording device (PD3, DLR) and used to measure SpO_2. From these data, average SpO_2 values were calculated per TST, N1–3 and REM as dependent variables. A further finger tip sensor (PalmSAT 2500 Series, Nonin) provided continuous online monitoring during sleep periods, ensuring the safety of the participants in the altitude chamber.

Statistical analysis

We analysed the single and combined effects of alcohol and hypobaric conditions on dependent variables using SAS version 9.4. In mixed ANOVAs with the main factors condition (alcohol, no alcohol), group (Control Group, InFlight Group) and the interaction between condition and group, we analysed dependent variables of sleep and heart rate. Individual baseline parameters of sleep in the sleep laboratory were included as covariates in the sleep analyses. Post hoc pairwise comparisons were adjusted for multiple testing according to the Tukey–Kramer test. An exploratory inclusion of sex, age and BAC into analyses did not impact the interaction results. In order to achieve a normal distribution, some parameters were transformed prior to analysis (TST, SE, N3, WASO, number of arousals). Normal distribution of residuals was assessed using Kolmogorov–Smirnov tests and Q–Q plots. The significance level was $\alpha<0.05$. SpO_2 and $SpO_2<90\%$ measured during TST and sleep stages (N1–3, REM) within and between groups were analysed with paired Wilcoxon signed rank tests and unpaired Wilcoxon rank sum tests as no normal distribution of residuals could be achieved. Bonferroni adjustment for multiple comparisons was applied and the significance level set to 0.0083 (0.05/6). The time period during sleep with $SpO_2<90\%$ was of special interest as this threshold is used as a definition of hypoxia in clinical guidelines.[26] If not otherwise mentioned, values are given as median (25th/75th percentile).

RESULTS

The demographic data of the participants did not differ between the groups (table 1).

Tables 2 and 3 provide an overview of the results.

Effects of moderate alcohol consumption

Comparing the alcohol and non-alcohol conditions of the Control Group, the following isolated effects of alcohol under normobaric conditions on sleep (figure 2), SpO_2 and heart rate (figure 3, online supplemental figures 1, 2) were observed: N1 (p=0.0448) and REM (p=0.0053) durations were shorter, SpO_2 during sleep was reduced (TST, N1–3, REM: p<0.0001) and heart rate accelerated (TST, N1–3, REM; p<0.0001) under alcohol exposure. During TST the median SpO_2 remained above the hypoxia threshold of 90%.

Table 1 Participant demographics and blood alcohol concentration (alcohol condition)

	Control Group	InFlight Group	P value (Wilcoxon)
Sample size	n=23	n=17	
Sex (% male)	61	47	0.3967
Age (years)	26.4±1.2	26.4±1.2	0.8274
BMI (kg/m^2)	24.3±0.6	23.5±0.6	0.3510
Usual alcohol intake (g/week)	24.4±4.15	39.6±8.2	0.2202
Heart rate, resting (bpm)	67.4±2.6	65.4±2.8	0.6153
Blood alcohol concentration (%)	0.042±0.003	0.043±0.005	0.7954

Values are shown as mean±SE.
bpm, beats per min

Effects of hypobaric inflight conditions

Comparing the non-alcohol condition between groups, a shorter REM (p=0.0005), longer N2 duration (p<0.0001) and longer WASO (p=0.0471) were observed in the InFlight Group. SE (p=0.0165, adjusted p=0.0822), N1 (p=0.0179, adjusted p=0.0886) and N3 duration (p=0.0133, adjusted p=0.0678) only changed on trend-niveau, but TST (p=0.0223, adjusted p=0.1059) and number of arousals (p=0.0448, adjusted p=0.1903) were not significantly different after adjustment.

In the InFlight Group, SpO_2 during sleep was reduced (TST, N1–3, REM; p<0.0001) and resulted in SpO_2 <90% in 81% of TST(figure 4). Heart rate was accelerated (TST, N1–3, REM; p<0.002).

Combined effects of alcohol and hypobaric conditions

In comparison to the normobaric, non-alcohol condition of the Control Group, N3 (p=0.0029) and REM (p<0.0001) duration decreased, N1 duration showed a decreased trend (p=0.0791) and N2 duration (p<0.0001) and WASO (p=0.0071) increased in the alcohol condition of the InFlight Group.

SpO_2 during sleep in the alcohol condition of the InFlight Group was reduced (TST, N1–3, REM; p<0.0001) and time spent with $SpO_2<90\%$ was prolonged (TST, N1–3 REM; p<0.0001). SpO_2 during TST fell from 95.88% (95.72/96.36) in the non-alcohol condition of the Control Group to 85.32% (82.86/85.93) under the combined exposure to alcohol and hypobaric conditions. Heart rate was accelerated (TST, N1–3, REM; p<0.0001).

What does alcohol add to the effects of hypobaric conditions?

The effect of alcohol in addition to that of the hypobaric environment can be quantified when comparing the alcohol and non-alcohol conditions of the InFlight Group. Alcohol led to a shortened REM (p=0.0467), a trend to longer N2 duration (p=0.0641), a trend to shorter SOL (p=0.0827), decreased SpO_2 (TST, N1–3, REM; all p<0.0002) and increased heart rate (TST, N1–3, REM; p<0.0001) (figures 2 and 3). SpO_2 during TST fell further from 88.07% (86.50/88.49) without alcohol to 85.32% (82.86/85.93) with alcohol in the InFlight Group (figure 4). During N3 and REM sleep, even lower SpO_2 values were registered after previous alcohol consumption (84.84% (82.18/85.88); 84.74% (83.63/85.81)). During TST, time spent with SpO_2 <90% (p=0.0034) was 201.18 min (188.08/214.42) under the combined condition compared

Table 2 Descriptive statistics and mixed ANOVA results: polysomnography and heart rate

Condition	Normal sleep	Alcohol	Hypobaric hypoxia	Combination of alcohol and hypobaric hypoxia	Mixed ANOVA		
Group	Control Group (Control NonAlc)	Control Group (Control Alc)	InFlight Group (InFlight NonAlc)	InFlight Group (InFlight Alc)	Condition	Group	Interaction Condition × Group
	Median (25th/75th percentile)	Median (25th/75th percentile)	Median (25th/75th percentile)	Median (25th/75th percentile)	P value	P value	P value
Polysomnography							
TST (min)	213.00 (211.25/216.75)	218.00 (209.75/221.75)	214.00 (194.00/217.50)	212.50 (199.00/222.00)	0.3972	**0.0117**	0.8725
SE (%)	88.75 (88.02/90.31)	90.83 (87.40/92.40)	89.17 (80.83/90.63)	88.54 (82.92/92.50)	0.3972	**0.0082**	0.8725
SOL (min)	22.50 (13.75/25.00)	16.00 (10.50/22.75)	19.00 (13.50/23.50)	12.50 (10.50/20.50)	**0.0060**	0.7180	0.4366
N1 (min)	9.50 (5.50/13.00)	**6.00 (3.50/9.00)**	7.00 (5.50/10.00)	6.50 (4.00/14.00)	0.0714	0.0870	0.0869
N2 (min)	88.00 (78.75/103.00)	99.00 (87.75/113.50)	**116.00 (105.00/132.00)**	**138.00 (116.00/150.50)**	**0.0017**	**<0.0001**	0.6193
N3 (min)	67.50 (58.50/87.75)	84.00 (62.25/92.75)	51.00 (47.50/66.00)	**46.50 (39.00/57.00)**	0.7250	**0.0002**	**0.0369**
REM (min)	37.00 (32.50/51.00)	**32.50 (23.75/36.75)**	**22.00 (20.00/31.00)**	**14.50 (9.50/19.50)**	**<0.0001**	**<0.0001**	0.7523
WASO (min)	5.50 (3.00/7.50)	5.50 (3.25/9.50)	**9.00 (5.00/20.50)**	**10.50 (6.50/20.50)**	0.2624	**0.0018**	0.7672
SSW per h TST (number)	12.86 (9.88/14.63)	10.54 (9.03/13.07)	10.69 (8.88/14.21)	13.47 (12.13/14.09)	0.9147	0.6036	0.0842
Arousals per h TST (number)	4.79 (3.14/7.22)	5.15 (4.49/6.40)	4.64 (3.29/5.50)	5.58 (4.73/6.99)	**0.0424**	0.2410	0.0746
Heart rate							
TST (bpm)	63.74 (55.55/70.98)	**76.97 (65.17/79.52)**	**72.90 (70.90/78.17)**	**87.73 (85.89/93.86)**	**<0.0001**	**<0.0001**	**0.002**
N1 (bpm)	62.99 (58.74/70.89)	**77.46 (67.82/81.49)**	**72.96 (71.04/79.41)**	**90.79 (88.04/94.25)**	**<0.0001**	**<0.0001**	**0.0088**
N2 (bpm)	61.99 (54.47/69.74)	**75.90 (64.31/78.70)**	**75.79 (71.93/81.20)**	**87.46 (85.14/93.46)**	**<0.0001**	**<0.0001**	0.3102
N3 (bpm)	63.50 (55.41/72.05)	**77.42 (65.75/81.39)**	**72.48 (71.04/79.88)**	**89.06 (85.85/94.38)**	**<0.0001**	**<0.0001**	**0.0425**
REM (bpm)	66.74 (59.33/71.12)	**75.65 (68.68/80.43)**	**77.02 (74.73/80.61)**	**90.89 (86.95/94.63)**	**<0.0001**	**<0.0001**	**0.0068**

Sleep was restricted to 4 hours from 0:00 hours to 04:00 hours in all conditions.
Results of mixed ANOVAs with the main factors condition, group and the interaction between condition and group and post hoc Tukey–Kramer adjustment ($\alpha<0.05$). Significant ANOVA results and significant differences compared to normal sleep are printed bold. Mixed ANOVAs for polysomnography were adjusted for baseline sleep in the sleep laboratory as covariate.
22 datasets of the Control Group and 17 datasets of the InFlight Group were taken into account (see online supplemental method).
Arousals per h TST, number of arousals per hour TST; N1–3 and REM, sleep stages; SE, sleep efficiency (ie, percent TST of complete time spent in bed); SOL, sleep onset latency; SSW per h TST, number of sleep stage changes per hour TST; TST, total sleep time; WASO, wake after sleep onset.

Table 3 Descriptive statistics: oxygen saturation

Condition	Normal sleep	Alcohol	Hypobaric hypoxia	Combination of alcohol and hypobaric hypoxia
Group	Control Group (Control NonAlc)	Control Group (Control Alc)	InFlight Group (InFlight NonAlc)	InFlight Group (InFlight Alc)
	Median (25th/75th percentile)	Median (25th/75th percentile)	Median (25th/75th percentile)	Median (25th/75th percentile)
Oxygen saturation				
TST (%)	95.88 (95.72/96.36)	**94.97 (94.59/95.33)**	**88.07 (86.50/88.49)**	**85.32 (82.86/85.93)**
N1 (%)	96.27 (96.04/96.97)	**95.52 (95.08/95.93)**	**87.72 (86.37/89.01)**	**85.83 (83.02/86.47)**
N2 (%)	95.83 (95.50/96.39)	**94.89 (94.59/95.36)**	**88.26 (86.68/88.60)**	**85.51 (83.04/86.18)**
N3 (%)	95.77 (95.33/96.47)	**94.80 (94.45/95.19)**	**87.27 (86.14/89.00)**	**84.84 (82.18/85.88)**
REM (%)	96.54 (95.78/96.88)	**95.50 (94.63/95.88)**	**88.15 (87.03/88.77)**	**84.74 (83.63/85.81)**
Oxygen saturation <90%				
TST (min)	0.00 (0.00/0.00)	0.00 (0.00/0.00)	**173.28 (133.25/199.03)**	**201.18 (188.08/214.42)**
N1 (min)	0.00 (0.00/0.00)	0.00 (0.00/0.00)	**4.08 (2.60/6.49)**	**6.98 (3.90/12.16)**
N2 (min)	0.00 (0.00/0.00)	0.00 (0.00/0.00)	**30.21 (19.27/51.00)**	**132.68 (119.74/147.93)**
N3 (min)	0.00 (0.00/0.00)	0.00 (0.00/0.00)	**51.00 (32.72/56.50)**	**46.32 (37.20/52.11)**
REM (min)	0.00 (0.00/0.00)	0.00 (0.00/0.00)	**17.08 (9.56/20.26)**	**14.50 (9.75/21.25)**

Sleep was restricted to 4 hours from 00:00 hours to 04:00 hours in all conditions. Significant differences compared to normal sleep are printed bold.
22 datasets of the Control Group and 14 datasets of the InFlight Group were taken into account (see online supplemental method).
N1–3 and REM, sleep stages; TST, time sleep time.

with 173.28 min (133.25/199.03) in the non-alcohol condition InFlight. Heart rate increased to 87.73 bpm (85.89/93.86) under the combined condition compared with 72.90 (70.90/78.17) in the non-alcohol condition InFlight. To quantify the strength of the alcohol-induced effects on SpO_2 and heart rate, a delta was calculated for each subject as the difference between conditions and compared between groups. The alcohol-induced reduction in SpO_2 (TST, N1–3, REM; $p<0.0004$) and increase in heart rate (TST, N1, N3, REM; $p<0.03$) was higher in the InFlight Group (TST SpO_2: 3.02 (2.28/3.74), TST heart rate: 13.94 (17.11/11.60)) than in the Control Group (TST SpO_2: 0.85 (0.56/1.41), TST heart rate: 9.96 (12.73/7.33)). In combination, hypobaric hypoxia and alcohol had a supra-additive effect on SpO_2 and heart rate.

What does the hypobaric condition add to the alcohol effect?

By comparing the alcohol conditions between the groups, the additional influence of hypobaric hypoxia was quantified. Sleep architecture under alcohol plus hypobaric conditions was characterised by a shortened REM ($p=0.0015$) and N3 duration ($p=0.0002$), while N2 duration ($p<0.0001$) was prolonged (figure 2). Participants spent more time awake (WASO, $p=0.0223$). SpO_2 (figure 3) was lower (TST, N1–3, REM; $p<0.0001$). Participants in the InFlight Group spent 95% of TST at a SpO_2 <90% in the alcohol condition compared with 0% in the Control Group in the alcohol condition ($p<0.0001$; figure 4). During sleep in the alcohol conditions, heart rate was higher in the InFlight Group compared with the Control Group (TST, N1–3, REM; $p<0.0001$).

DISCUSSION

Passengers frequently drink alcoholic beverages during a long-haul flight and fall asleep afterwards. Understanding the interacting effects of alcohol and sleep at altitude is therefore highly relevant. Such research provides insights for both passengers and healthcare professionals, facilitating the development of recommendations and guidelines for avoiding medical emergencies on board. The aim of this paper was to study the impact of moderate alcohol consumption and hypobaric conditions on sleep structure, SpO_2 and heart rate, with a special focus on the interacting effects of both conditions. An InFlight Group in a pressure chamber at a simulated altitude of 2438 m and a Control Group in the sleep laboratory were compared under two conditions of 4 hours of sleep: (1) sober and (2) with prior moderate alcohol consumption leading to a BAC of 0.04±0.003% just before going to sleep.

The combined impact of alcohol and hypobaric conditions led to an altered sleep architecture with shorter REM and N3 duration, prolonged N2 duration and increased WASO. During TST, SpO_2 decreased to a median of 85% which was accompanied by a compensatory increase in heart rate to a median of 88 bpm. Participants' SpO_2 was in total 95% of TST below the clinical hypoxia threshold of 90%. Together these results indicate that, even in young and healthy individuals, the combination of alcohol intake with sleeping under hypobaric conditions poses a considerable strain on the cardiac system and might lead to exacerbation of symptoms in patients with cardiac or pulmonary diseases. Cardiovascular symptoms have a prevalence of 7% of inflight medical emergencies, with cardiac arrest causing 58% of aircraft diversions.[27] The risk of venous thromboembolism is lower in comparison, with one out of 6000 affected per flight of >4 hours.[28] It has been shown that desaturations below the hypoxia threshold were associated with worse postoperative patient outcome[29] and increased mortality risk for emergency admissions.[30] Thus, elderly people and/or people with pre-existing conditions are in danger of clinically relevant desaturations due to impaired ability for compensation, resulting in greater hypoxaemia.[5 6 31] We have previously identified sleep as a potential exacerbating factor that reduces the ability to compensate for the decreased oxygen partial pressure in the atmosphere.[7] Likewise, a study in a hypobaric chamber simulating a 20-hour flight with healthy participants not acclimatised to altitude showed that SpO_2 was lower during sleep in a coach-class aeroplane seat compared with being awake, and that even

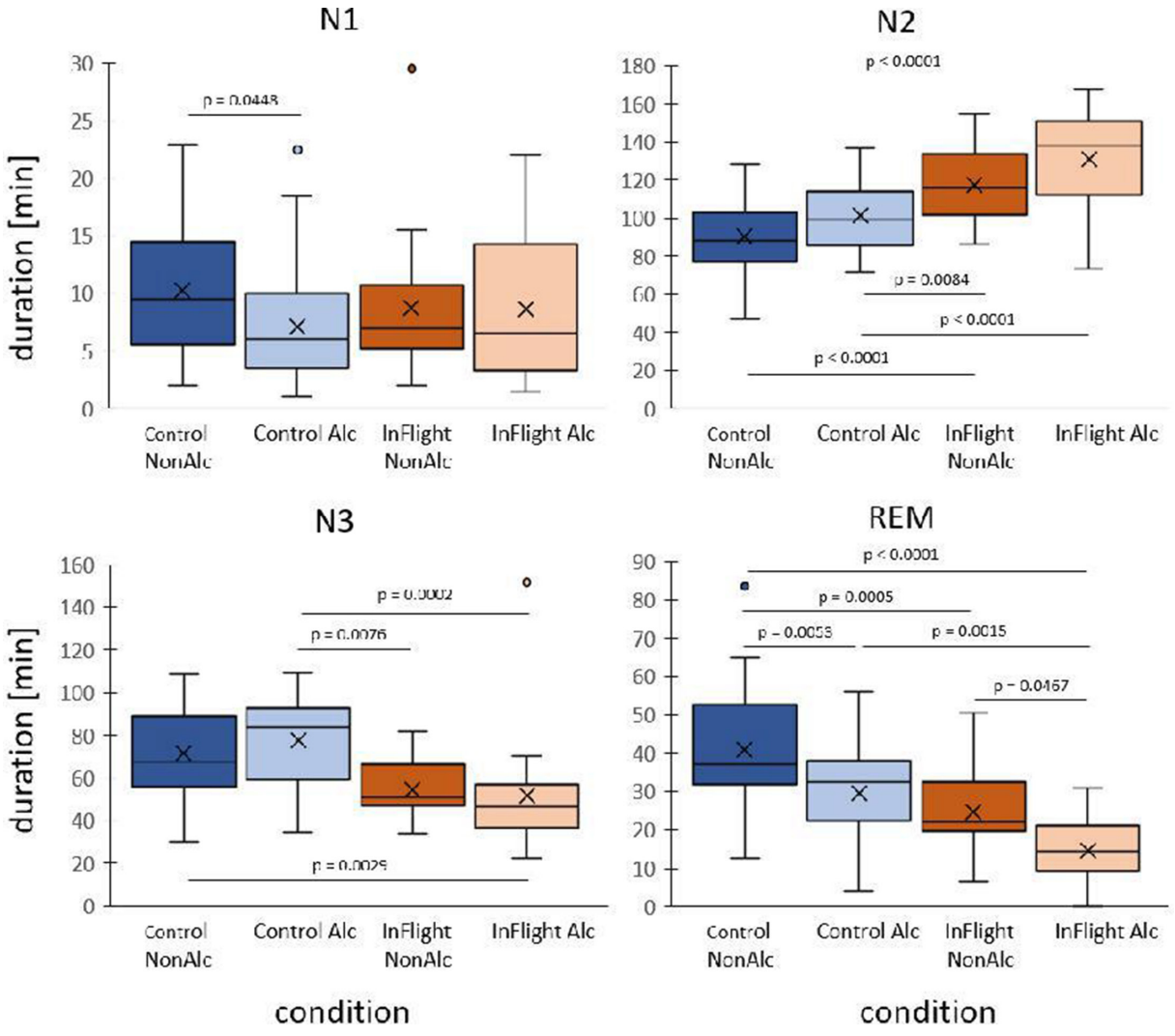

Figure 2 Duration of sleep stages (N1–3, REM) under two conditions (non-alcohol and alcohol) in the Control Group and InFlight Group. Mixed ANOVAs with the main factors condition, group and the interaction between condition and group and post-hoc Tukey–Kramer adjustment (α<0.05) for polysomnography. Mixed ANOVAs were adjusted for baseline sleep in the sleep laboratory as covariate. Data are from two independent groups recorded during 4-hour sleep episodes (00:00–04:00 hours) in an altitude chamber at a simulated flight level (ie, atmospheric pressure corresponding to 2438 m above sea level; n=17) and in the sleep laboratory (53 m; n=22). Box plots include mean values expressed as "X". Whiskers represent 1.5× IQR.

lower SpO_2 levels are to be expected in older passengers than in younger passengers.[4]

In agreement with our findings on the impact of hypobaric conditions on SpO_2 (median SpO_2 of 88% during TST), a reduction in SpO_2 levels from 93.8% to 84% has been reported in response to simulated (normobaric hypoxia) and real (hypobaric hypoxia) altitude of 2000–3000 m.[12 21 32 33] Hoshikawa *et al* simulated an altitude of 2000 m under conditions of normobaric hypoxia with 16.4% oxygen. As in our study, the duration of N3 and REM sleep was shortened, SpO_2 decreased (89.6% vs 95.4%) and heart rate increased (55.6 bpm vs 51.3 bpm) compared with normobaric normoxia.[21] The strikingly lower heart rate under both test conditions compared with our study can be explained by the fact that only medium and long distance runners were included in the study. Latshang *et al* reported a reduction in slow wave sleep (NREM stages 3 and 4) and a decreased SpO_2 during sleep at 2590 m compared with 490 m.[10] As N3 and REM sleep are considered important for the recuperative value of sleep,[19] sleeping at altitude is less recuperative and refreshing and might impair cognitive functioning.

The single exposure to moderate alcohol intake just before bedtime in our study reduced median N1 and REM duration by 3.5 min and 4.5 min, respectively. A variety of potential effects of alcohol consumption on sleep (including no effects) have been reported.[18] In line with our findings, moderate, high and intoxicating doses of alcohol have been reported to reduce the duration of REM sleep.[17 34] Thakkar *et al*, however, stated that alcohol before bedtime irrespective of the dose shortens SOL and increases slow-wave sleep.[14] Alcohol facilitates sleep by a rapid increase in cerebral adenosine receptor availability,[16] which explains why alcohol is often used as a self-prescribed sleep aid. Accordingly, reduced SOL has been found frequently[16 18] and deemed to be the most robust effect of alcohol on sleep.[17] Alcohol has also been reported to increase N2 duration.[34] In our study SOL seemed shorter and N2 longer under the influence of alcohol, but the effects were non-significant. Alcohol intake also decreased SpO_2 by 1% to a median of 95% during TST and increased heart rate by 13 bpm to a median of 77 bpm compared with normobaric normoxic conditions without alcohol. In this case, the decrease in SpO_2 is unlikely to account

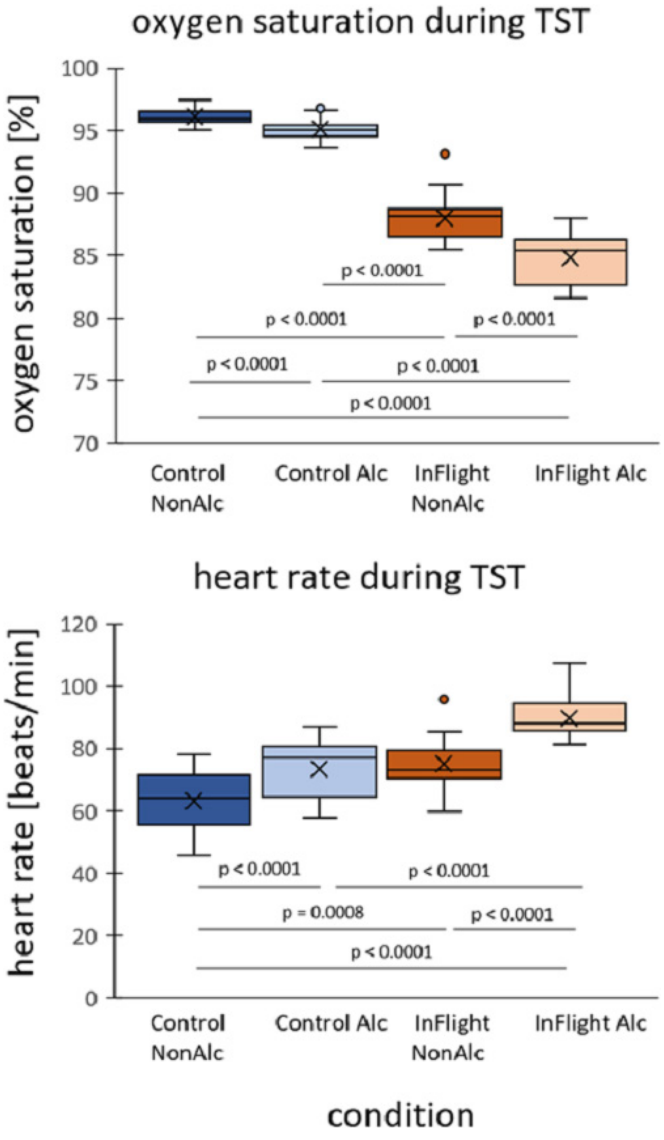

Figure 3 Top: Oxygen saturation under non-alcohol and alcohol conditions in the Control Group and InFlight Group. Paired and unpaired Wilcoxon tests were calculated and Bonferroni adjusted (α=0.05/6=0.0083). Data are from two independent groups recorded during 4-hour sleep episodes (00:00–04:00 hours) in an altitude chamber at a simulated flight level (ie, atmospheric pressure corresponding to 2438 m above sea level; n=14) and in the sleep laboratory (53 m; n=22). Box plots include mean values expressed as "X". Whiskers represent 1.5× IQR. Bottom: Heart rate under non-alcohol and alcohol conditions in the Control Group and InFlight Group. Mixed ANOVAs were performed with the main factors condition, group and the interaction between condition and group and post-hoc Tukey–Kramer adjustment (α<0.05). Data are from two independent groups recorded during 4-hour sleep episodes (00:00–04:00 hours) in an altitude chamber at simulated flight level (ie, atmospheric pressure corresponding to 2438 m above sea level; n=14) and in the sleep laboratory (53 m; n=22). Box plots include mean values expressed as "X". Whiskers represent 1.5× IQR. TST, total sleep time.

for the acceleration in heart frequency. Under normoxic conditions a SpO_2 range from 96% to 98% has been defined as normal.[12] During sleep an average SpO_2 of 96.5±1.5% has been reported in healthy participants,[35] confirming the slight decrease from normal due to alcohol in our study as well as in other studies.[18 20 36] De Zambotti *et al* reported a dose-dependent impact of alcohol consumption just before retiring on heart rate during sleep.[37] A plausible mechanism is that alcohol induces peripheral systemic vasodilation which triggers the baroreceptor reflex resulting in an increased heart rate.[20]

With different statistical comparisons, we tried to disentangle the additional and potentially synergistic impact that either alcohol had on top of hypobaric conditions or that hypobaric conditions had on top of alcohol intake. The additional exposure to alcohol primarily reduced REM duration further by 7.5 min compared with the hypobaric condition alone and showed a trend to shorten SOL and to prolong N2. It further decreased SpO_2 by 3% and led to an increase in the heart rate by 15 bpm. Comparing the change induced by alcohol intake (as the difference between both conditions) between the groups showed that alcohol also added a decrease in N3 duration to the hypoxia effect. Together these results fit well with the alterations that have been observed in response to alcohol intake alone, as discussed above. The additional exposure to the hypobaric condition reduced REM duration by 18 min, decreased N3 duration by 38 min, increased N2 duration, and WASO compared with alcohol exposure alone. It decreased SpO_2 and increased heart rate during TST by 10% and 11 bpm, respectively. Therefore, alcohol and hypobaric conditions have synergistic effects but the hypobaric condition contributes more to the observed changes than alcohol.

The results of this study refer only to a sleep duration of 4 hours, which limits the transferability to other sleep durations. However, the sleep duration was chosen to reflect realistic inflight sleep opportunities. Participants slept in supine positions, which resembles the situation of passengers travelling first and business class. Sleeping in a sitting position has been reported to impair sleep efficiency and REM duration.[38] Following the notion that hypobaric hypoxia is aggravated by sleep, passengers travelling in economy class might be affected to a lesser extent by the exposure to alcohol and hypobaric conditions. The free access of first and business class passengers to alcoholic beverages might increase the risk.

The sample examined in our study was of limited size and does not represent the average population. We derived the presented results from a subpart of a larger study,[22] so the absence of an a priori power calculation is a limitation. However, our findings are strong and robust and in line with existing literature. Even in these young and healthy subjects, critical oxygen desaturations below 90% were registered. In elderly and chronically ill people, the combined effects of alcohol consumption and hypobaric conditions on sleep architecture, SpO_2 and heart rate might be considerably stronger. Therefore, studying participants with stable treated respiratory disease is of wider public interest and is realistically feasible as it has already been done.[39] Barometric pressure was only one of several systematic differences between the sleeping environments. Factors such as personal comfort (real bed vs bunk bed as well as altitude chamber vs sleep laboratory) or ambient noise (quiet vs realistic inflight cabin noise) might have affected the outcome. Even though we provided two nights of recovery between conditions, carryover effects cannot be completely ruled out.

CONCLUSION

We conclude that the combined influence of alcohol and reduced atmospheric pressure has a supra-additive effect and even young and healthy participants suffered from clinically relevant desaturations (SpO_2 <90%) and heart rate accelerations during sleep.

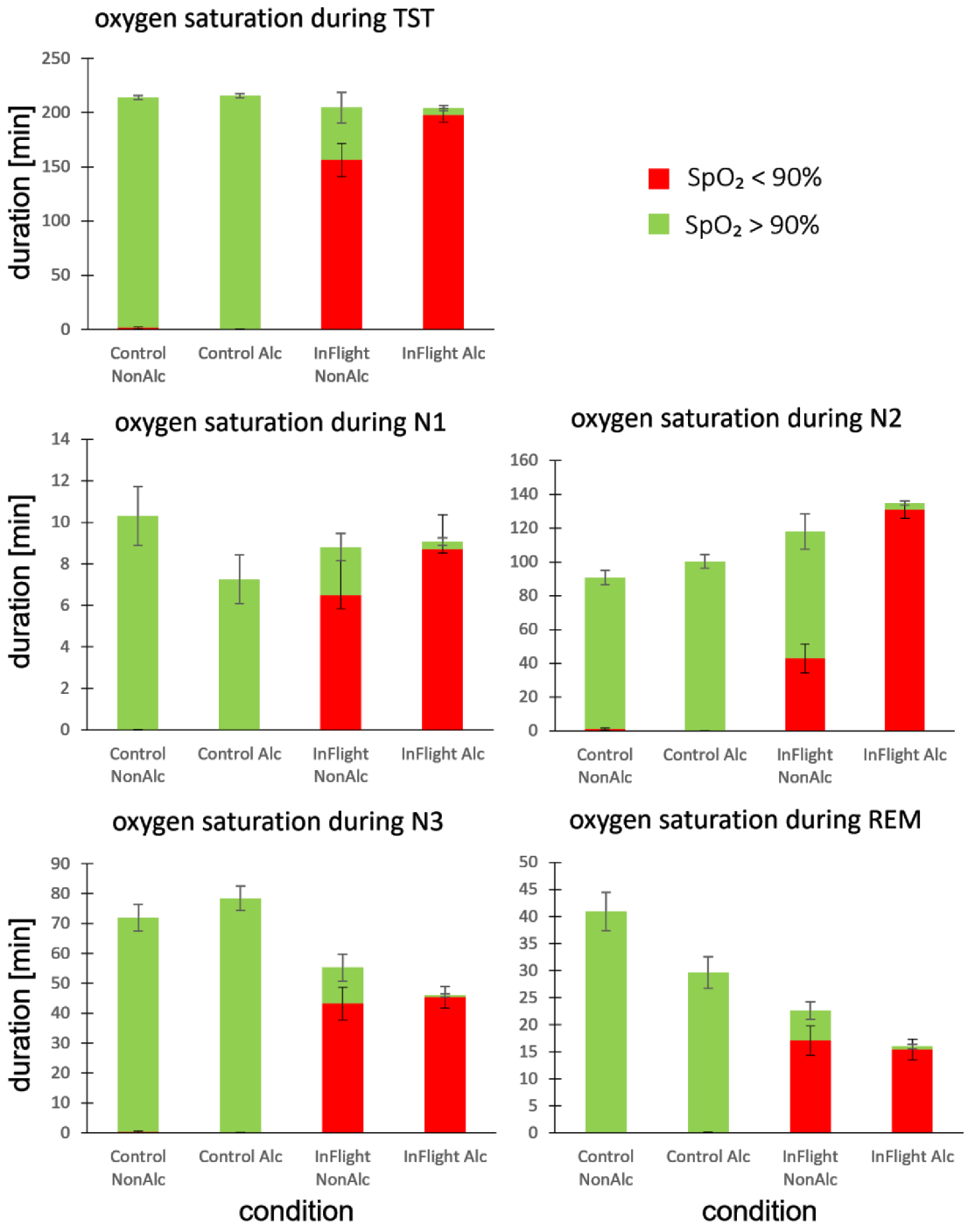

Figure 4 Comparison of blood oxygenation between non-alcohol and alcohol conditions in the Control Group and InFlight Group. Data are from two independent groups recorded during 4-hour sleep episodes (00:00–04:00 hours) in an altitude chamber at simulated flight level (ie, atmospheric pressure corresponding to 2438 m above sea level; n=14) and in the sleep laboratory (53 m; n=22). Mean±SE duration during sleep that participants spent with an oxygen saturation >90% and <90% (hypoxic state). N1–3, REM, sleep stages; TST, total sleep time.

Since sleep quality was compromised, inflight sleep cannot be considered as fully recuperative. This is even more true for passengers travelling first and business class because they have the possibility to sleep in a horizontal position. Our findings support the recommendations of the BTS Clinical Statement on Air Travel to avoid alcohol in the 12 hours preceding and during air travel when suffering from obstructive sleep apnea syndrome or obesity hypoventilation syndrome.[3] Moreover, public awareness of this topic should be raised through patient charities, public campaigns and written health advice of airlines. Technical and economic constraints make it unlikely that an increase in cabin pressure will be implemented by airlines.[6]

STATEMENT OF SIGNIFICANCE

Passengers frequently consume alcoholic beverages during long-haul flights before falling asleep. Despite this being a routinely occurring situation, the combined impact of moderate alcohol consumption and inflight hypobaric conditions on sleep, blood oxygen saturation (SpO_2) and heart rate is unknown. In young

and healthy adults we found a decrease in SpO_2 to a median of 85% during sleep under the combined exposure that was accompanied by an increase in heart rate and disturbed sleep. Higher doses of alcohol could amplify these observed effects, potentially escalating the risk of health complications and medical emergencies during flight, especially among older individuals and those with pre-existing medical conditions. Our findings strongly suggest that the inflight consumption of alcoholic beverages should be restricted.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the Ethics Committee of the North Rhine Medical Board, 2010100. Participants gave their signed informed consent according to the Declaration of Helsinki before taking part and were reimbursed for participation.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data will be made available by the corresponding author upon reasonable request.

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