

# Acute Moderate Alcohol Consumption Affects Cardiovascular Responses in Healthy Males with Different Tolerance Levels

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## Key Words

Respiratory sinus arrhythmia · Auditory stimulation · Acute alcohol · Alcohol tolerance · Lipids and lipoproteins

## Abstract

We investigated the effect of acute moderate alcohol consumption or placebo on respiratory sinus arrhythmia (RSA) in 48 healthy participants with different levels of alcohol tolerance but no abuse. In the electrocardiogram recording, auditory stimuli were presented at defined points in the respiratory cycle, which allows a non-invasive measure of CNS control over RSA. After alcohol consumption we found a decrease in RSA with auditory stimulation. Moreover, individuals with low tolerance showed only a slight change in the RSA after alcohol intake compared to baseline, whereas the placebo drink led to a reduced RSA. In subjects with high alcohol tolerance, alcohol consumption led to a reduction of RSA, with no change after placebo. These results suggest a centrally driven influence on RSA that is changed by alcohol ingestion depending upon subjects' levels of alcohol tolerance.

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## Introduction

Numerous investigations support the contention that acute alcohol ingestion results in a decrease of heart rate variability, which is partially mediated by brainstem centers via the vagal nerve [24, 35, 45, 56]. For example, Weise et al. [56] reported that acute alcohol (0.7 g ethanol/kg bodyweight) decreased heart rate variability. Similarly, Newlin et al. [35] found that the physiologically normal response to food or beverage intake, of an increased vagal tone is inhibited by moderate doses of alcohol (0.5 g ethanol/kg bodyweight). Respiratory sinus arrhythmia (RSA), i.e. the variation of heart rate with the rhythm of breathing, is considered an indicator of vagal tone [22]. It is characterized by acceleration of heart rate shortly after the beginning of inspiration and by deceleration shortly after the beginning of expiration. Reed et al. [41] investigated the influence of acute alcohol consumption on vagal regulation of heart rate in subjects with a history of poly-drug use. They found that alcohol reduces cardiac vagal tone, i.e. RSA and heart period was significantly lower after a high alcohol dose, in comparison to placebo. Variations in RSA are influenced by central and peripheral vagal mechanisms [16]. It is well known that RSA is controlled by changes in brainstem respiratory drive [2].

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Moreover, it is assumed that the brainstem centers which control breathing and heart rate cycles (and RSA) themselves receive input from higher cortical areas [55]. Warzel and Krell [55] developed a method to noninvasively investigate CNS control over RSA: They presented auditory stimuli and quantified the resulting modulation of RSA, i.e. the acoustic heart rate response. Using this method in a previous study with drunken drivers, we found that decreased RSA and reduced acoustic heart rate response was related to the blood alcohol concentration (ranging from 0.16 to 0.31%) at the time of the offense [47]. The data suggest that individual alcohol tolerance level, obtained by continuous alcohol consumption over time, modulates the central influence on RSA. In social drinkers, however, i.e. those not showing any sign of dependency [18], no studies have been conducted on the acute effect of moderate alcohol consumption on cardiovascular parameters and their relation to alcohol tolerance. According to the literature, alcohol tolerance can be defined as a less strong effect of alcohol after repeated consumption of the same quantity of alcohol [4, 21]. We have thus studied the association between cardiovascular parameters and biological alcohol markers in social drinkers in whom alcohol tolerance was known.

In epidemiological studies, cardiac autonomic activity, especially lower parasympathetic activity, as assessed by heart rate variability (e.g. RSA), has been found to be associated with postmyocardial infarction mortality and sudden death [30]. However, the association of heart rate variability and the incidence of coronary heart disease (CHD) is not well described. It is also known that heavy alcohol consumption is related to cardiovascular dysfunction [11, 42, 59]. Drinking at a greater than moderate rate, defined by a consumption of more than 2 drinks per day, is associated with an increased risk of cardiovascular disease [44]. In contrast, moderate alcohol consumption may have some beneficial effects on the cardiovascular system that are attributed to changes in lipid levels [23], especially to an increase in blood levels of high-density lipoprotein cholesterol (HDL-C) [25]. Alcohol may directly affect the hepatic production and secretion of apolipoproteins and lipoprotein particles, increase triglyceride lipase concentrations, and decrease removal of circulating HDL-C [32]. Indeed, increased apolipoprotein A-II levels, a constituent of high-density lipoproteins (HDLs), have been proposed as a biochemical indicator of alcohol abuse [38]. Elevated HDL-C levels have been shown to be associated with reduced cardiovascular risk [19]. However, it is unclear whether RSA and lipoproteins are associated in social drinkers.

In order to gain a more systematic view for psychophysiological processes related to alcohol, we monitored cardiovascular functions during acute alcohol ingestion with respect to biological blood parameters and individual alcohol tolerance. We studied whether there is an effect of acute, moderate alcohol doses on cardiovascular parameters (e.g. RSA, inter-beat intervals, blood pressure) and whether acute alcohol changes the modulation of RSA by auditory stimuli in social drinkers. Finally, we were interested in whether the level of individual alcohol tolerance has an influence on this relationship.

## Methods

### *Subjects*

We studied 48 male volunteers whose mean age was  $28.3 \pm 3.75$  years. Participants were recruited via newspaper advertisements and were paid DEM 80 for their participation. Inclusion criteria for the study were a healthy physical condition measured by blood parameters (standard clinical cut-off values) such as liver enzymes, full blood count, creatinine levels, and TSH. Furthermore, participants with a personal or family history of drug/alcohol abuse, with diabetes mellitus, with cardiovascular disease (i.e. arrhythmia, hypertension) or with hearing impairment were excluded (established by clinical in-depth interview and examination). No subject was taking medications. Prior to being accepted for inclusion, potential volunteers completed a questionnaire on their habits of alcohol consumption, e.g. the Magdeburg Alcohol Tolerance Test (MATT) [48]. Social drinkers in our experiment consumed approximately 14 ml ethanol/day on average, which is less than one drink/day. Written informed consent was obtained from all participants and the study was approved by the local ethics committee. Participants were instructed to stay abstinent from alcohol one day prior to testing and to avoid coffee or tea. The experiments were performed at the same time of day for each subject, commencing at least 2 h after the last meal consumed in our laboratory.

### *Procedure*

The design of the study involved a double-blind trial with an alcohol and a placebo condition, see Schulte et al. [49]. Smokers were instructed to stay abstinent from smoking during the experiment. Participants were quasi-randomly assigned to one of the two conditions, i.e. with respect to self-reported alcohol tolerance scores [48]. Measurements were taken before and after an oral dose of 0.6 g/kg alcohol (4 drinks of 200 ml containing a mix of vodka and orange juice) versus placebo (4 drinks of 200 ml of orange juice with 2 ml of vodka floating on top). Participants were instructed that all beverages (including placebo) contained alcohol. Beverages were consumed within 15 min. Then, blood alcohol level (BAL) was repeatedly measured using a breath alcohol analyser (AlcoQuant A 3020, EnviteC-Wismar) to monitor the absorption phase. For an additional assessment of BAL, we took venous blood samples. Post-alcohol/placebo recording started after the BAL had exceeded the maximum of the individual curve, i.e. when there was no further increase for four consecutive measurements (within 10 min). This peak was reached after approximately 30 min. All subjects were examined following the

same time schedule, starting at 11 a.m. A first venous blood sample was taken at 11 a.m. followed by a standard light meal. At 1 p.m., the pre-alcohol assessment started. Alcohol intake was scheduled at 2 p.m. At 2.30 p.m. the post-alcohol assessment was carried out. The second blood sample was then taken at 2.50 p.m. One experimenter prepared and handed out the drinks and also took the blood alcohol readings. The other experimenter, unaware of the subjects' previous drink, measured the cardiovascular parameters. Thus, because neither this experimenter nor the subject were informed about how much alcohol was contained in the drink, the study design was double-blind.

#### *Apparatus*

We employed standard Einthoven electrocardiogram (ECG) recording. The amplitude of RSA was measured as the mean difference between the minimum and the maximum of inter-beat intervals (IBIs) duration. Central nervous system control of respiratory-cardiac coupling in the method of Warzel and Krell [55] is defined as the momentary change of the RSA amplitude to auditory stimuli which occurs at defined time points in the respiratory cycle. Stimuli were a 90-dB white noise pulse of 750 ms duration, presented through headphones. Subjects followed a rhythm of breathing paced by an oscilloscope (adapted to the individual breathing; with an average frequency of respiration of  $11.9 \pm 1.4/\text{min}$ ).

Auditory stimuli were triggered by the first R wave occurring after a change in respiratory cycle (start of inspiration or of expiration). Twelve sequential IBIs following the respiratory phase change were recorded as one period of measurement. Forty-eight of these periods of measurement were selectively averaged into four separate groups of 12 periods each: (1) and (2) expiration with and without stimulation; (3) and (4) inspiration with and without stimulation. A phase-synchronizing averaging technique was used to remove the influence of phase variance between heart rate and respiratory cycle and thus achieve a phase-independent measure of the RSA amplitude: The shortest IBI during inspiration and the longest during expiration, respectively, were labeled as No. 1; the IBIs preceding these reference points were labeled as 0, -1, and those following the reference as 2, 3, 4 etc. IBIs having the same label were then averaged within a subject, and group means were obtained from these. Warzel and Krell [55] showed that the auditory effect on RSA is only present for stimulation in the early expiration phase, which may be interpreted as the efferent cardiac parasympathetic activity being either blocked or highly diminished during inspiration. For analyzing RSA we have chosen the time domain which allows analyzing the immediate cardiac response to acoustic stimulation [43, 47, 55]. The separation of inspiration and expiration phase which proves valuable to assess more central (medullar) control mechanisms amounts to a non-linear approach (a non-linearity in the respiration to heart rate transfer function) [9] that prohibits simple conversions between time and frequency domain analyses. In the peak-to-valley statistic, the RSA is quantified as the difference between the longest and shortest heart period within the respiratory cycle. The change of respiratory cycle was monitored by a thermo-element in a breathing mask that allows reliable measurement without hindrance of breathing. Systolic and diastolic blood pressure were measured by finger photoplethysmography (Finapres 2300, OHMEDA, Louisville, USA).

Determinations of biochemical markers of alcohol abuse, mean corpuscular volume (MCV) gamma glutamyl-transferase (GGT) and percent carbohydrate-deficient transferrin turbidimetric immunoassay (%CDT TIA) were made using routine clinical laboratory

methods. These markers have been shown to be sensitive and specific markers of alcohol abuse, especially when used in combination [51]. For the determination of blood cholesterol in very-low-density lipoproteins (VLDL), low-density lipoproteins (LDL) and high-density lipoproteins (HDL), the Lipid Research Clinic method was used, with the modification that LDL was precipitated by phosphotungstic acid/ $\text{Mg}^{2+}$ . The concentrations of total triglycerides (TG) and total cholesterol (TC) were determined by commercial enzymatic methods on a random-access analyzer (Hitachi 911, Roche Diagnostics, Germany). All reagents and calibrators were from Roche Diagnostics, Germany. Apolipoprotein A-I (APO A1) and A-II (APO A2) were determined using immunoturbidimetric assays [37].

Questionnaires can be an effective method for assessing alcohol tolerance by collecting information about personal experience with alcohol usage. Here, alcohol tolerance was assessed by a self-rating questionnaire, the Magdeburger Alcohol Tolerance Test (MATT). Unlike common scales of alcoholism, the MATT focuses on alcohol experiences as they relate to physical tolerance and performance levels and not on dependency-specific behavior. The complete test contains 50 items related to the effects of tolerance; typical items are, 'I can hold my liquor better than most people' or 'It really makes no difference if I've had something to drink or not, my performance is always the same'. Additionally, we asked for the amount of weekly alcohol consumption. The validity of this questionnaire has been described in a previous publication [48]. The MATT correlated significantly and positively with the Lübecker Alcohol Dependence and Abuse Screening Test (LAST) [46] and the maximum quantity that could be consumed before feeling the unpleasant effects of alcohol (dizziness, nausea, etc.), indicating that higher tolerance levels are associated with heavy drinking. As further psychological tests we used the d2 test [5] to assess concentration ability.

#### *Statistical Data Analysis*

Statistical data analyses were carried out with the SPSS package (Standard Version 9.0). For group comparisons, unpaired Student's *t* tests and once a  $\chi^2$  test were used. Group and condition effects were assessed by regression analysis and by a two-factorial repeated measures ANOVA. For biological variables, Spearman's rho correlation and for psychometric variables, Pearson correlation were calculated. Significance was accepted at  $p < 0.05$ .

## Results

There were, at baseline, no significant differences between the subject groups (low vs. high tolerant) in all the main variables: age (28.5 vs. 28 years), body mass index (BMI; 23.5 vs. 23.4  $\text{kg}/\text{m}^2$ ), d2 scores of attention (GZ-F: 465 vs. 464), drinks per week (5 vs. 7; one drink contains about 16 ml ethanol), the three biological markers of alcohol consumption: CDT (3.25 vs. 3.33%), MCV (87.9 vs. 89.3 fl) and GGT (0.38 vs. 0.37  $\mu\text{mol}/\text{s}\cdot\text{l}$ ) and the cardiovascular parameters: IBI (847 vs. 828 ms), RSA (112 vs. 110 ms; RSA with auditory stimulation: 118 vs. 109 ms), systolic blood pressure (SBP; 134 vs. 138 mm Hg), and diastolic blood pressure (DBP; 78 vs. 81 mm Hg).

Table 1. Correlation matrix (Spearman's rho) at baseline (pre-test) of cardiovascular parameters and lipid levels

Lipid parameters	Cardiovascular parameters				
	IBI	RSA without stimulation pre-test	RSA with stimulation pre-test	SBP	DBP
APO A1	0.19	0.02	0.02	0.08	0.04
APO A2	0.06	-0.32*	-0.32*	-0.02	-0.03
LDL	-0.24	-0.39**	-0.38**	0.22	0.25
HDL	0.08	0.14	0.10	0.06	-0.02
TC	-0.25	-0.44**	-0.47**	0.25	0.29*
VLDL	-0.03	-0.30*	-0.27	0.02	0.22
TG	-0.19	-0.32*	-0.34*	0.00	0.10

Cardiovascular parameters: IBI = inter-beat intervals; RSA = respiratory sinus arrhythmia; SBP = systolic blood pressure; DBP = diastolic blood pressure.

Lipid parameters: APO A1 = apolipoprotein A-I; APO A2 = apolipoprotein A-II; LDL = low-density lipoproteins; HDL = high-density lipoproteins; VLDL = very-low-density lipoproteins; TC = total cholesterol; TG = total triglycerides.

\* Correlation significant at the 0.05 level (2-tailed).

\*\* Correlation significant at the 0.01 level (2-tailed).

Table 2. Pre-post changes in the alcohol (n = 24) and placebo (n = 24) group

	Alcohol group (n = 24)			Placebo group (n = 24)			Alcohol/ placebo, mean difference	F	d.f.	p
	pre	post	Δ pre-post	pre	post	Δ pre-post				
IBI, ms	847.2 ± 26.8	791.6 ± 26.9	55.6 ± 8.8	827.9 ± 20.0	794.0 ± 22.4	33.9 ± 11.3	21.6 ± 14.3	2.26	1	0.13
RSA without auditory stimulation	112.9 ± 15.7	85.4 ± 17.6	27.5 ± 6.7	110.2 ± 12.9	92.0 ± 12.2	18.2 ± 5.3	9.3 ± 8.5	1.15	1	0.28
RSA with auditory stimulation	118.5 ± 17.7	89.6 ± 17.2	28.9 ± 4.3	109.0 ± 12.9	96.5 ± 13.5	12.5 ± 6.2	16.4 ± 7.6	4.59	1	0.04*
Diastolic blood pressure	78.0 ± 1.7	73.4 ± 1.2	4.6 ± 1.3	80.9 ± 9.5	81.7 ± 8.9	-0.8 ± 1.4	5.4 ± 2.0	7.01	1	0.01*
Systolic blood pressure	133.9 ± 2.2	125.8 ± 1.7	8.1 ± 2.0	137.8 ± 2.5	135.4 ± 2.3	2.4 ± 2.6	5.7 ± 3.3	2.98	1	0.09

Data are means ± SEM.

Two-factorial ANOVA, F values refer to the interaction term [time of measurement (pre, post) × group factor]. \* Significance level was set at  $p \leq 0.05$ .

We found no significant correlation (Spearman's rho, two-tailed) between the three conventional alcohol markers, GGT, CDT and MCV. One of the markers, CDT, was correlated with the number of drinks per week ( $r = 0.31$ ;  $p < 0.04$ ), but MCV and GGT were not. There was, however, a significant correlation between GGT and BMI ( $r = 0.41$ ;  $p < 0.004$ ).

We correlated alcohol indicators and lipoproteins before drinking and found significant correlations between

GGT and APO A1 ( $r = 0.48$ ,  $p < 0.01$ ), GGT and LDL ( $r = 0.36$ ,  $p < 0.05$ ), GGT and TC ( $r = 0.45$ ,  $p < 0.01$ ), GGT and VLDL ( $r = 0.36$ ,  $p < 0.05$ ), and GGT and TG ( $r = 0.40$ ,  $p < 0.01$ ). CDT was negatively correlated with LDL ( $r = -0.30$ ,  $p < 0.05$ ) and positively correlated with HDL ( $r = 0.27$ ,  $p = 0.07$ ). Additionally, drinks per week was correlated with APO A1 ( $r = 0.49$ ,  $p < 0.01$ ), APO A2 ( $r = 0.38$ ,  $p < 0.01$ ) and HDL ( $r = 0.26$ ,  $p = 0.07$ ).

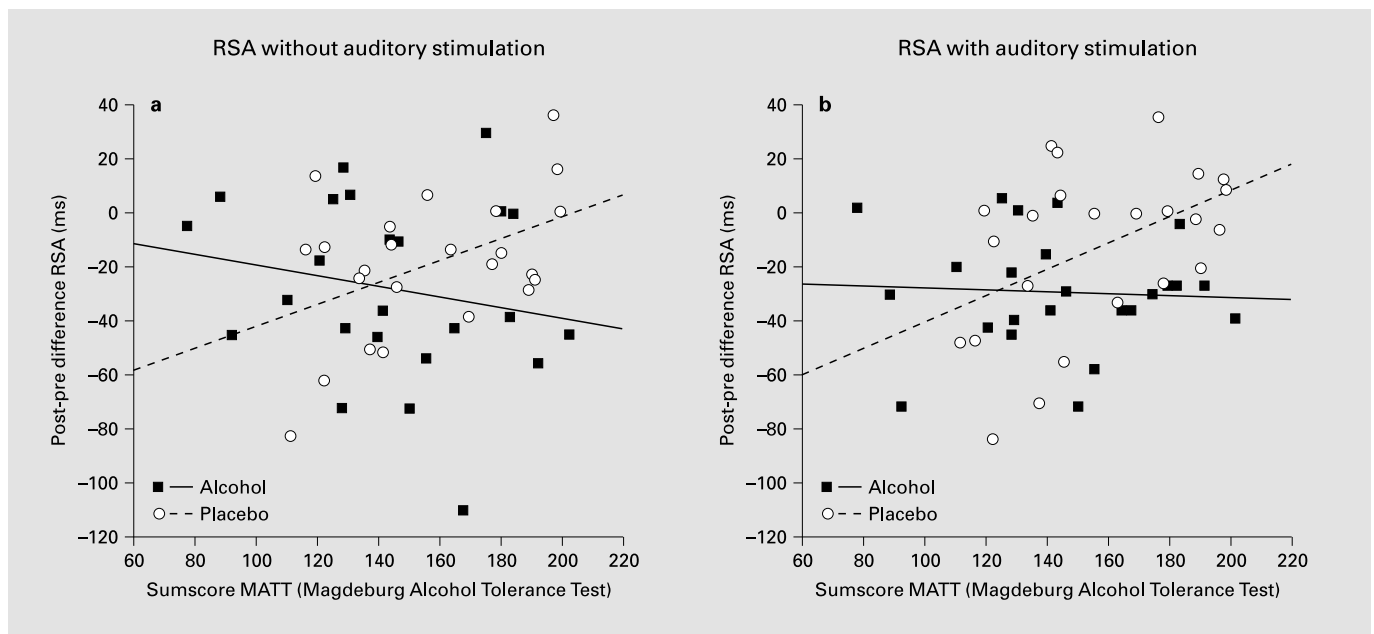


Fig. 1. Regression of the post-pre difference values of the RSA ( $\Delta$ RSA) without (a) and with (b) stimulation onto alcohol tolerance as assessed by the MATT score in the alcohol group (black) compared to the placebo group (gray). Negative difference values of RSA correspond to a reduction (and positive difference values to an increase) of RSA after the treatment.

The correlations between the cardiovascular parameters at baseline and the lipoproteins are shown in table 1. RSA was negatively correlated with a number of lipoproteins: APO A2 ( $r = -0.32$ ,  $p < 0.05$ ), LDL ( $r = -0.39$ ,  $p < 0.01$ ), TC ( $r = -0.44$ ,  $p < 0.01$ ) and TG ( $r = -0.32$ ,  $p < 0.05$ ). DBP further correlated with TC ( $r = 0.29$ ,  $p < 0.05$ ).

The mean breath alcohol concentration was 0.05% at its peak; the blood alcohol level as determined from the venous samples was slightly higher (0.06%). Table 2 shows the pre-post changes of cardiovascular parameters. The heart IBI after alcohol ingestion in comparison to placebo showed no significant effects [ $F(1, 46) = 2.3$ ,  $p = 0.13$ ] and also the RSA without auditory stimulation (90 dB) was not significantly different [ $F(1, 46) = 1.2$ ,  $p = 0.28$ ]. However, the pre-post change in RSA with auditory stimulation was significantly different between the two groups [ $F(1, 46) = 4.6$ ,  $p < 0.04$ ].

DBP (pre-post change) differed significantly between the alcohol and the placebo group [ $F(1, 43) = 7.0$ ,  $p < 0.01$ ] whereas the pre-post difference for SBP did not reach significance in the group comparison [ $F(1, 43) = 3.0$ ,  $p < 0.09$ ].

Analyzing the relation between alcohol tolerance and RSA changes following alcohol consumption, we found a

significant interaction between the two variables: the higher the MATT tolerance score, the higher the change in RSA after alcohol consumption, and the lower after placebo consumption. A regression of the RSA pre-post difference onto the MATT score is shown in figure 1a and b. The gradient of the two regression lines was significantly different (alcohol group:  $\beta = -0.195$ ; placebo group:  $\beta = 0.414$ ,  $F = 4.87$ ,  $p < 0.03$ , fig. 1a). Regression analysis of the relationship of RSA with stimulation and MATT scores (fig. 1b) also revealed a significant difference of the slope (alcohol group:  $\beta = -0.036$ , placebo group:  $\beta = 0.489$ ,  $F = 4.77$ ,  $p < 0.03$ ).

Regarding the effect of tolerance (MATT) on the post-pre change in DBP, we found no significant correlation ( $r = 0.16$ ,  $p = 0.47$ ) in the alcohol group but in the placebo group ( $r = -0.43$ ,  $p < 0.05$ ): in lower tolerant subjects assuming to have drunk alcohol showed an increase in DBP, whereas in higher tolerant subjects (placebo condition), no expectation effect was observable. Moreover, 20 min after alcohol consumption subjects scored their drunkenness from 0 (feeling nothing) to 10 (feeling totally drunk). This score correlated negatively with the MATT score both in the alcohol group ( $r = -0.46$ ,  $p < 0.03$ ) and placebo group ( $r = -0.39$ ,  $p < 0.06$ ), i.e., the more tolerant subjects reported feeling less drunk.

## Discussion

### *Blood Alcohol Markers, Lipoproteins and Alcohol Consumption*

As found by others [3, 40, 53], the blood alcohol markers GGT, CDT and MCV did not correlate with each other, suggesting that their respective response to alcohol occurs by different mechanisms. Currently, CDT is discussed as the most specific marker for chronic alcohol abuse [12, 50] because even moderate continuous consumption causes significant elevations in a healthy population [40]. In our study we also found CDT to be the most significantly correlated measure with the amount of weekly alcohol consumption, much higher than GGT which was predominantly correlated with BMI. This indicates that in healthy young men, GGT is a rather unspecific alcohol blood parameter. The interpretation of GGT should therefore take BMI into account when suspecting alcohol-related problems in young men [10]. From this we suspect that the correlation between GGT and the lipoproteins, APO A2, TC, VLDL, TG, mainly results from the use of carbohydrates in nutrition and not from alcohol consumption [31, 33]. However, the significant correlation of APO A1 and APO A2 with drinks per week indicates a specific sensitivity of these apolipoproteins to alcohol consumption. APO A1 and APO A2 have accordingly been suggested as biochemical indicators of alcohol abuse [38].

### *Lipoproteins and Coronary Heart Disease*

Furthermore, in our study CDT was negatively correlated with LDL. Alcohol is associated with lower LDL [7, 25, 57] and a strong positive association between LDL cholesterol and coronary heart disease (CHD) is well known [6, 8]. Most epidemiological studies found an inverse association between moderate use of alcohol and CHD [14, 23, 44]. The protective effect of moderate alcohol drinking is related to an increased HDL level, lower plasma fibrinogen, and inhibition of platelet aggregation [13, 39]. We found a low correlation between HDL and alcohol-related parameters in our group of healthy young men. However, especially in persons at increased risk for CHD, protective effects of alcohol were reported [32].

### *RSA with Auditory Stimulation in Healthy Subjects and the Risk of CHD*

It is well known that in heavy drinkers [47] and in chronic alcoholics [58], RSA is clearly reduced. In alcoholics, autonomic dysfunction and degeneration of the myelinated fibers in the vagal nerve have been observed

[34]. Furthermore, RSA is a measure of cardiac age [20] and a decreased cardiac vagal tone is associated with an increased risk of sudden cardiac death or coronary disease [52]. The significant negative correlation between RSA and the lipoproteins (LDL, CHOL, TG and VLDL) closely mirrors a risk for development of coronary artery disease due to a reduced cardiac parasympathetic modulation. Newlin et al. [35] and Weise et al. [56], using spectral analysis, found RSA in healthy subjects to be reduced after moderate alcohol consumption. With the time domain method, we did not find a significant decrease in RSA or a change in IBI after moderate alcohol intake, whereas RSA with acoustic stimulation did change significantly. Since the time domain allows analyzing central control mechanisms, e.g. auditory startle, it may be a more suitable method for centrally driven alcohol effects on RSA than the frequency domain. Cardiac acceleration is often associated with sympathetic activity [15, 17, 54]. Still, a relative acceleration from the tone during a phase of absolute deceleration (expiration phase) as in our paradigm suggests a reduced vagal heart rate downregulation [47]. In the polyvagal theory [36] the vagal system is part of a feedback loop in which the central nervous system regulates cardiac output. Thus, alcohol may moderate cardiac output by changes of the central influence of the vagal system. In our study, the effect of auditory stimulation on RSA under the influence of alcohol can be interpreted as an inhibition of the centrally driven influence on autonomic mechanisms. However, in both the alcohol and placebo groups we found a decrease of RSA amplitude, so that decrease is partially due to repeated test conditions.

### *Tolerance and the Effects of Moderate Drinking*

The acute effects of moderate drinking on behavior and body functions depend on tolerance, and we asked whether such effects can be shown by our data. As expected, we observed an interaction effect of alcohol/placebo and the MATT score on RSA (both with and without stimulation). Individuals with low self-reported tolerance showed hardly any change in RSA after alcohol consumption, whereas the placebo beverage led to a reduced RSA. In the placebo group the influence of an alcohol expectancy effect may be different depending on the familiarity with alcohol consumption [27], leading, in turn, to a higher arousal in low tolerant subjects. It is clear that a stressful situation, even as mild as expecting to receive alcohol with not much experience in drinking, can modulate the sensitivity of the baroreceptor-heart rate reflex [26]. This is supported by our finding that in the placebo group DBP

is significantly elevated in lower tolerant in contrast to higher tolerant subjects. Additionally, low tolerant subjects tend to misinterpret their own feeling of drunkenness, indicating little experience with the effects of alcohol. In low tolerant subjects, the presumably higher arousal from an administered placebo drink causes reduction of RSA, and this arousal might be lowered by alcohol resulting in no change of RSA after alcohol consumption. In highly tolerant subjects, i.e. those who had experience with the psycho-physiological effects of alcohol, alcohol consumption led to an activation (enhanced arousal) and thus a reduction of RSA compared to those who received placebo, showing no change in RSA.

## Conclusion

In conclusion, the findings suggest that RSA is a sensitive measure for cardiovascular status in healthy subjects. We showed that in healthy non-clinical subjects RSA is negatively correlated with lipoproteins, e.g. LDL and TC. LDL-C and TC are related to CHD, however, since we investigated healthy subjects, no direct conclusion on

RSA and CHD risk can be drawn. On the other hand, the number of drinks per week was significantly correlated with APO A1 and APO A2 known to act protectively against CHD that is mediated by a reverse cholesterol transport pathway [1]. Moreover, acute moderate alcohol consumption reduces RSA with auditory stimulation, which points to an alcohol-induced inhibition of the centrally driven influence on autonomic mechanisms in healthy subjects. For a full understanding of alcohol effects on cardiovascular parameters, the individual alcohol tolerance should be taken into account. RSA was shown to be diminished after alcohol ingestion only in subjects with higher scores of alcohol tolerance, thus alcohol had an activating effect. In contrast, subjects with low tolerances show a reduction of RSA and alcohol ingestion counteracts this in lowering the arousal, thus alcohol had a sedative effect. Thus, RSA with an auditory stimulation was discovered to be a sensitive indicator of acute alcohol intake as well as of different alcohol tolerance levels. The sample size in this study was small and additional work is required on the effects of alcohol and alcohol tolerance on cardiovascular functions in healthy individuals.

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