Effect of acute ethanol administration on the baroreceptor reflex control of heart rate in normotensive human volunteers

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Summary

1. The effects of acute ethanol administration on blood pressure, heart rate and the baroreceptor reflex control of heart rate were studied in normotensive subjects who served as their own control. Baroreceptor reflex control of heart rate was measured by two methods: the ramp method and the steady state method.

2. None of the doses of ethanol had any effect on blood pressure during the observation period, except for the highest dose where a slight elevation was evident for a short period of time. On the other hand, the heart rate showed a slight but consistent dose-related increase.

3. In general, ethanol attenuated the baroreceptor mediated bradycardia but this effect was dependent on the way in which blood pressure was elevated. A dose-related impairment of baroreceptors was evident when the ramp method was used, i.e. ethanol significantly depressed baroreflex sensitivity, expressed as $\Delta$heart period (HP)/$\Delta$mean arterial pressure (MAP). In contrast, $\Delta$HP/$\Delta$MAP was not influenced by ethanol when the steady state method was used. However, the steady state baroreflex curves were reset about a higher median blood pressure ($MAP_{50}$), suggesting that the baroreceptors will be operative at higher blood pressure levels after ethanol.

4. The pressor responsiveness was also influenced differently by ethanol depending on the method of injecting phenylephrine. An increase in pressor responsiveness was evident, though not dose-related, after ethanol only when blood pressure was elevated by the ramp method, suggesting that the inverse relationship between baroreflex sensitivity and pressor responsiveness is more prominent with the ramp method and/or when impairment rather than resetting of baroreceptors occurs.

5. That the decrease in baroreflex sensitivity and the increase in $MAP_{50}$ were related to peak ethanol levels in blood and that the blood pressure was not influenced by ethanol strongly suggest these effects were ethanol mediated. The weakened buffering action of the baroreflexes would be expected to favour the development of higher blood pressure.

Key words: baroreflex sensitivity, ethanol, pressor responsiveness, ramp method, steady state method.

Introduction

There is considerable epidemiological evidence which suggests a positive relationship between ethanol consumption and arterial blood pressure [1-5]. However, although the findings of more recent controlled clinical studies [1, 5] have supported this relationship, no study has clearly identified the mechanism(s) by which ethanol elevates blood pressure.

We have performed a series of experiments to evaluate the possibility that ethanol-associated hypertension may involve alteration of arterial baroreflexes. Except for our data in animals [6-8], there has been only one other study, to our know-
ledge, which has investigated the effect of ethanol on cardiovascular reflexes [9]. This study [9] showed that normotensive subjects who received 0.3 or 0.6 g of ethanol/kg had augmented reflex tachycardia in response to the Valsalva manoeuvre, a deep breath, hyperventilation and body tilt even though their baseline heart rate was higher after ethanol and their blood pressure did not change. Although data from our laboratory which showed that acute [6] and chronic [7] ethanol administration augmented the baroreflex mediated tachycardia are compatible with the findings of this study [9], there is no available information in the literature about the effect of ethanol on the baroreceptor reflex control of heart rate in response to evoked elevations in blood pressure in humans.

The baroreceptor heart rate response has been used in experimental [7, 10-12] and clinical studies [13-16] in both normotensive and hypertensive conditions. This technique, which involves recording heart rate responses during evoked changes in blood pressure, has provided definitive evidence that the baroreceptor heart rate response is attenuated in the hypertensive state [15, 16]. More importantly, this attenuation precedes and may be a factor in the development of some forms of hypertension [17-19]. In agreement with this view, our findings in rats have shown that chronic ethanol feeding attenuated the baroreceptor reflex control of heart rate [7] before the development of hypertension [8]. In fact, ethanol was able to attenuate the baroreceptor heart rate response in rats even after a single dose [6].

Assessment of baroreceptor function by the baroreceptor heart rate response can be achieved by administering either a bolus injection (ramp method) or a constant infusion (steady state method) of vasoactive agent. The differences between the results of the two methods have been reviewed by Korner et al. [14]. The present investigation deals with the acute effects of ethanol on the baroreceptor reflex control of heart rate in normotensive human volunteers when graded rises in their blood pressure were evoked by phenylephrine using the ramp (part I) or the steady state (part II) technique. The study also describes the effects of acute ethanol administration on baseline arterial pressure and heart rate and on the pressor responsiveness to phenylephrine. Whether the changes in baroreceptor reflex control of heart rate were ethanol mediated was tested by studying the relationship between blood ethanol concentration and baroreflex sensitivity (part I) or median blood pressure (part II). In this study, the term 'impairment' refers to a decrease in baroreflex sensitivity, whereas 'resetting' indicates an upward shift of the baroreflex curve.

**Methods**

**Subjects**

Sixteen subjects, eight male and eight female, were employed in part I of the study. The average age and weight of all subjects were 25.4 ± 0.7 years and 65 ± 3 kg, respectively. The mean age of the males was similar to that of females (24.7 ± 0.5 vs 26 ± 1 years), whereas the mean weight was significantly higher in males (78 ± 1 vs 54 ± 1 kg). To eliminate the possibility that either sex may respond differently to ethanol, the subjects were randomly allocated, with a similar male/female ratio, to three groups. All volunteers were professional students; two were ethanol naive and the remainder classified themselves as occasional drinkers. None admitted to any ethanol consumption in the 10 days before the experiment. All were screened by history and physical examination; they were normotensive and none had taken any medication within the past 3 months which could have interfered with the study. All were instructed to fast from 24.00 hours the previous day. The protocol of the study was approved by the University Policy and Review Committee on Human Research and informed consent was obtained from each subject. Each experiment was carried out at 08.00 hours to minimize the effects of diurnal variation on ethanol metabolism. In part II of the study, 13 subjects were employed, 10 of which had already participated in part I. This part of the study was carried out 3 months after part I and the subjects who participated in the two parts received the same dose of ethanol.

**Measurement of baroreceptor reflex control of heart rate**

The subjects were prepared similarly in the two parts of the study as regards their blood pressure and heart rate (HR) recording. With the subject in the recumbent position, in a quiet room, an arterial cannula was inserted into the ipsilateral brachial artery and an indwelling needle was inserted into the contralateral antecubital vein. The arterial cannula was connected to a Statham P23 pressure transducer and phasic blood pressure was displayed on a Grass polygraph (model 7D). HR was electronically computed from the blood pressure pulse using a tachograph and was simultaneously displayed on another channel. The venous cannula was used for either bolus injections (part I) or cumulative infusions (part II) of phenylephrine. After completing the cannulations, a 30 min time period was allowed for blood pressure and HR to stabilize. In part I of the study bolus injections of phenylephrine (25, 50, 75 and 100 µg) were
injected at 10 min intervals. The injection volume was 0.5 ml and flushed in with 2 ml of sterile 0.9% NaCl; an equal volume of saline injections failed to change blood pressure or HR. It typically took 30–45 s for blood pressure to reach its peak rise which was immediately followed by nadir fall in HR. These responses lasted 2 min and both variables returned to baseline level before the subsequent injection or ethanol ingestion. In part II, phenylephrine was cumulatively infused using the following doses: 25, 42, 82, 110 and 160 μg/min. An additional infusion of 220 μg/min was occasionally needed to reach the target blood pressure. Phenylephrine was prepared in sterile saline as 100 μg/ml; the lowest infusion rate was 0.25 ml/min and the highest was 2.2 ml/min; thus the total volumes given ranged from 21 to 32 ml over the experimental period. Each infusion rate was maintained for 5 min; it typically took 1–2 min after starting the infusion for blood pressure and HR to reach a plateau and it remained at that level for the rest of the 5 min period. After completing the cumulative infusion regimen and the target rise in blood pressure (25–50 mmHg) was reached, phenylephrine infusion was stopped and blood pressure and HR were allowed to recover to pre-infusion levels; this usually occurred within 5–10 min. However, this was not possible in the case of the higher dose of ethanol used as three out of the five subjects who received this dose felt they needed to void after completing the phenylephrine infusion.

In each experiment, the baseline values as well as the peak values of blood pressure and HR were tabulated for every bolus injection or infusion of the pressor agent. The changes in the primary variable, mean arterial pressure (MAP), and the dependent variable, heart period (HP, reciprocal of HR in ms), were obtained and used to calculate the baroreflex sensitivity from the ratio ΔHP/ΔMAP expressed as ms/mmHg [7, 10, 15]. In part II, steady state baroreflex (MAP–HP) curves were constructed according to the method of Korner et al. [14]. This was achieved by plotting HP against MAP starting with the baseline values of both variables and progressing to the plateau values obtained in response to each phenylephrine infusion. The two variables were positively related and a highly significant correlation coefficient \( r = 0.88 \) was obtained. The slope of this relationship was used to determine whether the shift of the baroreflex curve was of the parallel type. The MAP–HP relationship obtained from each subject was analysed for the following parameters: (a) heart period range (HPR, ms), which is the range of readings from baseline to peak HP response observed after the highest infusion rate of phenylephrine; (b) median blood pressure (MAP50, mmHg), which represents the MAP value corresponding to half the HPR; and (c) average gain \( G \), ms/mmHg, which was calculated from the equation \( G = a + b \log \Delta MAP \), where \( a \) and \( b \) were the intercept and regression coefficient respectively and \( \Delta MAP \) was the difference between baseline MAP and the maximum value of MAP [14].

**Protocol**

In both parts of the study each subject served as his/her own control. After measuring the baroreceptor reflex sensitivity as described above, ethanol was ingested and the same procedure was repeated again. Ethanol was given in the amounts of 0.5, 1.0 or 1.5 g/kg as pure ethanol in orange juice in a total volume of 360 ml and was consumed over a 10 min period. Subjects drank in the sitting position and were allowed to assume the recumbent position for at least 10 min before starting phenylephrine injections or infusions. This time period was found adequate for MAP and HR to stabilize and these values were taken as the baseline values for both variables after ethanol. Arterial blood samples were drawn at 15, 30 and 60 min in part I and at 30 min in part II after ethanol ingestion for the estimation of blood ethanol levels, which were determined by the method of Bonnichsen & Lundgren [20]. The peak rises in MAP obtained in response to the graded doses of phenylephrine were used to construct the dose–pressor response curves before and after each dose of ethanol.

**Statistical analysis**

Results are expressed as means ± SE. A two-tailed Student’s \( t \)-test was used in the analysis of paired and unpaired means with the level of significance chosen as \( P < 0.05 \). The baroreflex and pressor response curves were analysed by a one-way analysis of variance and a test for the equality of elevation was used to determine if the regression lines were identical.

**Results**

The average baseline values of MAP and HP of all subjects who participated in this study were 93.5 ± 1.9 mmHg and 918.5 ± 34.5 ms, respectively. For those in the first part of the study MAP and HP were 97.6 ± 2.7 mmHg and 879.9 ± 36.6 ms and the corresponding values for those subjects in the second part of the study were 89 ± 2 mmHg and 943.8 ± 63.6 ms. However, the values for baroreflex sensitivity (ΔHP/ΔMAP) were markedly different and probably reflected the different method of measurement in both experiments: 40 ± 5 ms/mmHg as determined by the ramp method and 17.2 ± 2 ms/mmHg by the steady state method. On
the other hand, the average gain (G) obtained according to the method of Korner et al. [14] under steady state conditions was 39 ± 7.4 ms/mmHg.

None of the doses of ethanol used, 0.5, 1 or 1.5 g/kg, had any effect on MAP throughout the 60 min experimental period after the administration of ethanol (Fig. 1b). On the other hand, there was a dose-related increase in HR after ethanol which began within 10 min and lasted for the duration of the experiment (Fig. 1a). It was important for us to establish that the doses of ethanol we used had no effect on baseline blood pressure for it allowed us to assess baroreflex sensitivity in the absence of any change in arterial pressure. Because of the steady state method we used in the second experiment we were unable to measure baseline MAP and HP throughout the post ethanol period. However, we did measure MAP and HP at 10 and 40 min after ethanol and they were similar to values recorded before ethanol (Table 1). We were assured that in the second experiment ethanol also produced no change in baseline MAP or HP.

Fig. 2 shows that when baroreflex sensitivity was assessed by the ramp method there was a dose-related, ethanol-induced attenuation, i.e. there was less of a bradycardia associated with a similar rise in blood pressure after ethanol than before. The depression of baroreflex sensitivity occurred within 10 min of ethanol ingestion; and with all three doses of ethanol employed it remained depressed throughout the 60 min post ethanol period except for the lowest dose used, 0.5 g/kg, where recovery to control levels occurred at 60 min (Fig. 2). Also shown in Fig. 2 is the blood ethanol concentration at 15, 30 and 60 min after ingestion of each dose. The high initial blood levels were undoubtedly due to the fasting state of all subjects.

The relationship between the peak blood ethanol level, 30 min after ethanol, and the change in baroreflex sensitivity measured at the same time is shown in Fig. 3. A highly significant negative correlation (r = -0.88) existed between blood ethanol concentration and the change in baroreflex sensitivity when measured by the ramp method. The slope of this linear regression line was -14.7, which indicates that a blood ethanol concentration of 1 mg/ml would result in an approximate decrease of 15 ms/mmHg in baroreceptor HR reflex sensitivity. Considering that the baseline control value of our subjects was 40 ms/mmHg, a blood ethanol level of 1 mg/ml would result in a decrease of 60 ms/mmHg in baroreceptor HR reflex sensitivity.

**Fig. 1.** Effect of drinking alcohol (ETOH) in different doses on basal mean arterial pressure (MAP) (b) and heart rate (HR) (a) in three groups of subjects. The male/female ratio was similar among the groups. Measurements, at 10 min intervals, were made after completing the drink (0 min). Volume of each drink was 360 ml. Blood samples were drawn at 15, 30 and 60 min through the arterial line. Values shown are means ± SE and the solid circles with the standard errors to the left of the vertical line represent the averaged basal values of the subjects in all three groups. Dose of ethanol: 0.5 g/kg, n = 6 (o—o); 1.0 g/kg, n = 6 (△—△); 1.5 g/kg, n = 4 (v—v).
**TABLE 1. Effect of ethanol on baseline values and maximally (Max.) evoked changes in mean arterial pressure (MAP) and heart period (HP) in response to phenylephrine infusion**

Recovery shows values of both variables 10 min after stopping phenylephrine infusion. Basal and recovery values after ethanol were obtained 10 and 40 min, respectively, after ethanol ingestion. The reason for absence of recovery values after the highest dose is given in the Methods section.

<table>
<thead>
<tr>
<th>Ethanol (g/kg)</th>
<th>Mean arterial pressure (mmHg)</th>
<th>Heart period (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Basal Before</td>
<td>Max. Before</td>
</tr>
<tr>
<td>0.5</td>
<td>83.3 ± 3.8 102.4 ± 2.9</td>
<td>84.7 ± 4.5</td>
</tr>
<tr>
<td>1.0</td>
<td>91.4 ± 3.1 117.8 ± 1.9</td>
<td>94.0 ± 3.5</td>
</tr>
<tr>
<td>1.5</td>
<td>88.4 ± 3.5 124.7 ± 1.2</td>
<td>87.8 ± 5.7</td>
</tr>
</tbody>
</table>

**Fig. 2. Effect of alcohol drinking on baroreflex sensitivity measured by the ramp method (a).** Blood ethanol concentration (mg/ml) is shown in (b) for the three groups which received the three doses of ethanol. For further explanation see Fig. 1. Dose of ethanol: 0.5 g/kg, n = 6 (○—○); 1.0 g/kg, n = 6 (△—△); 1.5 g/kg, n = 4 (∇—∇).

Concentration of 1 mg/ml impairs baroreflex sensitivity by 37%.

In contrast to the significant ethanol-induced decrease in baroreflex sensitivity when assessed by the ramp method, none of the doses of ethanol used had any effect on baroreflex sensitivity when it was measured by the steady state method. As shown in Fig. 4, baroreflex sensitivity, expressed as ΔHP/
Blood ethanol (mg/ml)

![Graph showing the relationship between blood ethanol concentration and baroreflex sensitivity change.](image)

Fig. 3. Relationship between the change in baroreflex sensitivity (ΔHP/ΔMAP) measured by the ramp method and blood ethanol concentration (mg/ml) obtained at peak blood ethanol values (30 min after ethanol ingestion). The relationship is highly significant ($r = 0.88$) with a slope of $-14.7$ and an intercept of 3.14.

$\Delta$MAP, was not significantly depressed by any dose of ethanol. However, even though ethanol had no effect on baroreflex sensitivity it produced a significant downward shift of the steady state baroreflex curve and this effect was related to the dose of ethanol (Fig. 5). Since neither the slope of the linear regression line relating HP and MAP nor HPR changed (Table 2), the rightward shift of the baroreflex curve produced by ethanol was a parallel shift and suggested resetting of baroreceptors had occurred.

Baseline MAP$_{50}$ values for each of the three groups which later received ethanol were quite comparable (Table 2). The increase in MAP$_{50}$ produced by 0.5, 1 and 1.5 g/kg of ethanol was $6.4 \pm 1.2$, $11.6 \pm 3.2$ and $13.6 \pm 4.1$ mmHg, respectively, which clearly showed the increase was dose-related. This was further supported by the positive correlation which existed between blood ethanol concentration present 30 min after ethanol and the change in MAP$_{50}$ ($r = 0.66$). Thus for every 1 mg/ml increase in blood ethanol concentration there would be a corresponding increase of 8 mmHg in MAP$_{50}$ (Fig. 6).

There was a marked difference in the effects of ethanol on pressor responsiveness when it was assessed by the two methods. When phenylephrine was injected by the bolus method each dose of ethanol used shifted the pressor response curve upward (Fig. 7), indicating increased pressor responsiveness after ethanol. The maximal rise in MAP in the pre-ethanol period averaged approximately 15 mmHg, whereas after ethanol the rise was approximately 27 mmHg and only reached a plateau after the 1 g/kg dose of ethanol (Fig. 7). In contrast, when pressor responsiveness was measured by the steady state method there was no shift in the pressor response curve after any dose of ethanol (Fig. 8).

Discussion

No work has yet been reported which has measured the effect of acute ethanol administration on baroreceptor function in humans and determined if this important regulator of blood pressure is altered in ways which may promote an increase in blood pressure. In this study we used the baroreceptor HR response as an index of baroreceptor function. This technique has been used in many experimental and clinical studies [10–16] and involves evoked changes in blood pressure and evaluating the associated reflex changes in HR or its reciprocal, HP.

![Graph showing the gain in baroreflex sensitivity (ΔHP/ΔMAP) before and after ethanol ingestion.](image)

Fig. 4. Gain in baroreflex sensitivity (ΔHP/ΔMAP) obtained before (○) and after (□) ethanol ingestion (doses are shown at top of each panel). The results shown are means ± se and represent the averages of the five and six steady-state measurements obtained before and after treatments.
Ethanol and baroreflexes

0.5 g/kg \((n = 3)\)

1.0 g/kg \((n = 5)\)

1.5 g/kg \((n = 5)\)

FIG. 5. Steady-state baroreceptor reflex curves relating heart period (HP) to mean arterial pressure (MAP), showing the effects of three doses of ethanol consumed by three groups of normotensive human volunteers. In each sequence, curves were obtained before (open symbols) and after (closed symbols) the particular dose shown at the top of each panel. Larger symbols on each curve are resting values. Results are means ± SE. In each case, the slopes of the linear regression lines before and after treatments were similar (see Table 2). For method and times of constructing the curves see the Methods section.

TABLE 2. Effect of ethanol on median blood pressure (MAP\(_{50}\)), heart period range (HPR) and baroreflex sensitivity (slope of the regression line)

<table>
<thead>
<tr>
<th>Ethanol (g/kg)</th>
<th>MAP(_{50}) (mmHg)</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>After</td>
<td></td>
</tr>
<tr>
<td>0.5</td>
<td>94.0 ± 3.6</td>
<td>+6.4 ± 1.2*</td>
</tr>
<tr>
<td>1.0</td>
<td>103.1 ± 4.9</td>
<td>+11.6 ± 3.2*</td>
</tr>
<tr>
<td>1.5</td>
<td>99.9 ± 4.3</td>
<td>+13.6 ± 4.1*</td>
</tr>
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<table>
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<tr>
<th>HPR (ms)</th>
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<tbody>
<tr>
<td>Before</td>
</tr>
<tr>
<td>0.5</td>
</tr>
<tr>
<td>1.0</td>
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<tr>
<td>1.5</td>
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<table>
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<tr>
<th>Slope (ms/mmHg)</th>
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<tbody>
<tr>
<td>Before</td>
</tr>
<tr>
<td>0.5</td>
</tr>
<tr>
<td>1.0</td>
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<td>1.5</td>
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Since blood pressure and HR were determined by intra-arterial recording, the results of this study as regards the acute effects of ethanol on blood pressure and HR should be more accurate than those obtained by indirect recording.

Previous findings have shown that HR is consistently increased after alcohol [9, 21], whereas blood pressure has been reported to be unchanged [9] or slightly increased [21]. Our findings support the view that acute ethanol causes an increase in HR but does not affect blood pressure. The only time blood pressure was increased after ethanol was at 10 min after the highest dose; this increase was small and short lived (Fig. 1), and may have been a
non-specific effect associated with the high dose of ethanol. Ireland et al. [21] have reported a small and short lived increase in systolic pressure in response to acute ethanol ingestion in normotensive human subjects. That the small rise in blood pressure in our study and in that of Ireland et al. [21], preceded, and subsided before, the blood ethanol concentration reached its peak, suggests this effect may not be alcohol mediated.

The fact that blood pressure was not altered by ethanol was important to establish since it allowed us to be assured that all measurements of baroreceptor HR response were made in the presence of a stable blood pressure. In the first part of our study, using the ramp method, we were clearly able to show that baseline arterial pressure was not changed throughout the experimental post ethanol period. However, the protocol in the second experiment, the steady state procedure, did not allow us to determine this as accurately. Nonetheless, since baseline MAP at 10 min after ethanol and at the end of the experiment was similar to pre-ethanol levels and since 80% of the subjects were the same in both parts of the study and received the same dose of alcohol in both parts, we feel confident that baseline MAP was not changed in either experiment.

The doses of ethanol used produced blood alcohol levels comparable with those which are encountered during social drinking. Signs of intoxication were observed in two of the five subjects who

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**Fig. 6.** Relationship between elevations in median blood pressure (MAP_{50}) and blood ethanol concentration obtained in 13 normotensive human volunteers. The correlation is significant ($r = 0.66$) and has a slope of 8, indicating that for every 1 mg/ml rise in blood ethanol concentration, MAP_{50} will be elevated 8 mmHg.

**Fig. 7.** Phenylephrine dose-pressor response relationship before and after ethanol. Pre-ethanol responses were similar in the three groups. Phenylephrine was given as a bolus injection. The increases in mean arterial pressure (MAP) were always greater after ethanol for a given dose of phenylephrine but there was no dose-related effect for ethanol on the increase in pressor responsiveness. Results are expressed as means ± se. Doses of ethanol are shown at the top of each panel and the number of subjects in each group is given in parentheses.
received the dose of 1.5 g/kg. These were limited to slight ataxia and mild euphoria.

The present findings clearly show that, regardless of the method used to evaluate baroreceptor function, acute ethanol administration produced an attenuation of arterial baroreceptor function. However, qualitative differences were noted between the two experiments which were most likely related to the methods used to elevate blood pressure. In the ramp method ethanol produced a dose related impairment of baroreflex sensitivity (Fig. 2) which was significantly correlated with blood ethanol concentration (Fig. 3). On the other hand, when the method of steady state elevation of blood pressure was used, impairment of baroreflex control of HR was not noted (Fig. 4). Instead the baroreflex curves were reset about a significantly higher median blood pressure (MAP_50) suggesting that the baroreceptors would be operative at a higher pressure after ethanol. This resetting was also related to blood ethanol concentration (Fig. 6) in such a way that for every increase of 1 mg/ml in blood alcohol concentration MAP_50 will increase approximately 8 mmHg.

Our baseline values and the properties of the baroreflex curves measured under steady state conditions agree well with those reported by Korner et al. [14], the first to use this procedure in humans. The subjects in both studies were normotensive and of the same average age. Starting from similar baseline MAP (89±2 vs 92±2.5 mmHg) and HP (944±64 vs 904±39 ms) values, and using phenylephrine as a pressor agent, the baroreflex (MAP–HP) curves in the two studies had very similar properties. The average gain in our study (39±7.4 ms/mmHg) calculated according to the method of Korner et al. [14] was very similar to that reported by these authors (41±5 ms/mmHg). Furthermore, the MAP_50 (98±2 mmHg) and HPR (419±35 ms) obtained in our study compare very well with those of the Korner et al. study calculated from that part of the baroreflex curve which deals with the increments in MAP (MAP_50, 95 mmHg; HPR, 350 ms). These comparisons demonstrate the validity of our baseline steady state data.

The HR response to phenylephrine-evoked increases in blood pressure is entirely reflex in origin since it may be abolished by cardiac autonomic blockade [22, 23]. In animals the reflex HR response is mediated mainly through arterial baroreceptors with only minor contributions from cardiopulmonary receptors [11, 23]. Studies, using the same techniques as in this report, have shown that baroreflex mediated bradycardia is due to an increased vagal and a decreased sympathetic outflow [10]. In the ramp method the HR response at the onset of the pressure change is thought to be due solely to changes in vagal outflow with the sympathetic contribution beginning shortly afterwards [24–26]. In fact, our finding that the gain of the HR response was significantly higher in the ramp versus the steady state method, 40±5 vs 17.2±1.2 ms/mmHg, is consistent with this view. Korner et al. [14] have concluded that impairment of the vagal component of the baroreceptor HR response would be most evident during rapid (ramp) rises in blood pressure. Indeed this may be an important factor in explaining the different effects of ethanol on baroreceptor HR response which we showed to be dependent, at least in part,

FIG. 8. Dose–pressor response curves relating peak elevations in mean arterial pressure (MAP) to the rate of phenylephrine infusion before (open symbols) and after (filled symbols) ingestion of ethanol in three groups of normotensive human volunteers; doses of ethanol are shown at the top of each panel and the number of subjects in each group is given in parentheses. Results are expressed as means ± se.
on the method used to evoke arterial pressure increases.

Our findings that the pressor responsiveness to phenylephrine was enhanced by acute ethanol administration is consistent with the inverse relationship which exists between baroreceptor sensitivity and pressor responsiveness [15]. Since this effect was only observed when arterial pressure was elevated by the ramp method (compare Figs. 7 and 8), it seems likely this inverse relationship is present when impairment rather than resetting of baroreceptors is involved. Ethanol may also have a direct as well as an indirect effect on pressor responsiveness since we have previously shown in the rat that ethanol, per se, has an α-blocking like activity [7]. If this also occurs in humans it should act opposite to the indirectly enhanced pressor responsiveness and may explain, at least in part, the absence of a dose related increase in pressor responsiveness in spite of an attenuation of baroreceptor function.

References