Effect of Alcohol on Vagal Regulation of Cardiovascular Function:
Contributions of the Polyvagal Theory to the Psychophysiology of Alcohol

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Research was conducted to evaluate the influence of acute alcohol consumption on vagal regulation of heart rate. Nine men with histories of polydrug use participated in this residential study. On 5 separate days, they drank liquids consisting of cold water (on 2 days), a moderate dose of alcohol (0.64 g/kg), a high dose of alcohol (1.12 g/kg), and a placebo. Continuous recordings of heart period were quantified to produce 3 measures of heart rate variability, reflecting the amplitude of 3 neurophysiologically mediated rhythms. Heart period, respiratory rhythm (i.e., respiratory sinus arrhythmia [RSA]), and the 0.06–0.10-Hz vasomotor rhythm were significantly lowered during the high alcohol dose condition, relative to the placebo and water conditions. Because the neural regulation of the heart by the vagus contributes to these variables, these findings suggest that alcohol reduces cardiac vagal tone. In support of this explanation, alcohol also decreased the coupling between changes in heart period and changes in RSA. This study demonstrated that alcohol produces a dysregulated state in which heart rate is relatively uncoupled from vagal activity.

Alcohol is a drug with a broad array of physiological and behavioral effects. The acute cardiovascular effects of alcohol include tachycardia, dampening of the cardiovascular response to a discrete stressor (e.g., Levenson, Sher, Grossman, Newman, & Newlin, 1990; Sayette, 1993), and reduction of heart rate variability (Newlin, Byrne, & Porges, 1990; Weise, Krell, & Brinkhoff, 1986). It is unclear which of the diverse acute effects of alcohol, including cardiovascular effects, are related to the abuse potential and addictive properties of the drug. In terms of chronic cardiovascular effects, prolonged alcohol consumption may describe a J-shaped function in which moderate use of alcohol appears to have beneficial effects on the heart, whereas heavy use has predominantly deleterious consequences (Secretary of Health and Human Services, 1990). The precise pharmacological effects of alcohol that contribute to this nonlinear relationship have not been identified. Finally, the relationship between acute and chronic cardiovascular effects of alcohol remains fertile ground for research.

Newlin (1992, 1995) proposed that factors that are common to a broad array of different abused drugs have direct implications for the addictive mechanisms of these compounds. For example, most drugs of abuse are readily self-administered by animals that are naive to the drugs (e.g., Pickens & Thompson, 1968). In humans, many abused drugs produce short-term decreases in global brain metabolism, as measured with positron emission tomography (Newlin, 1992). Most abused drugs that are administered acutely increase locomotor activity in rodents, a common effect thought to reflect the activation of mesocorticolimbic dopamine circuits (Wise & Bozarth, 1987). Low-dose locomotor activation is viewed as a strong correlate but not a direct cause of abuse (Wise & Bozarth, 1987).

Evidence that alcohol (Newlin et al., 1990), cocaine (Newlin, 1995), and several other abused drugs (Newlin, 1992) decrease cardiac vagal tone suggests that this acute cardiovascular effect represents activation of a final common pathway that reflects, rather than causes, the abuse liability of these drugs. Thus, decreased cardiac vagal tone may result from activation of output circuits downstream from dopaminergic midbrain systems that are intimately involved in drug-induced reward and reinforcement. Therefore, it is important to understand the neurophysiological link between the higher nervous system structures that regulate the psychological and behavioral processes that are vulnerable to alcohol and the acute cardiovascular effects of the drug. To the extent that withdrawal of vagal control of the heart is a common factor among drugs of abuse, the depression of cardiac vagal tone might be used as an index of their abuse liability and may shed light on the addictive properties of these drugs.

Porges (1995) proposed the polyvagal theory, in which cardiovascular physiology plays an important role in the regulation of adaptive behaviors, ranging from prosocial behaviors to fear responses. The vagus is a cranial nerve that...
conveys neural influences from the brain stem to the heart's pacemaker (i.e., the sinoatrial node). When vagal tone is increased, heart rate slows. When vagal tone is reduced, heart rate increases. According to the polyvagal theory, vagal output to the heart originates in two different brain stem nuclei: the dorsal motor nucleus of the vagus and the nucleus ambiguus. Via unmyelinated afferent pathways, the output of the dorsal motor nucleus of the vagus influences heart rate level. In contrast, via myelinated afferent pathways, the output of the nucleus ambiguous influences heart rate level and components of heart rate variability. Because the output of vagal fibers from the nucleus ambiguous has a respiratory rhythm, shifts in the neural output of the vagal pathways originating in the nucleus ambiguous have a direct measurable effect on the respiratory component of heart rate variability. This effect is observed as a change in the amplitude of the periodic increases and decreases in heart rate associated with spontaneous breathing, a phenomenon known as respiratory sinus arrhythmia (RSA). In humans, the primary vagal control of heart rate is determined by nucleus ambiguous pathways. Therefore, it is possible to monitor a dimension of cardiac vagal tone by quantifying the amplitude of RSA.

The polyvagal theory (Porges, 1995) emphasizes the importance of regulating cardiac output (i.e., a function of heart rate and stroke volume) through vagal effector pathways to support the changing metabolic demands (e.g., oxygen consumption) associated with behavioral responses to environmental challenges. The analogy that is made is that of a "vagal brake," which is applied in situations characterized by low metabolic demands to reduce cardiac output and facilitate homeostatic processes. Alternatively, the vagal brake may be withdrawn in times of high metabolic demands to increase cardiac output and to support, for instance, fight-or-flight behaviors (Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996). The polyvagal theory also emphasizes a view of the vagal system as part of a feedback loop in which the central nervous system (CNS) regulates cardiac output via vagal effector pathways and monitors cardiac output via vagal afferent pathways. Thus, the ability to regulate cardiac output by the vagal system is essential for optimal behavioral regulation, and failure or deficits of this system are potential sources of behavioral dysregulation.

Vagal regulation of cardiac output contributes to humans' ability to regulate behavior (e.g., level of performance or responses to stress), and there is a documented decrease in vagal output to the heart in response to alcohol (Newlin et al., 1990). We hypothesized that the alcohol-related decrease in vagal control of the heart may contribute to the dysregulated neurophysiological states produced by the drug. This question may be addressed by investigating whether alcohol compromises the ability of the vagal system to regulate changes in heart rate, in addition to the influence of alcohol on the level of vagal tone.

In previous research, the efficiency of the vagal brake has been evaluated as a shift in the regression slope between simultaneously measured measures of heart rate level and RSA (Porges, Doussard-Roosevelt, Stifter, McClenney, & Riniolo, 1999). When the vagal brake is functioning efficiently, slight withdrawals and reengagements of the brake, measured by changes in RSA, are associated with stronger coupling (indicated by steeper regression slopes and higher correlations) of simultaneously measured RSA and heart rate.

On the basis of the previous research and theory, we conducted this research (a) to replicate Newlin et al.'s (1990) results demonstrating that alcohol reduces vagal tone in human participants with an entirely within-subjects design and higher doses of alcohol (0.64 and 1.10 g/kg body weight); (b) to evaluate whether this effect is dependent on the dose of alcohol; (c) to determine whether this effect is specific to the RSA frequency band (i.e., to determine whether alcohol also reduces heart rate variability at lower frequencies than RSA); and (d) most important, to apply the polyvagal theory (Porges, 1995) to interpret the effect of alcohol on heart rate by using a newly developed measure of vagal–cardiac coupling (Porges et al., 1999) to assess the efficiency of the vagal brake.

This study was conducted to evaluate the influence of acute alcohol consumption on the efficiency of the vagal brake. Because the amplitude of RSA is the functional output of vagal pathways originating in the nucleus ambiguus, cardiac vagal tone may be assessed by quantifying RSA. Specifically, we hypothesized that alcohol would decrease the efficiency of the vagal brake and, thus, would contribute to difficulties in the regulation of psychological and behavioral adaptive processes. Hypothetically, the decrement in efficiency of the vagal brake, by promoting a physiologically based state characterized by a loss of control, may contribute to the rewarding characteristics of the drug.

Method

Participants

Nine men between 24 and 42 years of age participated in this study. Their mean age was 30.4 years. Seven participants were black and 2 were of European descent. Their mean body weight was 80.5 kg (range = 60.5–102.3 kg). Six (67%) of the participants were chronic cigarette smokers. On intake into the study, the participants showed no evidence of Diagnostic and Statistical Manual of Mental Disorders (3rd ed., rev.; American Psychiatric Association, 1987) Axis I disorders other than substance abuse disorders. The participants had no serious medical conditions that required medication.

The participants were selected because they reported extensive histories of using both alcohol and cocaine but were not seeking treatment. They were housed for the duration of the study on an inpatient residential ward dedicated to research on drug abuse. They had no access to drugs other than caffeine and nicotine (cigarettes) for several days before and during the study. During the study (which lasted about 2 weeks), they received only the alcohol that was provided as part of this experiment. The participants were not allowed to smoke during each actual study session. The Institutional Review Board of the Frances Scott Key Medical Center approved this protocol.

Apparatus

The computerized psychophysiology laboratory used a Grass alternating-current bioelectric amplifier (Grass Instruments; Astro-Med, Inc., West Warwick, RI) for the electrocardiogram (ECG) and a Compaq 386 microcomputer with an intelligent (microprocessor-
based analog–digital conversion board (Microstar Laboratories, Bellevue, WA). This board was programmed to measure and store successive interbeat intervals (milliseconds between successive R waves on the ECG), which are the reciprocals of heart rate (in beats per minute). Timing accuracy of R–R intervals was 1 ms. Instructions to the participant (e.g., to “rest comfortably” or to “drink the beverage now”) were displayed on a computer terminal in a sound-attenuated chamber in which the participant sat in a comfortable armchair. All other equipment was located outside of this chamber. Disposable electrodes were attached to the skin over the ribs on each side of the participant’s chest in a bipolar configuration. Other psychophysiological and subjective measures (e.g., “craving” for cocaine on a visual–analog scale) were recorded but are not reported here.

Procedure

The heart-period data analyzed in this study were collected as part of a larger study carried out by researchers at the Addiction Research Center of the National Institute on Drug Abuse (Newlin, 1992). The main purpose of the study from which the present data were obtained was to investigate the ways in which drinking alcohol interacts with responses to stimuli associated with cocaine in cocaine abusers.

The design of the experiment was entirely within subjects, with each participant receiving all conditions. Participants were in the laboratory on 5 alternate days (usually Monday, Wednesday, and Friday, depending on scheduling, but always at least 48 hr apart) and received a different condition on each day. The 1st day was used to familiarize the participants with the procedures of the study. All participants received water to drink in the amount calculated to body weight. On all 5 study days, participants were asked to first eat a light lunch at approximately 11 a.m. At 1 p.m., participants were instructed to drink a beverage containing some undisclosed amount of alcohol or water. The conditions were a moderate dose of alcohol (0.64 g/kg body weight), a high dose of alcohol (1.12 g/kg), placebo, and distilled (cold) water (used during 2 of the 5 study sessions) in a volume equal to the mixed drink. Water was administered during the first session. During the subsequent four sessions, water, placebo, moderate alcohol, and high alcohol were administered in pseudorandom order such that there was no preponderance of any one order for the four conditions. Participants were instructed that all beverages (including placebo) except water contained alcohol. The alcoholic drinks consisted of Smirnoff’s 100 Proof Vodka and cold Canada Dry Sugar Free Tonic Water. The placebo drink consisted of the tonic water, equal in volume to the mixed drink, with a small amount of vodka placed on the rim of the glass to disguise the placebo.

Each session lasted approximately 120 min, during which heart rate and skin temperature were measured from the surface of the skin. Participants were not allowed to smoke during the experiment. They were required to rest for at least 10 min before physiological monitoring. After this rest period and before the participants drank the fluids, physiological activity was monitored during three 5-min baseline trials. The participants were then required to drink the fluids during three 5-min trials. Following the fluid consumption, physiological activity was monitored for fifteen 5-min trials. The total time of the experiment was slightly longer than the sum of these trials because there were variable-length periods between trials, during which data were saved.

Data Analysis

Heart period and RSA were calculated from ECG recordings and quantified in sequential 30-s epochs. Heart period was calculated as the mean of all heart-period values within each 30-s epoch. RSA was calculated with edit software (Porges, 1996). MXedit uses the Porges method (Porges, 1985), which quantifies RSA in adult participants from a heart-period time series and includes the following steps: (a) The heart-period data are resampled every 500 ms, (b) a 21-point moving cubic polynomial filter is stepped through the time-sampled series to produce a smooth template series, (c) the template series is subtracted from the original series to produce a residual time series, (d) a digital band-pass filter with 25 coefficients is stepped through the residual series to extract variance in the 0.12–0.40-Hz frequency band, and (e) the remaining variance is transformed by its natural logarithm and used as a measure of RSA. The smoothing techniques contained in these steps function to remove variance in the heart-period data with frequency characteristics that fall outside of the frequency band of spontaneous respiration, allowing for accurate quantification of the amplitude of RSA.

Mean values for heart period and RSA were calculated for the ten 30-s epochs within each 5-min trial. The entire experimental session, including the 15-min predrink baseline, consisted of twenty-one 5-min trials. In addition, a new measure of RSA–heart-period coupling (see Porges et al., 1999) was generated from the regression of trial-by-trial values of RSA and heart period. Coupling was measured in terms of the correlation coefficient and slope values produced by regressing trial means for RSA (N = 15) onto trial means for heart period (N = 15). In addition, the Traube–Hering–Meyer (THM) rhythmicity—a measure related to baroreceptor feedback (Hatch, Klett, Porges, Schroeder-Jaschewski, & Supik, 1986; Hayano et al., 1990; Penaz, 1978)—and the presumed angiotensin-resin-mediated vasomotor (AVR) rhythmicity—a measure assumed to be influenced by the peripheral vascular system resulting from angiotensin control (Akselrod et al., 1985; Hyde & Izard, 1997)—were calculated. These rhythms were calculated with the same methods as those used to quantify RSA, by modifying the filter coefficients to pass frequencies only between 0.06 and 0.10 Hz for THM and between 0.02 and 0.06 Hz for AVR.

We calculated repeated measures analyses of variance (ANOVA) to determine the effect of time (i.e., trial) and treatment condition on heart period and RSA and to evaluate the treatments relative to pretreatment baseline on heart period and the three measures of heart-period rhythmicity. These analyses were based on the difference between the 15 min of baseline (i.e., the mean of the six 5-min trials before drinking) and the mean of Trials 7–16 (the period when the pharmacological effect of alcohol should be most apparent).

In addition, to determine whether the known influences of alcohol on heart rate are mediated by vagal influences, we calculated analyses of covariance (ANCOVAs) using the changes in RSA and the coupling between heart period and RSA as covariates. We used Greenhouse–Geisser (Greenhouse & Geisser, 1959) corrections for univariate repeated measures to adjust for possible violations of the constant covariance assumption required for repeated measures ANOVAs. We used Systat (Wilkinson, 1998) for statistical analyses, and we adopted an alpha level of p < 0.05 for rejecting null hypotheses.

Results

As illustrated in Figure 1, heart period and RSA were sensitive to both the alcohol manipulation and the time experienced in the experimental environment. The significant condition effects for heart period, F(3, 24) = 6.6, p < .01, and RSA, F(3, 24) = 7.9, p < .01, support the observed level of difference between the alcohol and the nonalcohol treatments in heart period and RSA. Moreover, the signifi-
significant trial effects illustrate the natural adaptation across trials within each session as the participants habituated to the laboratory environment on each day of the experiment. Note that in Figure 1 the significant Treatment × Trial interactions for heart period, $F(51, 408) = 2.9, p < .001$, and RSA, $F(51, 408) = 3.1, p < .001$, are represented by a gradual increase (suggesting increased vagal influence) across trials in the water and placebo conditions and that administration of alcohol at both doses inhibited these increases.

The primary focus of this study was to evaluate the differential sensitivity of the physiological measures to the treatment conditions. To evaluate this question, the change from baseline to time of maximum pharmacological effect of alcohol was evaluated for each variable during each treatment condition. Figure 2 displays the means and the standard errors for each of these dependent variables. Repeated measures ANOVAs were then calculated to determine treatment effects. If a significant treatment effect was identified, contrasts between the treatment conditions were calculated.

**Heart Period**

The treatment effect was statistically significant, $F(3, 24) = 7.8, p < .005$. Both the high dose, $F(1, 8) = 26.5, p < .001$, and the low dose, $F(1, 8) = 12.9, p < .007$, of alcohol,
compared with placebo, were associated with lower heart period. However, the effect of the high dose did not differ from the effect of the low dose, nor did the placebo and water sessions differ from each other.

Table 1

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Slope</th>
<th>Pearson’s $r$</th>
<th>Pearson’s $r$ (z transform)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High alcohol</td>
<td>10.3</td>
<td>.16</td>
<td>.19</td>
</tr>
<tr>
<td></td>
<td>(30.1)</td>
<td>(.39)</td>
<td>(.43)</td>
</tr>
<tr>
<td>Low alcohol</td>
<td>21.9</td>
<td>.33</td>
<td>.46</td>
</tr>
<tr>
<td></td>
<td>(30.6)</td>
<td>(.40)</td>
<td>(.61)</td>
</tr>
<tr>
<td>Placebo</td>
<td>55.2</td>
<td>.46</td>
<td>.64</td>
</tr>
<tr>
<td></td>
<td>(60.4)</td>
<td>(.46)</td>
<td>(.66)</td>
</tr>
<tr>
<td>Water</td>
<td>57.7</td>
<td>.55</td>
<td>.81</td>
</tr>
<tr>
<td></td>
<td>(33.8)</td>
<td>(.32)</td>
<td>(.65)</td>
</tr>
</tbody>
</table>

Note. $N = 9$ for all conditions. Standard deviations are in parentheses.

*Milliseconds per vagal tone unit.

Respiratory Sinus Arrhythmia (RSA)

Analyses of RSA yielded similar results. The effect of treatment was significant, $F(3, 24) = 9.6, p < .001$. The high dose of alcohol was associated with significantly, $F(1, 8) = 10.8, p < .01$, lower RSA compared with placebo. The difference in level of RSA during the low-dose alcohol condition compared with placebo, although in the same direction, only approached significance, $F(1, 8) = 4.5, p < .07$. Similar to the heart-period data reported earlier, comparisons between high and low doses and between placebo and water were not significant.

Traube–Hering–Meyer Rhythmicity (THM)

The effect of treatment on THM rhythmicity was significant, $F(3, 24) = 11.1, p < .001$; both high, $F(1, 8) = 5.6, p < .017$, and low, $F(1, 8) = 7.5, p < .025$, doses of alcohol were associated with lower THM rhythmicity relative to placebo, and placebo resulted in significantly lower THM rhythmicity compared with water, $F(1, 8) = 5.6, p < .05$.

Angiotensin–Resin-Mediated Vasomotor Rhythmicity

The effect of treatment was not significant for ARV rhythmicity.

Coupling

The functional impact of alcohol on the vagal control of heart rate was assessed by the degree of coupling between heart period and RSA across trials. Differences in the degree of coupling between conditions were analyzed to assess the effects of alcohol on the vagal control of heart rate. Coupling was measured in terms of the slope and the correlation generated from the regression of heart period on RSA. Means for slope and correlation values are presented in Table 1. There was a significant effect of treatment on slope, $F(3, 24) = 6.98, p < .01$ (see Table 1). Pairwise comparisons (Table 2) showed slope to be significantly higher during the placebo and water conditions compared with the high-dose and low-dose alcohol conditions. Similarly, the covariation between heart rate and RSA measured by correlation...
was significantly influenced by treatment (see Table 1). Pairwise comparisons (Table 3) showed a lower correlation in the high-dose alcohol condition than in both the placebo and water conditions. Although alcohol could potentially influence the range of the cardiac variables, and thus the magnitude of the correlation coefficients, according to Cohen and Cohen (1983), distributions of regression line slopes, compared with correlation coefficients, are relatively immune to the influence of range.

To further investigate the relationship between the presumed vagal control of the heart and heart rate reactivity, we performed ANCOVAs to determine whether the effects of alcohol remained significant after controlling for alcohol-induced changes in RSA and in the new metric describing the dynamic vagal influence on heart period (i.e., the coupling between heart period and RSA). These ANCOVAs were comparable to those of Newlin et al. (1990), which demonstrated that the tachycardia from a low dose of alcohol was no longer significant after correcting for the alcohol-induced change in vagal tone (i.e., RSA).

When change in RSA (from baseline to time of maximum pharmacological effect of alcohol) was entered as a covariate, the effect of alcohol on heart period was no longer statistically significant, \( F(3, 21) = 2.5, \) ns. In fact, only 20% of the variance due to condition remained after we controlled for change in RSA. Similarly, the effect of alcohol was reduced to nonsignificance when the coupling between heart period and RSA, measured in terms of slope, was entered as a covariate, \( F(3, 21) = 2.4, \) ns. The variance due to condition was reduced to 28% of its original value after we removed the effects of RSA. Thus, the ANCOVA indicated that the significantly lower heart period associated with alcohol was due substantially to alcohol-induced decreas in vagal activity (i.e., whether indexed by RSA or by the trial-by-trial coupling between heart period and RSA).

The correlation between the alcohol-induced changes in the two vagal indexes was moderate (RSA vs. slope: \( r = .74 \)). Therefore, the vagal indexes were not entirely redundant with each other despite showing parallel effects from alcohol.

## Discussion

Alcohol influenced the pattern of heart period and RSA during the experimental session. As illustrated in Figure 1, both alcohol treatments blocked the adaptive slowing of heart rate (i.e., increases in heart period) and the increases in RSA that were clearly observable during the placebo and water treatments. These findings, in conjunction with the observed decrease in the coupling between RSA and heart period, confirm that alcohol influences the vagal regulation of the heart. Additional support for this proposed alcohol-induced inhibition of vagal control of the heart was obtained from the ANCOVAs, which indicated that when the alcohol-induced changes in RSA or the RSA-heart-period coupling were used as covariates, the heart-period pattern during the alcohol treatments was no longer statistically different than that in the water and placebo treatments. Although these findings are consistent with those reported by Newlin et al. (1990), the present study used a more powerful within-subjects experimental design and included manipulations with higher doses of alcohol and additional measures of heart rate variability as indexes of neural regulation of the heart (i.e., RSA, THM, ARV, and coupling).

Consistent with the aforementioned findings of a selective alcohol-induced inhibition of vagal control of the heart, alcohol was associated with decreased THM but did not influence ARV. It is accepted in the literature that THM, being a manifestation of a baroreceptor feedback loop, has a substantial vagal component (Bernstorf et al., 1997). Research has demonstrated (Goddard, Porges, Fleg, & Wright, 1995; Jokkel, Bonyhay, & Kollai, 1995) that THM, similar to RSA, is sensitive to atropine. Because atropine blocks the transmission of acetylcholine, the neurotransmitter of vagal effector fibers, these data support the assumption that both RSA and THM are mediated primarily by vagal fibers. The neural contributions to rhythms slower than THM are not well understood.

Although previous research by Newlin et al. (1990) documented similar reductions in RSA, the present study assessed more directly the functional significance of these changes on heart rate regulation. The results support the

### Table 2

**All Pairwise Multiple-Comparison Procedures for Slope Analysis (Student Newman–Keuls Method)**

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Difference of means</th>
<th>( p^a )</th>
<th>( q^b )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water vs. high</td>
<td>47.35*</td>
<td>4</td>
<td>5.27</td>
</tr>
<tr>
<td>Placebo vs. high</td>
<td>44.85*</td>
<td>3</td>
<td>4.99</td>
</tr>
<tr>
<td>Water vs. low</td>
<td>35.73*</td>
<td>3</td>
<td>3.97</td>
</tr>
<tr>
<td>Placebo vs. low</td>
<td>33.23*</td>
<td>2</td>
<td>3.70</td>
</tr>
<tr>
<td>Low vs. high</td>
<td>11.62</td>
<td>2</td>
<td>1.29</td>
</tr>
<tr>
<td>Water vs. placebo</td>
<td>2.50</td>
<td>2</td>
<td>0.28</td>
</tr>
</tbody>
</table>

*Note. high = high-dose alcohol condition; low = low-dose alcohol condition.

*aNumber of means spanned in the comparison. *bStudent Newman–Keuls test statistic.

\( *p < .05. \)

### Table 3

**All Pairwise Multiple-Comparison Procedures for Correlation Analysis (Student Newman–Keuls Method)**

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Difference of means</th>
<th>( p^a )</th>
<th>( q^b )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water vs. high</td>
<td>.62*</td>
<td>4</td>
<td>5.88</td>
</tr>
<tr>
<td>Placebo vs. high</td>
<td>.45*</td>
<td>3</td>
<td>4.26</td>
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<tr>
<td>Water vs. low</td>
<td>.35</td>
<td>3</td>
<td>3.33</td>
</tr>
<tr>
<td>Low vs. high</td>
<td>.27</td>
<td>2</td>
<td>2.55</td>
</tr>
<tr>
<td>Placebo vs. low</td>
<td>.18</td>
<td>2</td>
<td>1.71</td>
</tr>
<tr>
<td>Water vs. placebo</td>
<td>.17</td>
<td>2</td>
<td>1.62</td>
</tr>
</tbody>
</table>

*Note. high = high-dose alcohol condition; low = low-dose alcohol condition.

*aNumber of means spanned in the comparison. *bStudent Newman–Keuls test statistic.

\( *p < .05. \)
hypothesis that alcohol consumption leads to a relatively specific reduction in the neural regulation of heart rate by vagal pathways. By examining the slope of the regression of heart period onto RSA, we were able to estimate the magnitude of the change in heart period associated with a unit change in RSA. By examining the correlation between heart period and RSA, we were able to estimate the amount of variance in heart period that could be accounted for by changes in RSA. The results showed that the magnitude of change in heart period associated with a unit change in RSA decreased significantly with alcohol. For example, during the water and placebo conditions, a unit change in vagal tone (natural logarithm of milliseconds squared) resulted, on average, in a change of more than 50 ms in heart period. For an individual with a basal heart rate of 70 beats per minute, a 50-ms reduction in heart period would result in a heart rate of approximately 74 beats per minute. In contrast, during the high dose of alcohol, a unit change in vagal tone resulted in only a 10-ms shift in heart period. The correlation coefficients illustrated that the impact of vagal influences on the dynamic shift in heart period was significantly reduced during the alcohol conditions. On average, 30% of the variance in heart period was accounted for by changes in RSA during the water treatment, whereas less than 3% of the variance was accounted for during the high dose of alcohol. These results support the conclusion that the regulation of heart rate by vagal pathways was compromised during the alcohol manipulations. It is important to note that the alcohol did not eliminate the vagal influence on the heart but appears to have resulted in a more selective deficit in the regulation of heart rate. This deficit in vagal regulation may be observed by contrasting the alcohol treatments with the water and placebo treatments. In response to alcohol, the coupling between RSA and heart period was significantly depressed, and the normal adaptive recovery of heart period and RSA observed during the water and placebo treatments was blocked.

The importance of vagal regulation in prosocial behavior has been introduced by Porges in his polyvagal theory (Porges, 1995, 1998; Porges et al., 1996, 1999). The polyvagal theory (Porges, 1995, 1998) describes the evolution of a mammalian system for regulating behavior that relies on efficient and finely tuned modulation of cardiac output. According to the polyvagal theory, the neural regulation of the heart by the vagus functions as a brake to modulate metabolic output during periods of social engagement. When the regulation of the heart by vagal mechanisms is inefficient (Porges et al., 1996), behavior is less social and potentially more aggressive (see Porges, 1998). According to the polyvagal theory, the neural regulation of the heart by the vagal pathways reflects an output system that originates in frontal areas of the cortex and monosynaptically regulates medullary nuclei, such as the source nucleus of the chronotropic control of the heart (i.e., nucleus ambiguus), by corticobulbar pathways. As part of a social engagement system (Porges, 1998), this system is integrated with the corticobulbar regulation of components of the cranial nerves that modulate the striatal muscles of the head, which determine facial expressions as well as looking, listening, vocalizing, and ingestive behaviors.

On the basis of the polyvagal theory, behavioral dysregulation occurs when this support system is compromised (Porges et al., 1996). Therefore, the behavioral dysregulation that results from acute alcohol intake (e.g., social incompetence, impaired performance, aggression) may be indexed by the cardiac dysregulation that results when short-term variations in heart rate are no longer controlled by the vagal pathways that typically make subtle adjustments to the system. Our data demonstrated this alcohol-related loss in vagal control of heart rate by documenting a decoupling between heart period and RSA. Thus, the vagal regulation of the heart may provide a sensitive index of the debilitative influences of alcohol and other substances on the neural system that regulates prosocial behavior.

The withdrawal of vagal control of heart rate observed in response to alcohol must be understood in relation to the effect of other drugs (Newlin, 1995). Acute cocaine and other abused drugs (Newlin, 1992, 1995; Newlin, Wong, & Cheskin, 1992) have the common feature of producing tachycardia with reduced RSA. We hypothesize that this common factor reflects disruption of CNS integrity (i.e., loss of cortical regulation of the brain stem by corticobulbar pathways) or functioning of the nucleus accumbens from abused drugs, in much the same way that the common factor of low-dose locomotor activation from abused drugs reflects activation of mesolimbic dopamine systems in the midbrain (Wise & Bozarth, 1987) and deficits in the corticospinal regulation of movement. Furthermore, we propose that the organismic counterresponse to this disruption of CNS integrity (the latter indexed by withdrawal of vagal tone) may play a role in the etiology of drug addiction, as discussed by Poulos and Cappell (1991) and Ramsay and Woods (1997).

The results of this study have implications for the cardiovascular effects of chronic alcohol consumption. Recent evidence (Liao et al., 1997) from a 3-year prospective study has linked low RSA amplitude in healthy individuals to increased risk of subsequent coronary heart disease. It is possible that the decreased RSA observed in response to acute alcohol intake may suggest a mechanism for the decreased RSA observed in chronic alcoholics (Weise et al., 1986).

Three important limitations of this study are the absence of dose dependency (the low and high doses of alcohol produced similar cardiovascular responses), the lack of significant differences between the water and placebo conditions, and the issue of declining cardiovascular function in the two control conditions (water and placebo). We were unable to account for the lack of dose dependency, although this sample was a cocaine-abusing group, which may have altered cardiovascular dynamics. A ceiling effect is also a plausible interpretation.

The absence of an effect of placebo could have been due to (a) ineffective placebo manipulation, (b) some characteristic of this drug-abusing population that would mitigate
against placebo responding, or (c) a floor effect in which cardiovascular function could not decrease further. There was no significant placebo effect (difference from water ingestion) in the earlier study (Newlin et al., 1990).

Finally, the question may be raised of whether alcohol increased cardiovascular function, or merely prevented the decrease from water and placebo. Given the large literature indicating that alcohol increases heart rate (Levenson et al., 1980), we conclude that alcohol increased cardiovascular function and that the high baselines only made it appear that alcohol prevented declines from water and placebo. However, the latter interpretation cannot be ruled out definitively with the present data.

Future research should include behavioral and performance measures with the psychophysiological measures assessed in this study. In addition, although there is no research to suggest that the effects of alcohol on vagal regulation of the heart are specific to the clinical population used in this study, the generalizability of these findings could be increased by replication in a nonclinical population.

Although this study clearly implicates the effect of alcohol on the vagal regulation of the heart, measures of sympathetic activity are needed to complete the model. Perhaps the inability to discriminate between the two alcohol doses with the measures of vagal regulation suggests a special role of the sympathetic nervous system in the autonomic and behavioral responses to alcohol. Possibly, as proposed by the polyvagal theory, sympathetic activation, at least to the heart, would be a secondary response occurring after vagal withdrawal, with the magnitude of the sympathetic response determined not only by the amount of alcohol ingested but also by the environmental demands challenging the individual.

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