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A Pilot Study of Brief Heart Rate Variability Biofeedback to Reduce Craving in Young Adult Men Receiving Inpatient Treatment for Substance Use Disorders

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Abstract

The present pilot study investigated the implementation feasibility, and efficacy for reducing alcohol and drug craving, of a brief, 3-session heart rate variability biofeedback (HRV BFB) intervention added to a traditional 28-day substance abuse disorder (SUD) inpatient treatment program. Forty-eight young adult men received either treatment as usual (TAU) plus three sessions of HRV BFB training over three weeks, or TAU only. Participants receiving HRV BFB training were instructed to practice daily using a handheld HRV BFB device. HRV BFB training was well tolerated by participants and supported by treatment staff. Men receiving TAU + HRV BFB demonstrated a greater, medium effect size reduction in alcohol and drug craving compared to those receiving TAU only, although this difference did not reach statistical significance. In addition, an interaction effect was observed in analyses that accounted for baseline craving levels, wherein heart rate variability (HRV) levels at treatment entry were predictive of changes in craving in the TAU group only. Low baseline levels of HRV were associated with increases in craving, whereas higher baseline HRV levels were associated with greater decreases in craving from start to end of treatment. In the TAU + HRV BFB group, however, there was no such association. That is, HRV BFB appeared to dissociate individual differences in baseline HRV levels from changes in craving. Given that alcohol and drug craving often precipitates relapse, HRV BFB merits further study as an adjunct treatment to ameliorate craving experienced by persons with substance use disorders.

Keywords

Heart rate variability biofeedback; substance use disorders; craving

Introduction

Substance use disorders (SUDs) represent a major public health concern, and are resistant to treatment. A number of psychological and pharmacological addiction treatments have demonstrated efficacy, yet maintaining abstinence during and after treatment is a challenge for the majority of clients (O'Brien, 2005). While there are many obstacles to long-term SUD remission, substance craving represents one of the most commonly experienced, and pernicious impediments. In a process known as incentive-salience, many individuals attempting recovery from SUDs experience intense 'wanting' or craving for alcohol and drugs, even after alcohol and drug 'liking' has drastically diminished. Incentive-salience processes are believed to heighten the reward value of substances and their related cues,

leading to drug seeking and use behaviors in spite of minimal hedonic reward, and maximal negative consequences of use (Robinson & Berridge, 1993; Tindell, Smith, Berridge, & Aldridge, 2009).

In addition to playing an important antecedent role in the development and maintenance of SUD related behaviors (Hasin, Fenton, Beseler, Park, & Wall, 2012), craving is a robust predictor of relapse after periods of abstinence (Paliwal, Hyman, & Sinha, 2008; Sinha, 2011). To complicate matters further for the individual striving for abstinence, the disinhibitory psychopharmacological actions of substances of abuse lead to impaired behavioral control, reducing an individual's ability to appropriately manage interoceptive challenges such as craving, amplifying a "vicious cycle" that contributes to the persistent nature of relapse (Berkling et al., 2011; Koob & Le Moal, 2001).

Craving processes, and the specific influence of these processes on SUD treatment outcome, are controlled by integrated brain-body systems (Ingjaldsson, Thayer, & Laberg, 2003; Porges, 2009; Quintana, Guastella, McGregor, Hickie, & Kemp, 2013). Thus, craving can be conceptualized as a biobehavioral phenomenon because it involves integrated psychological and physiological processes, some of which occur in conscious awareness, while others occur outside of conscious awareness (Diamond & Aspinwall, 2003; Forgas, 2008; Gross, 1998; Verheul, van den Brink, & Geerlings, 1999). The conscious components of craving have been well studied (Franken, 2003; Weinstein, Feldtkeller, Law, Myles, & Nutt, 2000), as have associated processes such as thought suppression and reappraisal (Gross, 2002), cognitive restructuring (Andreotti et al., 2011), and rumination (Nolen-Hoeksema, 2012).

Parallel physiological processes, on the other hand, have received less attention, particularly in the context of SUD treatment development. This oversight is unfortunate because adaptive cognitive and affective regulation is heavily mediated by an individual's ability to make moment-to-moment physiological adjustments outside of conscious awareness (Thayer & Lane, 2000, 2009). As such, a flexible autonomic nervous system allows for rapid generation or modulation of physiological states in accordance with situational demands (Porges, 2009; Thayer, Hansen, Saus-Rose, & Johnsen, 2009). The ability for the autonomic nervous system to make rapid fine-grained adjustments to situational demands is perhaps nowhere more evident than in its control of heart rhythm. The physiological phenomenon of heart rate variability (HRV), therefore, reflects the degree to which the autonomic nervous system is adaptively responding to changing situational demands (Appelhans & Luecken, 2006).

Alcohol dependence (Malpas, Whiteside, & Maling, 1991) and chronic drug use (Brody, Krause, Veit, & Rau, 1998) tend to be associated with reduced HRV, as is the expression of craving (Ingjaldsson, Laberg, & Thayer, 2003; Quintana et al., 2013). In addition, previous research has shown that HRV is negatively associated with perseverative thinking, indicating that lower levels of HRV in substance dependent individuals could be related to the level of craving or conscious preoccupation with thoughts of drinking and using drugs (Thayer & Friedman, 2002; Thayer & Lane, 2000; Tiffany, 1990). These findings are consistent with a psychobiological perspective of substance craving which suggests that stimuli and mental representations associated with substance use produce the quality of

incentive salience, and therefore automatically capture the attention of the substance dependent individual (Berridge, 2012).

Taken together, this suggests that SUD treatments may be more effective if they target the problem of craving at multiple psychological and physiological levels. We test here whether heart rate variability biofeedback (HRV BFB), an intervention used previously to reduce substance craving in individuals with post traumatic stress disorder (PTSD; Zucker, Samuelson, Muench, Greenberg, & Gevirtz, 2009), and reduce food craving in high food cravers (Meule, Freund, Skirde, Vögele, & Kübler, 2012), may reduce the experience of craving, compared to treatment as usual (TAU) in individuals seeking inpatient treatment for SUDs.

Mechanism of heart rate variability biofeedback

Maximal increases in the amplitude of heart rate oscillation are produced when the cardiovascular system is rhythmically stimulated by paced breathing at a frequency of about 0.1Hz (6 breaths per minute; Song & Lehrer, 2003; Vaschillo, Lehrer, Rishé, & Konstantinov, 2002). This effect is linked to respiratory sinus arrhythmia and resonance properties of the cardiovascular system resulting from activity of the baroreflex (Vaschillo, Vaschillo, Buckman, Bates, & Pandina, 2010), a closed-loop feedback mechanism responsible for controlling blood pressure fluctuations (Benarroch, 2008). Resonance usually occurs in the low frequency range (Wills et al., 2001), typically between 0.075 and 0.120 Hz, with the average resonance frequency being slightly less than 0.1 Hz, or approximately 5 to 6 breaths per minute (Vaschillo et al., 2002).

HRV BFB has been shown to produce acute and chronic increases in baroreflex gain (Lehrer et al., 2003), and improve symptom severity in disorders characterized by autonomic nervous system dysfunction including asthma (Lehrer et al., 2004), and hypertension (McCraty, Atkinson, & Tomasino, 2003). Other controlled studies suggest it may be a useful intervention for anxiety (Paul & Garg, 2012; Thurber, Bodenhamer-Davis, Johnson, Chesky, & Chandler, 2010; Wells, Outhred, Heathers, Quintana, & Kemp, 2012), and major depression (Karavidas et al., 2007), as well as for ameliorating depressive symptomology in patients with fibromyalgia (Hassett et al., 2007) heart-disease (Nolan et al., 2005), and PTSD (Zucker et al., 2009). Additionally, as mentioned earlier, HRV BFB has shown to reduce substance craving in patients with PTSD (Zucker et al., 2009), as well as food cravings in high food cravers (Meule et al., 2012).

The autonomic pathway by which HRV BFB works is of theoretical interest, but is not entirely clear at this time. One hypothesis is that it increases balance between the sympathetic and parasympathetic branches. HRV BFB produces an interaction between baroreflex and respiratory effects on HRV, both primarily mediated by the parasympathetic system. Although lasting increases in respiratory sinus arrhythmia have not been definitively found, effects on what appears to be the vagal baroreflex (Reyes del Paso, Langewitz, Mulder, Roon, & Duschek, 2013) are significant (Lehrer et al., 2003). During HRV BF, vagally mediated respiratory effects are found in the low-frequency (Lf) range (0.05-0.15 Hz), because people are breathing at this low frequency (Vaschillo, Vaschillo, & Lehrer, 2006). Thus, although Lf HRV has been hypothesized to reflect both sympathetic and

parasympathetic activity, compared to high-frequency (Hf) HRV (0.15 – 0.40 Hz), which is known to be entirely parasympathetically mediated, this interpretation of autonomic balance cannot be made in HRV BFB.

Current study and predictions

Based on HRV BFB's potential to help reduce craving, we posited that this intervention might be an effective complement to traditional SUD treatment. We thus developed and pilot tested a concise HRV BFB protocol designed to be easily delivered concurrently with an intensive 28-day inpatient SUD treatment program. The HRV BFB training was modified from the protocol developed by Lehrer, Vaschillo, and Vaschillo (2000). The adapted protocol included three sessions of HRV BFB training with instructions to practice daily.

The present pilot investigation had two primary goals, 1) To qualitatively test the feasibility (including patients' ability to tolerate the intervention) of providing HRV BFB in addition to treatment as usual (TAU) within the confines of a 28-day inpatient treatment program, and 2) to quantitatively test whether TAU + HRV BFB would affect reductions in alcohol and drug craving more than TAU alone. We predicted TAU+ HRV BFB would be associated with larger decreases in alcohol and drug craving during the course of inpatient treatment compared to TAU alone.

Methods

Participants

All patients at the young adult male unit at a private substance use treatment facility (ages 20–25) who met the inclusion criteria were eligible for participation. Inclusion criteria included a SUD diagnosis, fluency in the English language, at least 72 hours since last use of alcohol or other drugs to guard against acute withdrawal effects, and near 20/20 or corrected vision. Exclusion criteria included having received previous HRV BFB training, or a serious medical (pacemaker, cardiac arrhythmia, hypertension, diabetes), psychiatric (e.g., psychosis), or neurological condition (e.g., Parkinson's disease) that would complicate interpretation of physiological data. Patients currently taking medications such as MAOIs, alpha/beta blockers, or withdrawal or maintenance medications (e.g., Librium, methadone) were excluded due to their potential to affect HRV. Substance use disorder diagnoses were confirmed at intake by clinical psychologists using the Structured Clinical Interview for DSM-IV (First & Gibbon, 2004). Participants also were assessed for comorbid Axis-I general psychopathology, and Axis-II personality disorder pathology.

Of the initial 48 participants, four experimental and two control participants left the treatment facility prematurely. One additional experimental participant was excluded from analysis due to an ECG recording error. The final sample included 21 participants in the HRV BFB group, and 20 participants in the TAU only control group. The experimental and control groups were on average 21.7 ($SD= 1.8$) and 22.0 ($SD= 1.9$) years of age respectively, and the majority of participants in each group reported some college or technical education. The two groups did not differ significantly in proportions of substance use disorders (all $p > .05$; see Table 1), or Axis-I and Axis-II diagnoses (all $p > .05$; see Table 2). The groups were

not significantly different on pre-treatment baseline measures of craving or HRV (all $p > .05$; Table 3).

Physiological measures

Electrocardiogram (ECG) and respiration were measured using Thought Technology Infiniti hardware and software (Thought Technology Inc. SA9306M). Sequences of heart beat-to-beat intervals (RRI) were recorded via ECG and exported to WinCPRS software (Absolute Aliens Oy, Turku, Finland) for analysis and calculation of HRV indices and mean heart rate. After cubic interpolation of the non-equidistant waveform, the RRI sequence was checked for artifacts and irregular beats and edited manually where necessary. Mean respiration frequency was calculated from the abdominal respiration record.

Heart rate, expressed as beats per minute, was derived by calculating the average number of R-spikes in the ECG signal occurring each minute during the 5-minute recording period. HRV was calculated from edited sequential RR intervals derived from the ECG signal. Frequency domain HRV indices were calculated using Fourier analysis (Cooke et al., 1999; Taylor, Carr, Myers, & Eckberg, 1998). Frequency domain indices provided information about how power distributed as a function of frequency (Task-Force, 1996). We calculated very low frequency variability (VLF: 0.005-0.04 Hz), low frequency variability (LF: 0.04-0.15 Hz), and high frequency variability (HF: 0.15-0.4 Hz) indices.

Time domain indices included the standard deviation of all normal-to-normal intervals (SDNN) and the root of the mean squared differences of successive normal-to-normal intervals (RMSSD), both of which useful for gauging autonomic activity. In addition, the number of pairs of adjacent normal-to-normal intervals differing by more than 50ms throughout each 5min recording (NN50) was used to derive the percentage of NN50 (pNN50), a measure of parasympathetic vagal activity (Task-Force, 1996).

Psychological measures

The Penn Alcohol Craving Scale (PACS) is a five-item self-administered instrument that assesses frequency, intensity, and duration of thoughts about drinking alcohol, ability to resist drinking, and average craving in the past week (Flannery, Volpicelli, & Pettinati, 1999). The questions use descriptors coupled with numerical ratings ranging from 0 to 6. The scale has high internal consistency ($\alpha = .92$) and has been validated in clinical samples (Flannery et al., 1999). Garland and Lewis (2013) modified the PACS to measure drug craving by changing key words in the questionnaire. This adapted version of the PACS was found to have similar internal consistency to the original form ($\alpha = .90$). Due to the heterogeneity of substances used both within and across men in our inpatient sample, the PACS was modified in the present investigation to capture both alcohol and drug craving by adding the words “drug” and/or “using drugs” respectively to the words “drink” and/or “drinking”. Cronbach's alphas for this modified PACS were .90, .93, and .94 respectively for the first, second, and third administrations of the questionnaire. Further, we explored concurrent and discriminant validity by testing for correlations between the modified PACS and the Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983), and the Reasons for Drinking Questionnaire (Labouvie & Bates, 2002; not discussed). Evidence for

convergent and discriminant validity of the modified PACS scores was obtained in our data. Modified PACS scores were positively associated with total score on the Perceived Stress Scale ($r = .35$), and the suppression subscale of the Reasons for Drinking Questionnaire ($r = .29$)—measures theoretically linked to craving, but there was no significant association between the modified PACS and the social reasons subscale of the Reasons for Drinking Questionnaire ($r = .05$), which is conceptually unrelated to craving.

The Perceived Stress Scale (PSS) is a widely used, Likert-type, 10-item measure of perceived stress (Cohen et al., 1983). Items are designed to tap how unpredictable, uncontrollable, and overloaded respondents find their lives. The scale also includes a number of direct queries about current levels of experienced stress. The PSS is well validated (Cohen, 1988) and has adequate internal consistency (Hewitt, Flett, & Mosher, 1992)

Procedures

Participation was voluntary and did not affect access to any other services provided by the treatment facility. The HRV BFB training was provided in addition to TAU that included psycho-educational lectures, process groups focused on addiction, community activities, 12-step meetings, and a family treatment program. The study was approved by the Rutgers Institutional Review Board for the Protection of Human Subjects, and written informed consent was obtained from each participant. Rolling admissions entering the treatment facility were offered the opportunity to participate in the study. To avoid between group contamination of the HRV BFB intervention on the unit, HRV BFB + TAU participants were run at a separate time from TAU participants, with a wash-out period between groups, such that no study participant had contact with anyone previously involved in the other study condition.

Heart rate variability biofeedback Intervention

Participants completed one 60-75 minutes session each week for three weeks for a total of 3.5 hours of physiological monitoring and breathing training. The three sessions were conducted by clinical psychology doctoral students (D.E. and C.K.). The PSS was completed at the beginning of session 1 only, while the adjusted PACS craving measure was completed at the start of each session. Physiological data were recorded during sessions 1 and 3.

In session 1, after calibrating the respiration belt, participants performed a standardized low-cognitive-demand task (Plain Vanilla; Jennings, Kamarck, Stewart, Eddy, & Johnson, 1992) in which they viewed rectangles of various colors appearing one at a time on a computer screen and were asked to silently count the number of rectangles of a certain color. This commonly used pre-test baseline task engaged all participants in a low cognitive load activity to facilitate a stable baseline measure.

Participants were then introduced to the EZ-Air Plus visual breathing pacer (Biofeedback Foundation of Europe, Montreal, PQ, Canada), to guide their inhalation and exhalation according to fixed rate. They were asked to breathe along with the pacer set at a six-breaths

per minute rate for 5 minutes. Next, to identify participants' resonance frequency, they were then asked to breathe for 2 minutes at five different breathing frequencies (4.5, 5, 5.5, 6, & 6.5 breaths per minute). Resonance frequency was determined based on participant's physiological indices as well as their subjective level of comfort. Participants were asked to breathe with the pacer set at this frequency for 5 minutes. The session ended with a repeat of the baseline plain vanilla task.

In session 2, participants were asked to breathe along with the EZ-Air Plus pacer set at their identified resonance frequency. Physiological data were monitored to determine if participants were accurately breathing at their resonance frequency. If not, they were coached on how to do so, or asked to breathe at a rate 0.5 BPM faster or slower until the optimum frequency was identified. Next, for the BFB component of the training, participants' instantaneous heart rate and respiration rate data were shown on the screen as cardiometer and respiratory tracings. Participants were asked to breathe so that these two rates were as close to synchronous as possible.

In session 3, HRV BFB group members completed respiration calibration, the pre-test baseline task, breathing with the pacer set at their resonance frequency, breathing in synchrony with the cardiometer line, and the post-test assessment.

Throughout the three-week intervention, participants were instructed to practice HRV BFB for two 20-minute sessions each day, on their own, using handheld EmWave biofeedback devices provided by the researchers (HeartMath Institute, Boulder Creek, CA). In addition, they were instructed to practice the technique whenever they were experiencing alcohol or drug craving. Total time spent practicing daily was recorded by the experimenters using a timeline follow-back interview at the beginning of sessions 2 and 3.

Treatment as usual condition

Control group participants were administered the same plain vanilla baseline task at sessions 1 and 3. In addition, to provide additional physiological data, they did 5 minutes of paced breathing at six-breaths per minute, though no theoretical education, instruction or biofeedback was provided, and participants were not instructed to practice any type of paced breathing. Control participants completed the craving questionnaire once weekly, consistent with the HRV BFB + TAU group. In an attempt to encourage control group participation and reduce attrition, these participants were offered instruction in HRV BFB following completion of the study.

Analyses

Testing for multivariate outliers was conducted using Mahalanobis distance (D^2) with a criterion set at $p < .001$ (de Maesschalck, Jouan-Rimbaud, & Massart, 2000). No outliers were detected. Student's t-Tests were used to examine differences between TAU and HRV BFB + TAU groups in how much physiological indices and craving changed from Session 1 to Session 3.

To assess changes in craving that took into account individual differences in craving level at treatment entry, we regressed each participant's craving scores at Session 3 onto their

baseline craving score taken at Session 1. Residual scores greater than zero indicate increased levels of craving while residual scores less than zero indicate decreased levels of craving. This residual score was then used as the dependent variable in a hierarchical linear regression model. Baseline HR and HRV (from the first plain vanilla baseline task in session 1), and group (0 = TAU, 1 = TAU + HRV BFB) were entered in Step 1 of the hierarchical regression model. The interaction term between these two main effects was entered in Step 2 to examine whether treatment group moderated the relationship between initial HRV levels and residual changes in craving. Baseline craving data for one participant was lost.

Results

Preliminary analyses examined the comparability of the TAU and TAU + HRV BFB groups prior to treatment. Between group differences in SUD diagnoses, and comorbid psychopathology are presented in Tables 1 and 2. Chi-square tests indicated the proportions of different diagnoses represented in the groups were not statistically significant (all $p > .05$). Next, the TAU and TAU+HRV groups were compared on pre-treatment basal measures of heart rate, HRV, craving, and stress. There were no significant differences between groups on any measure (all $p > .05$; see Table 3). In the full sample at baseline (session 1) craving scores were positively correlated with stress scores ($r = .36, p < .05$), and stress scores were positively correlated with measures of HRV, including SDNN ($r = -.44, p < .01$), Rmssd ($r = -.35, p < .05$), Hf HRV ($r = -.33, p < .05$), and Lf HRV ($r = -.36, p < .05$). Craving scores at session 1 and session 3 were positively correlated ($r = .71, p < .001$).

An HRV biofeedback training manipulation check was conducted in the experimental group. We compared HRV measures during the baseline and resonance frequency breathing tasks of session 1. Statistically significant physiological and respiratory changes in the expected direction were observed (Table 4), indicating that participants were able to perform the breathing training as instructed. The 20 cumulative minutes of HRV BFB training resulted in significant increases in HRV levels from pre-session baseline to the post-session assessment obtained at the session's end (Table 4). Experimental participants reported practicing outside of sessions with the EmWave biofeedback device for an average of 21.02 minutes per day ($SD = 12.01$).

The t-test comparisons of the TAU and TAU+HRV BFB groups at the pre-session baseline in session 3 revealed no statistically significant differences in HRV, indicating that two weeks of HRV BFB training did not affect chronic changes in HRV (Table 5). The TAU + HRV BFB group showed a medium effect size trend (Cohen's $d = .35$) toward a larger mean total reduction in alcohol and drug craving over the course of treatment compared to TAU (mean reduction = 5.5 points versus 3.7 points), although this difference did not reach statistical significance, $t(39) = .99, p > .05$.

Hierarchical regression analyses revealed a main effect of pre-treatment baseline Hf HRV on residual change in craving, but did not reveal any main effects of group (Table 6). There were, however, significant interaction effects, such that the relationship between pre-treatment HRV and residual change in craving was moderated by group. Significant group $\times$ pre-treatment HRV interactions were observed for pNN50 ($r^2 = .22$), SDNN ($r^2 = .18$),

Rmssd ($r^2 = .26$), and Hf HRV ($r^2 = .31$). Figure 1 graphically represents the slopes of residual change in craving scores as a function of HRV level in the TAU and TAU+ HRV BFB groups. In order to clarify interpretation of the significant group by baseline HRV interactions, tests were conducted to determine whether the simple slopes within groups were significantly different from zero. These tests revealed that slopes were significantly greater than zero for pNN50 ($t = -2.98, p < .01$), SDNN ($t = -2.67, p < .01$), Rmssd ($t = -3.44, p < .001$), and Hf HRV ($t = -3.91, p < .001$) in the TAU only condition. However, none of the slopes were significantly different from zero in the TAU+HRV BFB group (all $p > .05$). Note that the interpretation of residual changes in craving is different from absolute increases versus decreases in craving. For example, in the context of the strong positive association between craving scores at session 1 and session 3, these results show that in the TAU only group, low baseline levels of HRV predicted significantly greater craving at session 3 than the average association between craving at baseline and session 3 shown by the combined sample. This larger than expected relationship was not observed in the TAU + HRV BFB group.

Discussion

The present study investigated the feasibility and efficacy of a brief heart rate variability biofeedback (HRV BFB) intervention to reduce craving, in the context of an intensive inpatient substance use disorder (SUD) treatment program. Pre-treatment baseline levels of HRV were negatively associated with perceived stress. This is in line with previous reports of negative relationships between HRV and stress (Dishman et al., 2000), and further supports the integrated operation of psychological and physiological processes of affective regulation (Porges, 2009; Thayer & Lane, 2000).

The experimental group received 3 sessions of HRV BFB + treatment as usual (TAU), while the control group received TAU only. Craving decreased in both groups as would be expected given that all participants were receiving inpatient SUD treatment. Further, individual differences in craving were positively correlated over time, and shared approximately 50% variance ($r = .71$). Although there were no statistically significant differences between groups in the absolute level of craving recorded just prior to the final session (session 3), participants receiving TAU + HRV BFB did demonstrate a medium effect size greater reduction in craving compared to TAU.

The significant group $\times$ baseline HRV interaction effect on several key indices of HRV in the hierarchical regression analyses of residual changes in craving (i.e., taking into account participants' pre-treatment level of craving) suggests that one benefit of the HRV BFB intervention may be in mitigating the disadvantage of having low levels of HRV at treatment entry. Specifically, the interaction effects suggested that pre-treatment baseline levels of HRV were predictive of greater than expected (in view of the positive correlation between craving scores over time) changes in craving only in the TAU group, wherein low baseline levels of HRV were actually associated with greater than expected levels of craving at session 3, whereas higher baseline HRV levels were associated with lower than expected levels of craving at session 3. In the TAU + HRV BFB group, however, there was no association between baseline HRV levels and residual changes in craving. That is, HRV

BFB appeared to dissociate individual differences in baseline HRV levels from changes in craving. Thus, even though TAU + HRV BFB was associated with a medium effect size greater absolute reduction in craving compared to TAU, this potential clinical benefit was not systematically related to baseline HRV levels, and those with low baseline HRV were not at a disadvantage in terms of showing greater than expected levels of craving at the end of treatment. Similarly, higher levels of HRV at baseline appeared advantageous in the TAU only group in fostering greater than expected decreases in craving. This preliminary finding, if replicated, may have useful clinical implications, as well raises interesting questions for future patient-treatment matching research.

The group $\times$ baseline HRV interactions were observed across two indices of HRV known to characterize vagus nerve activation (pNN50 and Hf HRV), and two indices thought to be a more general indicators of overall HRV (SDNN and Rmssd). Vagal tone is believed to be a robust physiological marker of general health, as well as one's ability to self-regulate emotion (Kemp & Quintana, 2013; Thayer & Lane, 2000). Vagal withdrawal, characterized by low levels of pNN50, SDNN, and Hf HRV, which results in decreased parasympathetic tone acting on the heart, has been associated with certain anxiety disorders and depression (Carney et al., 1995; Gorman & Sloan, 2000; Lyonfields, Borkovec, & Thayer, 1995), and level of alcohol craving in individuals with alcohol dependence (Quintana et al., 2013). The present findings in the TAU only group are consistent with this literature in that the interaction effect showed that patients with relatively lower levels of these HRV indices showed greater than expected levels of craving toward the end of treatment. The slope in the TAU + HRV BFB group, however, suggested that HRV BFB may be useful in breaking this association and in a sense "leveling the playing field" for patients with low or high levels of HRV. It is plausible that individuals who have low levels of Hf HRV and other indicators of parasympathetic dysregulation, also experience concomitant difficulties regulating intrusive cognitions such as craving. Baseline assessment of HRV could play an important role in treatment planning for individuals with substance abuse problems. Additionally, HRV BFB may prove to be an effective treatment component among individuals with initially low levels of HRV.

There were no statistically significant physiological differences between the experimental and control groups at pre-session baseline in session 3, indicating that two weeks of HRV BFB training + practice did not affect chronic changes in HRV. Because clients were discharged the following week, we could not assess differences following session 3 that would not be confounded with acute changes during that session. The absence of chronic increases in HRV is consistent with findings from other studies that showed HRV BFB did not induce persistent changes in HRV, even though it affected improvements in clinical symptoms such as craving and depression (e.g., Hassett et al., 2007; Meule et al., 2012; Zucker et al., 2009). It is possible that participants trained in HRV BFB may have used the technique more acutely, to help regulate alcohol and drug craving in the moment.

With respect to feasibility of implementation, HRV BFB participants were generally enthusiastic about the intervention and counselors on the unit were supportive of the intervention. Anecdotal reports from patients and counselors about the benefits of HRV BFB

led the young adult male unit at the treatment facility to incorporate HRV BFB training into their standard inpatient treatment protocol.

Limitations and caveats

The lack of significant overall HRV BFB effects, despite a medium effect size reduction in craving, may have resulted from the relatively short training period used in this study, with relatively little practice. Previous clinical trials of HRV BFB that have produced clinically significant changes have taken longer (4–12 weeks; Hassett et al., 2007; Karavidas et al., 2007; Meule et al., 2012; Tan, Dao, Farmer, Sutherland, & Gevirtz, 2011; Zucker et al., 2009). Further, power was limited by the modest sample size. It was not feasible to inferentially compare craving changes in the relatively small numbers of participants who had high HRV levels at treatment entry in the TAU only versus TAU + HRV BFB groups, although this is an important question for future research. A post-hoc power analysis indicated that a minimum of 102 participants would be required per group to have 80% power for detecting a medium sized effect with alpha set to .05, although the effect size may also be increased through the use of additional sessions of HRV BFB training during inpatient treatment. In addition, participant reports of daily practice, although assessed by timeline follow-back at each session, were not independently verified. Thus, it was not certain that the reported/recalled average of 20 minutes of daily practice accurately reflected actual time spent practicing. Daily practice logs, verified by staff, or electronic monitoring of biofeedback equipment use could enhance accuracy of practice assessment.

Conclusion

In summary, the present findings support an interpretation of potential added clinical benefit in craving reduction from HRV BFB, within the context of intensive inpatient treatment, particularly for more autonomically dysregulated individuals experiencing low HRV. In participants receiving TAU only, level of HRV at treatment entry appeared to be a factor contributing to craving regulation wherein lower levels of HRV predict less positive changes in craving over time. HRV biofeedback may break this link. In addition, participant feedback was extremely positive and the intervention was well received by clinical staff at the treatment facility. The results support the further examination of HRV assessment as a component in treatment planning for people with SUDs, and the use of HRV BFB as a complement to SUD treatment programs using larger samples, verified daily practice logs, and perhaps additional HRV training sessions.

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Figure 1.

The relationship between residual change in craving scores, and pNN50 ($SD= 20.0$), SDNN ($SD= 0.4$), Rmssd ($SD= 0.6$), and Hf HRV ($SD= 1.4$) in the heart rate variability biofeedback + treatment as usual, and treatment as usual only groups. X-axes show heart rate variability scores at treatment entry. Y-axes show residual change in craving scores ($SD= 4.5$). Scores above zero on the y-axis represent greater residuals than expected, i.e., greater craving at session 3 than would be predicted by the average association between baseline and session 3 in the combined sample, whereas scores below zero indicate smaller residuals than expected, i.e., less craving at session 3 than would be predicted by the average association between baseline and session 3 in the combined sample.

Notes. pNN50= percent of normal-to-normal intervals greater than 50ms, SDNN= standard deviation of normal-to-normal intervals, Rmssd= square root of the mean squared difference of successive normal-to-normal intervals, Hf HRV= high frequency range of the power spectral analysis, TAU Only= Treatment as usual, TAU + HRV BFB= Treatment as usual + heart rate variability biofeedback

Table 1

Participants' Substance Use Disorder Diagnoses by Group

	# Alcohol Dependence Diagnoses	# Opiate Dependence Diagnoses	# Cannabis Dependence Diagnoses	# Stimulant Dependence Diagnoses	# Sedatives Dependence Diagnoses	# Hallucinogen Dependence Diagnoses	Average # Dependence Diagnoses per Participant	# Participants with Co-occurring Substance Abuse Diagnosis
HRV BFB + TAU Group	7	9	11	8	2	0	1.94	6
TAU Only Group	3	12	13	3	0	1	1.78	5

Table 2
Participants' Co-occurring Psychopathology Diagnoses by Group

	# Anxiety Disorder Diagnoses	# Depressive Disorder Diagnoses	# Bipolar Disorder Diagnoses	# ADHD Diagnoses	# Cluster A Personality Disorder	# Cluster B Personality Disorder	# Cluster C Personality Disorder	Total # Participants with Co-occurring Axis-I Diagnosis	Total # Participants with Co-occurring Axis-II Diagnosis
HRV BFB + TAU Group	6	6	2	6	0	2	2	14	3
TAU Only Group	7	5	2	6	0	2	0	13	2

Table 3
Between Group Differences in Heart Rate Variability, Craving and Perceived Stress at Baseline Session 1

Variable	Experimental Group <i>n</i> = 21	Control Group <i>n</i> = 20	<i>t</i>
HR	76.09 (12.50)	75.05 (10.60)	-0.29
pNN50	19.34 (19.33)	21.84 (21.19)	0.39
SDNN (log)	3.84 (0.45)	3.93 (0.45)	0.62
Rmssd (log)	3.44 (0.71)	3.62 (0.56)	0.87
Hf HRV (log)	5.67 (1.50)	6.08 (1.20)	0.96
Lf HRV (log)	6.39 (1.09)	6.56 (1.18)	0.47
Vlf HRV (log)	6.11 (0.80)	6.15 (1.01)	0.16
Respiration	0.26 (0.08)	0.27 (0.05)	0.13
Craving	15.00 (7.45)	13.70 (6.51)	-0.57
Perceived Stress	27.09 (5.41)	24.55 (5.90)	-1.45

Notes. Standard deviations in parentheses; HR= heart rate, pNN50= percent of normal-to-normal intervals greater than 50ms, SDNN= standard deviation of normal-to-normal intervals, Rmssd= square root of the mean squared difference of successive normal-to-normal intervals, Hf HRV, Lf HRV, and Vlf HRV = high frequency, low frequency, and very low frequency range of the power spectral analysis, respectively; Respiration= respiration frequency, Craving= Total PACS craving score, Perceived Stress= Total Perceived Stress Scale Score; *df*= 39, except for craving, *df*= 38, all *p*>.05

Table 4
Physiological Changes in Experimental Group from Pre-session Baseline Assessment (Plain Vanilla), to Resonance Frequency Breathing Task, to Post-session Assessment (Plain Vanilla), During Session 1

Variable	Pre-session Assessment ^a	Resonance Freq. Breathing ^b	Post-session Assessment ^c	<i>t</i> a-b	<i>t</i> a-c
HR	76.09 (12.50)	75.90 (10.17)	74.03 (10.71)	0.12	1.90
pNN50	19.34 (19.33)	23.47 (17.06)	19.64 (19.02)	-2.11 *	-0.13
SDNN (log)	3.84 (0.45)	4.42 (0.43)	4.06 (0.41)	-9.88 **	-3.33 **
Rmssd (log)	3.44 (0.71)	3.87 (0.59)	3.60 (0.66)	-5.26 **	-1.67
Hf HRV (log)	5.67 (1.50)	6.09 (1.24)	5.91 (1.45)	-1.98	-1.42
Lf HRV (log)	6.39 (1.09)	8.45 (0.93)	7.13 (1.04)	-9.27 **	-3.48 **
Vlf HRV (log)	6.11 (0.80)	5.95 (0.92)	6.37 (0.73)	0.66	-1.36
Respiration	0.26 (0.08)	0.10 (0.02)	0.20 (0.08)	9.76 **	3.31 **

Notes. Standard deviations in parentheses; HR= heart rate, pNN50= percent of normal-to-normal intervals greater than 50ms, SDNN= standard deviation of normal-to-normal intervals, Rmssd= square root of the mean squared difference of successive normal-to-normal intervals, Hf HRV, Lf HRV, and Vlf HRV = high frequency, low frequency, and very low frequency range of the power spectral analysis, respectively.; Respiration= respiration frequency; *df*= 39

**
p < .01,

*
p < .05

Table 5
Physiological Differences Between Experimental And Control Groups At Pre-Session
Baseline, Session 3

Variable	Experimental Group <i>n</i> = 21	Control Group <i>n</i> = 20	<i>t</i>
HR	82.10 (17.01)	77.20 (12.35)	-1.05
pNN50	14.39 (16.61)	16.19 (13.80)	-0.25
SDNN (log)	3.90 (0.61)	3.86 (0.33)	0.29
Rmssd (log)	3.40 (0.83)	3.47 (0.52)	0.29
Hf HRV (log)	5.60 (1.64)	5.87 (1.06)	0.61
Lf HRV (log)	6.77 (1.44)	6.61 (0.80)	-0.04
Vlf HRV (log)	6.00 (1.10)	6.17 (0.91)	0.53
Respiration	0.24 (0.09)	0.26 (0.06)	1.14
Craving	9.62 (6.78)	9.95 (5.95)	0.07

Notes. Standard deviations in parentheses; HR= heart rate (*df*= 39), pNN50= percent of normal-to-normal intervals greater than 50ms (*df*= 39), SDNN= standard deviation of normal-to-normal intervals (*df*= 31), Rmssd= square root of the mean squared difference of successive normal-to-normal intervals (*df*= 34), Hf HRV= high frequency range of the power spectral analysis (*df*= 39), Lf HRV= low frequency range of the power spectral analysis (*df*= 32), Vlf HRV= very low frequency range of the power spectral analysis (*df*= 39), Respiration= respiration frequency (*df*= 33), Craving= Total PACS craving score (*df*= 39); all *p* > .05

Table 6

The Relationship Between Change in Craving (Dependent Variable), and Measures of Mean Heart Rate and Heart Rate Variability in the Inpatients Receiving Treatment as Usual Only, and Treatment as Usual + Heart Rate Variability Biofeedback

Variable		R ²	β	B	SE
Mean Heart Rate					
Step 1	Group (0=TAU, 1=TAU + HRV BFB)	0.04	-0.13	-1.19	1.43
Mean Heart Rate					
			0.15	0.06	0.06
Step 2	Group $\times$ Mean Heart Rate	0.09	-2.12	-0.24	0.12
pNN50					
Step 1	Group	0.12	-0.13	-1.17	1.40
	pNN50		-0.24	-0.06	0.04
Step 2	Group $\times$ pNN50	0.15*	0.68*	0.18	0.07
SDNN (Log)					
Step 1	Group	0.08	-0.14	-1.27	1.40
	SDNN		-0.25	-2.64	1.64
Step 2	Group $\times$ SDNN	0.10*	2.90*	6.60	3.17
Rmssd (Log)					
Step 1	Group	0.07	-0.15	-1.34	1.41
	Rmssd		-0.23	-1.71	1.17
Step 2	Group $\times$ Rmssd	0.19**	2.08**	6.93	2.27
Hf HRV (Log)					
Step 1	Group	0.15	-0.17	-1.51	1.36
	Hf HRV		-0.36*	-1.23	0.56
Step 2	Group $\times$ Hf HRV	0.17**	2.02**	2.95	1.00
Lf HRV (Log)					
Step 1	Group	0.02	-0.13	-1.17	1.44
	Lf HRV		-0.05	-0.20	0.66
Step 2	Group $\times$ Lf HRV	0.04	1.13	1.53	1.31
Vlf HRV (Log)					
Step 1	Group	0.04	-0.13	-1.15	1.43
	Vlf HRV		-0.14	-0.69	0.81

Variable		R ²	β	B	SE
Step 2	Group $\times$ Vif HRV	0.05	1.60	2.28	1.62

Notes: TAU= Treatment as usual, TAU + HRV BFB= Treatment as usual + heart rate variability biofeedback;

*
= $p < .05$,
**
= $p < .01$