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Objective and specific tracking of anhedonia via event-related potentials in individuals with cocaine use disorders*

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Abstract

Background—Hyposensitivity to non-drug reward, behaviorally manifested as anhedonia, is a hallmark of chronic substance use. Anhedonia is a transdiagnostic symptom underpinned by neurobiochemical disturbances in the reward circuit, yet an objective measure to assess anhedonia severity still eludes the field. We hypothesized that the Reward Positivity (RewP) component of the event-related potentials (ERPs) will specifically track anhedonia as the RewP is attributed to the same brain regions that are also implicated in anhedonia.

Methods—Forty-six individuals with cocaine use disorders (iCUD) performed a gambling task predicting whether they would win or lose money on each trial, while ERP data was acquired. RewP in response to predicted win trials was extracted from the ERPs using the principal component analysis. State anhedonia and depression severity were assessed using the Cocaine Selective Severity Assessment (CSSA).

Results—Although RewP amplitude correlated with both anhedonia and depression, only the RewP-anhedonia correlation survived a correction for depression severity. Further, a hierarchical multiple regression analysis revealed that anhedonia explained a significant amount of variance in the RewP amplitude, and this variance was significantly greater than that explained by demographics, severity and recency of drug use and even depression.

Conclusions—These results show that RewP amplitude in response to rewarded trials tracks state anhedonia severity in iCUD. We argue that this association is perhaps driven by the activity in the dopaminergic mesocorticolimbic reward pathway that may underlie anhedonia symptomology as well as modulate RewP amplitude.

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Keywords

Anhedonia; EEG; Event-related potentials; Reward positivity; Cocaine; Addiction

1. INTRODUCTION

Substance use disorders (SUD) are often characterized by hypersensitivity to drug-related rewards with a concomitant hyposensitivity to non-drug-related rewards (Berridge and Robinson, 1998; Di Chiara, 1998). Preclinical as well as human neuroimaging studies have consistently implicated alterations within the mesocorticolimbic reward circuit (Hyman et al., 2006; Koob and Le Moal, 2001) in mediating such reward dysregulation in SUD. Within this circuit, the ventral striatum (VS) is a critical subcortical node that underlies response to reward behaviors and pleasurable experiences associated with reward (Heinz et al., 1994; Willner et al., 2005). At the cortical level, the medial prefrontal cortex (mPFC) plays a crucial role in the processing of the motivational value of rewards (Grabenhorst and Rolls, 2011; Grabenhorst et al., 2008; Harvey et al., 2007; Keedwell et al., 2005), in goal-directed behavior (Hare et al., 2008) and its adaptive adjustments after reward contingency changes (Hikosaka and Watanabe, 2000). In SUD, however, both the VS and the mPFC show hyposensitivity to non-drug-related rewards, such as food, sex and even to more abstract rewards such as money (Childress et al., 2008; Goldstein et al., 2007; Volkow et al., 2010). Previous studies have posited an attenuated tonic dopamine activity, partially due to a prolonged allostatic overload on the reward circuit by chronic drug use, to underpin such hyposensitivity to non-drug rewards in SUD (e.g., see Koob and Le Moal, 2005).

Similarly, anhedonia, the decreased capacity to experience pleasure, is a clinical symptom that reflects deficits of reward processes. While it is a core symptom of depression (Gorwood, 2008), anhedonia is a salient feature across many neuropsychiatric disorders (Whybrow, 1998), including SUD (Ahmed and Koob, 1998; Volkow et al., 2002). It has been argued that abnormalities in the dopaminergic neuronal reward circuitry underlying anhedonia can be induced by dopamine-inducing drugs, such as cocaine (Volkow et al., 2010; Vollm et al., 2004). Subsequently, this drug-induced dopamine surge influences reward-guided decision making (Bechara, 2005), and plays a crucial role in the development and maintenance of SUD (Ahmed and Koob, 1998; Goldstein and Volkow, 2002, 2011; Koob and Le Moal, 2001). Therefore, the objective quantification of anhedonia in individuals suffering from SUD is critical in gaining better understanding of the impaired reward-related brain functions that are specific to anhedonia. However, anhedonia is a subjective clinical measure, which reflects a wide range of deficits in reward processes.

Anhedonia has traditionally been assessed via self-report questionnaires, either as a composite measure [e.g., using the Snaith-Hamilton Pleasure Scale (SHAPS; Snaith et al., 1995)] or in SUD as a constituent score of a higher-level construct, such as withdrawal [e.g., using the Cocaine Selective Severity Assessment (CSSA, Kampman et al., 1998)]. Indeed, there have been attempts to objectively assess anhedonia behaviorally (Pizzagalli et al., 2005; Treadway et al., 2009) as well as using event-related potential (ERP) components, such as the Oddball P3 component in healthy individuals (Franken et al., 2006), and the

feedback-related negativity (FN) (Foti et al., 2014) and reward positivity (RewP; Liu et al., 2014) in individuals with major depressive disorder. The RewP [also termed the feedback correct-related positivity; Holroyd et al., 2008)] is the positive-going deflection in correct (or win/reward) trials; its absence in incorrect (or loss/punishment) trials yields the FN (Baker and Holroyd, 2011; Foti et al., 2011; Holroyd et al., 2008). The RewP amplitude is posited to specifically reflect the activity of the mesencephalic dopamine system underlying reward processing (Foti et al., 2011; Proudfit, 2015), specifically with the activity in the VS and the mPFC (Carlson et al., 2011; Foti et al., 2014).

Here we sought to investigate ERPs correlates of anhedonia in adults with SUD. Given that activity in the VS-mPFC loop contributes to both anhedonia and the RewP amplitude and that chronic drug use is presumed to act as an allostatic overload on this loop (Koob and Le Moal, 2001), we hypothesize that the RewP amplitude would be specifically associated with the severity of anhedonia, and not that of depression, in individuals with cocaine use disorders (iCUD).

2. METHODS

2.1. Participants

Fifty-five iCUD (10 females, 43.4 ± 6.9 years old) participated in this study. Forty-six participants (7 females, 43.0 ± 6.9 years old) yielded useable data (Table 1); the other nine participants either did not yield adequate number of trials (< 15 trials, n=6) or their electroencephalography (EEG) data was of low fidelity (n=3). All participants were recruited through advertisements in local newspapers, word of mouth, and local treatment facilities. Additionally, participants were right-handed, native English speakers, and free of sustained/maintenance medications for >30 days prior and throughout the study. Further exclusionary criteria included (A) history of head trauma or loss of consciousness (>30 min) or other neurological diseases of central origin (including seizures); (B) current medical diseases that required hospitalization or regular monitoring; (C) history of major psychiatric disorder [other than substance abuse/dependence and disorders of high comorbidity with substance abuse/dependence (inclusive of depression and post-traumatic stress disorder) and/or nicotine dependence]; (D) positive urine screens for psychoactive drugs or their metabolites (phencyclidine, benzodiazepines, cannabis, opiates, barbiturates, and inhalants) other than cocaine; and (E) more than two standard deviations below the norm on a verbal intelligence measure. Note that data from 28 of the current 46 participants have already been published elsewhere (Parvaz et al., 2015). However, the current study focuses exclusively on previously un-reported data from these participants. All participants were fully informed of all study procedures and risks, and they provided written consent in accordance with the Stony Brook University Institutional Review Board and the associated treatment facility's Institutional Review Board.

2.2. Diagnostic Interview

All participants underwent a full diagnostic interview including: (A) the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Axis I Disorders (First et al., 1996); (B) the Addiction Severity Index (McLellan et al., 1992), a

semi-structured interview instrument that assesses the severity as well as recent and lifetime history of alcohol- and drug-related problems, as they relate to seven problem areas (medical, employment, legal, alcohol, other drug use, family-social functioning, and psychological status); (C) the 5-item Severity of Dependence Scale (Gossop et al., 1992); (D) the 18-item Cocaine Selective Severity Assessment Scale (CSSA; Kampman et al., 1998), designed to evaluate cocaine abstinence/withdrawal signs and symptoms (including anhedonia and depression) 24 hours within the time of interview. Single items on the CSSA were used to quantify anhedonia and depression, using scales from '0' to '7' [0 = "ability to enjoy themselves remain unchanged" (anhedonia), "no feelings related to sadness or depression" (depression); 3–4 = "able to enjoy themselves half the time" (anhedonia), "feels sad or depressed half the time" (depression); 7 = "unable to enjoy themselves at all" (anhedonia), "feels depressed all the time" (depression)].

This interview determined that iCUD met criteria for current cocaine dependence (n=33), or cocaine dependence in partial (n=4) or sustained remission (n=9). Current comorbidities in this sample included marijuana use disorder (n=1), alcohol use disorder (n=1), opiate use disorder (n=1), anti-social personality disorder (n=2), post-traumatic stress disorder (n=1), and major depression disorder (n=1). All other comorbidities were in partial or sustained remission.

2.3. Task

The overall design of the task was similar to what has been previously described (Parvaz et al., 2015) and similar to Experiment 2 reported in a previous study by Hajcak et al. (2007). In brief, participants' primary objective on each trial was to guess which of four doors hid a prize by pressing one of four keys on a keypad corresponding to each door (Figure 1). At the beginning of each trial, after an initial presentation of a fixation cross (1000ms), a white cue of "1," "2," or "3" appeared on the screen for 1000ms, which indicated the number of doors (out of four) that contained a monetary prize (60¢); thus, these cues indicated the probability of reward on the upcoming trial (25, 50, and 75%, respectively). Following the presentation of the cue, an inter-stimulus delay of 500ms was presented followed by a presentation of the graphic of the doors, which remained on-screen until the participant made a selection to indicate their prediction of the winning door. Immediately following their choice, the question "Do you think you won or lost in this trial?" appeared on the screen and remained there until participants indicated via button press a predicted win or loss. Thus, participants were first presented with a cue that conveyed the objective probability of reward on the upcoming trial, and then asked to make a choice and, finally, predict whether or not they thought they chose correctly. Five hundred milliseconds following their prediction, a feedback stimulus appeared on the screen for 1000ms: a green arrow pointing upward indicated a win (i.e., a win of 60¢), or a red arrow pointing downward indicated a loss (i.e., a loss of 30¢; Figure 1). Winning probability was always consistent with the cue type (e.g., 75% winning probability for three-cue trials). Such a task design specifically allows for modulating valence-related variability in FN by explicit prediction errors (Hajcak et al., 2007).

This task was administered using Presentation software (Neurobehavioral Systems) to control the presentation and timing of all stimuli. All stimuli were positioned in the center of the screen. The cue and feedback stimuli occupied 21° of visual angle horizontally and 21° vertically. A fixation cross was then presented during each intertrial interval for 500ms. The task consisted of six blocks of 50 pseudorandom trials (i.e., a total of 300 trials; 100 trials per cue type) interspaced by a brief break. Participants were told that the task earnings would be given to them at the end of the EEG session. Unbeknownst to the participants, the task earnings were not dependent on their choice and they were always paid $75 for the task.

2.4. Psychophysiological recordings and data reduction

Electroencephalogram (EEG; Neuroscan) recordings were obtained using a 64 silver–silver chloride electrode cap positioned according to the International 10/20 system. Electro-oculogram electrodes at the left supraorbital and infraorbital sites and the right and left outer canthi recorded the blinks (and vertical eye movements) and horizontal eye movements, respectively. EEG recordings were sampled at 500 Hz and bandpass filtered from DC to 70 Hz. Electrode impedances were kept <50 kΩ.

Offline preprocessing of the EEG signal was performed using SPM8 (Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm) and custom Matlab (The MathWorks) scripts. Data were first bandpass filtered (0.01–30 Hz) and re-referenced to the averaged electrical activity from all 64-scalp sites. To evaluate the effect of the participant's actual predictions on the feedback-locked ERP and to maximize the number of trials for each analysis across the objective winning probabilities (25, 50, and 75%), averaged waveforms were created for all feedback trial types: Predicted Win, Unpredicted Win, Predicted Loss, and Unpredicted Loss. Therefore, the continuous EEG data were segmented beginning 200ms before the feedback onset and continuing for 1000ms. For each trial, the 200ms baseline was subtracted from the post-stimulus data for baseline correction. Eye-blink and ocular corrections were performed using the partial signal space projection method proposed by Nolte and Hamalainen (2001), such that the contribution to the estimated spatial structure of eye-blink artifact was removed only from the artifact-ridden epochs, leaving as much information as possible in the data. This artifact-rejection procedure identified a voltage step of >75 μV between sample points and a peak-to-peak voltage difference of 150 μV within an epoch. Additional artifacts were identified through visual inspection, and the contaminated epochs were subsequently rejected. Finally, robust averaging was used to create artifact-free ERPs (Wager et al., 2005) separately for each of the four conditions. To test our hypothesis, we only used data from the Predicted-Win condition, as this condition signals reward outcome without being influenced by reward prediction error (in contrast to the unpredicted-win condition). Nevertheless, to inspect for specificity of results, data from the other conditions were also extracted and the results are presented online as Supplementary Material[1]. The average number of artifact-free epochs used for ERP averaging of the Predicted Win condition was 110.85 (Range: 60 – 134).

[1]Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:…

Following recently published studies, temporospatial principal components analysis (PCA) [EP-Toolkit, version 2.51b (Dien, 2010)] was used to isolate RewP amplitude from the Predicted Win ERP waveform (Foti et al., 2011; Liu et al., 2014). First, a temporal PCA was performed to capture variance across time and maximize the initial separation of the ERP components (Dien et al., 2005). A Promax rotation was used (Dien, 2010; Dien et al., 2007) and 11 temporal factors were extracted based on the resulting Scree plot (Cattell, 1966). Following the temporal PCA, a separate spatial PCA was performed for all 11 temporal factors obtained in the previous step. The Infomax rotation was used and based on the results of the parallel Scree plot five spatial factors were extracted from each temporal factor, yielding a total of 55 temporospatial factor combinations. To directly assess timing and spatial voltage distributions, we then translated the factors back into voltages. Seventeen factor combinations accounted for more than 1% of the variance each. Of these, one factor combination was identified to reflect the RewP (Spatial factor 1 of the temporal Factor 3, or TF3SF1; Figure 2) based on its latency (between 250 – 400ms), scalp topography (frontocentral maxima) and statistically computed source location (medial orbitofrontal cortex), consistent with proposed characteristics of RewP (see, Proudfit, 2015). The latency and amplitude of PCA factors in other task conditions are presented online as Table S1[2].

2.5. Statistical analyses

First, the association between the amplitude of the isolated PCA factor (i.e., TF3SF1) denoting RewP and the severity of anhedonia and depression (assessed via CSSA) were ascertained using the Spearman Rank correlation. Next, a hierarchical multiple regression analysis was conducted to assess whether anhedonia and depression predicted unique and significant variance in the RewP amplitude. The first model included participants' demographic characteristics (age and gender), the second included the measures of severity and recency of drug-use [i.e., severity of cocaine dependence (assessed via the severity of dependence scale), current cocaine abstinence (in days) and cigarette smoking status (current, past, or non-smoker)]. Anhedonia and depression (assessed via CSSA) were entered in the last two models. This way the predictive value of either anhedonia or depression on RewP amplitude was tested beyond the predictive value of participants' demographics and drug-use measures.

3. RESULTS

3.1. Correlations

As hypothesized, the RewP amplitude was negatively correlated with anhedonia (r_S=−0.409, p=0.005) and depression (r_S=−0.287, p=0.05) scores, such that reduced RewP amplitude was associated with greater anhedonia and depression severity in iCUD (Figure 3). As expected, both anhedonia and depression severity scores were significantly intercorrelated (r_S=0.389, p=0.003).

[2]Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:…

3.2. Hierarchical Multiple Regression

The hierarchical multiple regression analyses revealed that the RewP amplitude were significantly associated with the anhedonia scores (β=−0.32, p=0.046) and not with the depression scores (β=−0.14, p=0.428) (Table 2). Further, a total of 24.9% of the variance in the RewP amplitude was explained by the full regression model. Demographic (i.e., age and gender) and drug use variables [i.e., severity of cocaine dependence, current cocaine abstinence (in days) and cigarette smoking status (current or past/non-smoker)] explained 2.3% ($F_{change}(2,43)=0.50$, p=0.607) and 7.7% ($F_{change}(3,40)=1.13$, p=0.347) of the variance in the RewP amplitude, respectively. Anhedonia score significantly predicted 13.7% of the variance ($F_{change}(1,39)=6.97$, p=0.012), whereas depression score only predicted 1.3% of the variance ($F_{change}(1,38)=0.64$, p=0.428) in the RewP amplitude. Standardized and unstandardized regression coefficients and the test statistic for each independent variable in the model are listed in Table 2.

To rule out order effects in model specification, a similar hierarchical multiple regression was conducted again, but with depression and anhedonia scores in the third and the fourth model, respectively. This time depression marginally predicted 6.6% of the variance ($F_{change}(1,39)=3.06$, p=0.088), whereas anhedonia still significantly predicted 8.4% of the variance in the RewP amplitude ($F_{change}(1,38)=4.24$, p=0.046), highlighting the specificity of the association between anhedonia and the RewP amplitude in iCUD.

4. DISCUSSION

The goal of this study was to determine an objective and specific electrocortical marker of anhedonia in individuals with SUD. Using ERPs in response to a monetarily rewarded condition in a probabilistic gambling task, the current study titrated the specific association between RewP amplitude and anhedonia severity. Indeed, recent studies have reported that modulation in FN (a complimentary ERP component of RewP) amplitude stems from stimuli that signal reward (Foti et al., 2011; Holroyd et al., 2011, 2008) and is associated with depressive symptoms (Foti et al., 2014; Foti and Hajcak, 2009), including anhedonia (Liu et al., 2014). Thus, the current study replicates these findings by showing an association between the RewP amplitude in response to rewarding feedback and the severity of anhedonia and depression (both assessed via the CSSA) in individuals with SUD. More importantly, this study extends the existing literature to further highlight the specificity of the association between RewP amplitude and anhedonia, irrespective of the depressed mood, severity and recency of drug use and demographic characteristics in iCUD.

Although novel, these results are not surprising. Both anhedonia and depressed mood are key symptoms of depression that is highly comorbid in SUD, but they are empirically distinct – each can occur without co-occurrence of the other (Zimmerman et al., 2006), have distinct underlying neural correlates (Wacker et al., 2009) and are posited to be distinct endophenotypes of the depression syndrome (Hasler et al., 2004). Having an objective and unique marker of anhedonia (RewP) is clinically significant in SUD as more severe anhedonia is associated with increased likelihood of relapse among nicotine dependent individuals (Cook et al., 2010; Leventhal et al., 2009) and with increased drug craving among alcohol (Martinotti et al., 2008a, 2008b), opioid (Janiri et al., 2005; Martinotti et al.,

2008a) and nicotine dependent individuals (Cook et al., 2004; Leventhal et al., 2009). Increased anhedonia severity has also been reported in recent as well as in protracted abstinent substance-dependent populations (Hatzigiakoumis et al., 2011).

A substantial body of research has suggested that psychostimulants (i.e., drugs that activate mesolimbic dopamine system, such as cocaine) usurp the dopamine-mediated process of assigning salience to reinforcers by reducing tonic dopaminergic transmission in the striato-cortical loop, resulting in hyposensitivity to non-drug-related reward and related motivational disturbances such as anhedonia (Di Chiara and Bassareo, 2007; Gorwood, 2008; Melis et al., 2005; Romer Thomsen et al., 2015). Similar dopaminergic neural substrates that are implicated in reward sensitivity, mainly in the striato-cortical loop, are also posited to generate the RewP amplitude (mainly from the findings in FN; Carlson et al., 2011; Foti et al., 2014). Thus, it can be speculated that the specific association between the RewP amplitude and anhedonia in our sample is mediated by dopaminergic signaling in the mesocorticolimbic reward circuit, especially in individuals with chronic stimulant use disorders, such as the iCUD.

Indeed, anhedonia-related modulations of ERP amplitude have been studied previously. For example, studies in healthy individuals have shown that, compared to those with low anhedonia, those with higher anhedonia score [assessed via the Chapman's Physical Anhedonia Scale (PAS; Chapman et al., 1976), the Beck-Weissman's Dysfunctional Attitude Scale (DAS; Weissman, 1979), or the SHAPS] manifest deficits in the orienting response and motor preparation processes quantified via the contingent negative variation (Pierson et al., 1987) and P3 amplitude (elicited using an Oddball paradigm; Franken et al., 2006). Similarly, a recent multimodal study in healthy individuals has shown a unique association between anhedonia [assessed via the anhedonic depression scale of the Mood and Anxiety Symptoms Questionnaire (MASQ-AD; Watson et al., 1995a, 1995b)] and the resting-state EEG delta band power reflecting the activity in the rostral anterior cingulate cortex (Wacker et al., 2009). Compared to healthy controls, a recent study has shown reduced FN amplitude as correlated with increased anhedonia and depressive symptoms in a clinical cohort of patients with major depressive disorder (Liu et al., 2014). However, the significant anhedonia-FN correlation was reduced to a trend significance when controlled for overall depression severity (Liu et al., 2014). In another recent clinical study, more pronounced N2 and reduced P3 amplitudes during successful response inhibition (in a Go/No-Go task) were associated with more severe anhedonia, but only in healthy control and not in iCUD (Morie et al., 2014). The authors speculated that the diverging results might be driven by the interaction between diagnostic groups and the distinct neural substrates underlying No-Go N2 and P3 amplitudes (i.e., response inhibition) and anhedonia severity (i.e., reward processing deficits; Morie et al., 2014). Thus, the current results extend the literature by using RewP amplitude that is specifically elicited by reward-signaling stimuli (i.e., Predicted Win condition), and by using data-driven approaches (i.e., temporospatial PCA and dipole source modelling) to systematically show the specificity of the RewP-anhedonia association in a population with specific impairments in reward processing (Di Chiara and Bassareo, 2007; Parvaz et al., 2012).

Here, it is important to distinguish the RewP from what has previously been termed as the reward-related P3. The RewP is a positive-going deflection that is elicited only in response to reward-related stimuli and shows peak amplitude between 250 – 400 msec at fronto-central scalp location (Holroyd et al., 2011, 2008). The RewP has specifically been implicated as a functional marker of dopaminergic reward processing (Carlson et al., 2011; Foti et al., 2014, 2011; Proudfit, 2015). In contrast, the P3, also a positive-going deflection, is elicited by both reward- and loss-related trials (or outcomes of motivational importance; Wu and Zhou, 2009; Yeung and Sanfey, 2004), showing a comparatively delayed maxima (350 – 600 msec) at centro-parietal scalp locations (Goldstein et al., 2006; Sato et al., 2005). Although there have been reports of increased P3 amplitude to positive compared to non-positive feedback (Hajcak et al., 2007), perhaps due to increased motivational salience attributed to positive feedback, functionally, the reward-related P3 is sensitive to outcome magnitude (Bellebaum et al., 2010; Parvaz et al., 2012; Sato et al., 2005), regardless of its valence (win or loss; Yeung and Sanfey, 2004).

It is important to note that the current study used individual items from the CSSA to assess state anhedonia and depression severity in iCUD. The CSSA is a clinician-administered instrument that measures early cocaine abstinence signs and symptoms. The literature-informed questions seek to quantify severity of symptoms that are most often associated with early cocaine abstinence, including depression, fatigue, anhedonia, anxiety, irritability, sleep disturbance, and inability to concentrate (Brower et al., 1988; Cottler et al., 1993; Watson et al., 1992). Thus, similar to using the Beck Depression Inventory to quantify depression severity in patients with mood disorders, the CSSA provides a targeted quantification of anhedonia and depression in iCUD. Individual items of the CSSA have been previously used to investigate unique withdrawal-related state measures, such as craving (Hendricks and Greenway, 2011; Reid and Thakkar, 2009). Nevertheless, the use of individual items of a questionnaire instead of a composite score, and the resulting limited variability in the scores (evident in Figures 3 and 4), is a limitation of this study. Therefore, it is important that future studies test if this unique association of the RewP amplitude with the CSSA-derived anhedonia score also generalizes to anhedonia measured using other scales (i.e., PAS, SHAPS, and MASQ-AD). Another limitation of the current study is the absence of a healthy control group. However, since differences between iCUD and healthy controls have consistently been reported in anhedonia severity (see, Leventhal et al., 2010) and the RewP (or FN) amplitude (Franken et al., 2007; Parvaz et al., 2015; Torres et al., 2013), inclusion of a control group might only have served the purpose of yet another validation of group differences, which was not the focus of the current study.

In sum, the current study reported a unique association between reduced RewP amplitude in response to rewarding feedback stimuli and increased anhedonia severity in iCUD, even after controlling for demographics, drug use variables and, importantly, depression severity. Since RewP amplitude has been posited to be a marker of depression (Proudfit, 2015), the current results help titrate this association specifically to anhedonia, a core transdiagnostic neuropsychiatric symptom. Although anhedonia is typically assessed via psychometrically validated subjective (self-report) scales, their utility in populations with known self-awareness and insight impairments, such as in individuals with SUD (Goldstein et al., 2009), remains questionable. Therefore, our results suggest that the RewP amplitude can potentially

serve as an objective biomarker that reliably tracks anhedonia severity in iCUD. These results also speak to the overall utility of EEG markers in clinical settings to facilitate objective assessments of clinical symptomology.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Anhedonia is a core symptom of drug addiction but assessed only subjectively.
- Reward positivity (RewP) is a reward-sensitive event-related potential.
- RewP amplitude is correlated with anhedonia and depression severity
- However, anhedonia explains a significant variance in RewP amplitude
- Significantly more than demographics, drug-use, and depression.

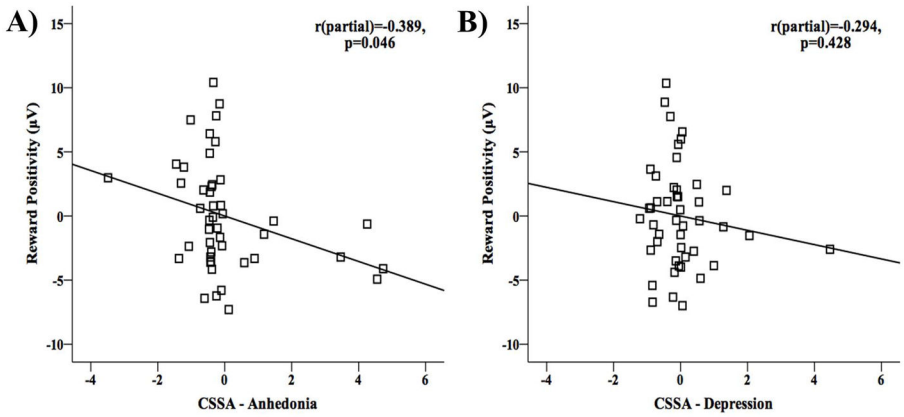

Figure 1.

Task schematic during a win trial of the gambling task. Based on a cue (1, 2, or 3), the participants select a door and then identify if they expect to win or lose in that trial. A feedback of their accuracy is provided at the end of each trial.

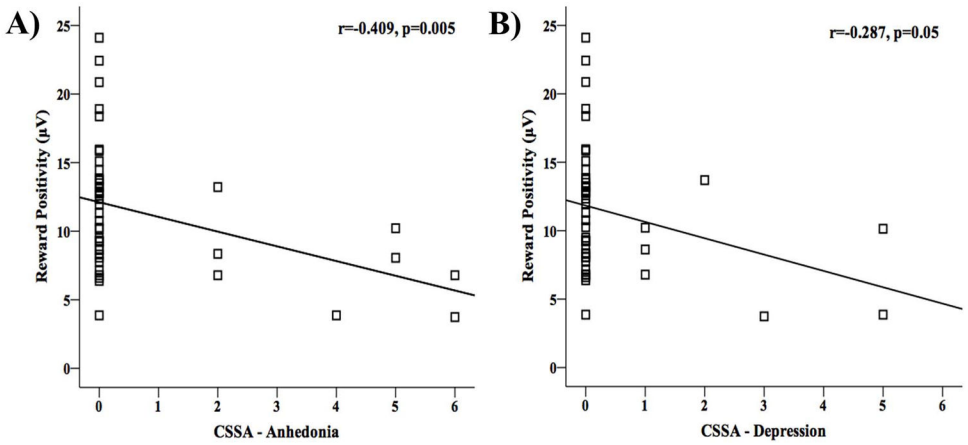

Figure 2.

(A) The time series waveforms of the ERP (red) in response to the predicted win condition, and its derived PCA factor (TF3SF1) that reflects RewP (blue). **(B)** The scalp topography with frontocentral maxima and **(C)** the dipole source location in the medial orbitofrontal cortex (Tailarach coordinates: x=0, y=21, and z=−6), are consistent with previous reports of RewP.

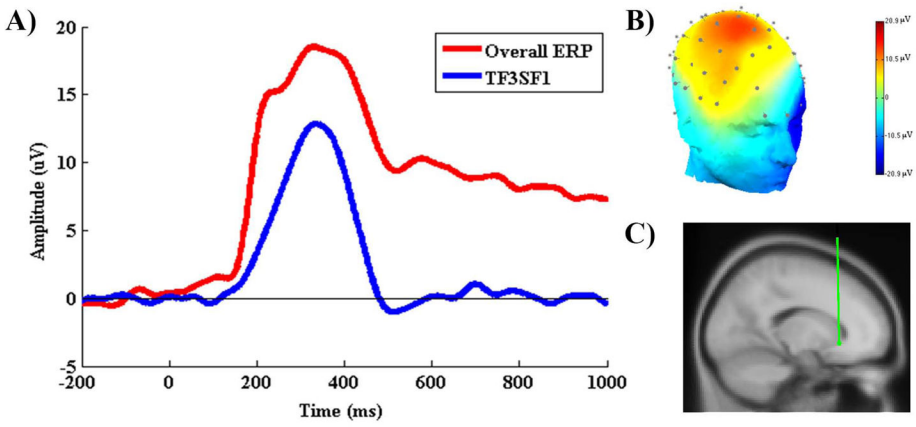

Figure 3.

The correlations between the (PCA derived) RewP amplitude and subjectively assessed (via CSSA) **(A)** anhedonia and **(B)** depression scores show that iCUD who presented higher scores on anhedonia and depression also presented lower RewP amplitudes.

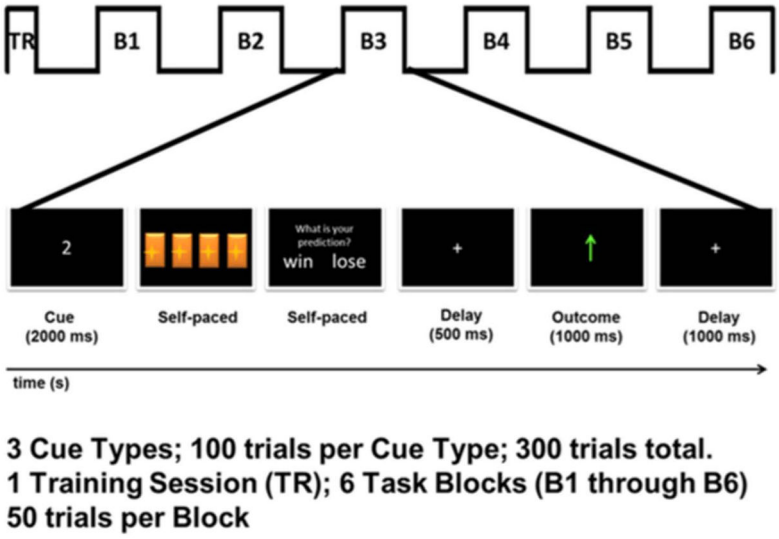

Figure 4.

The partial correlation plots (from the hierarchical multiple regression) between the RewP amplitude and **(A)** anhedonia, and **(B)** depression scores, show that unlike depression scores, anhedonia scores significantly predict the RewP amplitude.

Table 1

Demographic characteristics and drug use-related measures for iCUD.

	iCUD (*N*=46)
Demographics	
Age (years)	43.03 ± 6.9
Gender (male/female)	39/7
Race (African-American/Caucasian/Other)	28/15/3
Education (years)	12.83 ± 1.7
Drug Use	
Cigarette smokers (current/past/nonsmoker)	32/10/4
Daily cigarettes in current smokers	4.02 ± 4.6
Lifetime duration of cocaine use (years)	15.30 ± 7.9
Duration of current abstinence (days)	70.89 ± 137.6
Cocaine Craving (Cocaine Craving Questionnaire)	16.74 ± 12.65
Total Substance Dependence Scale	7.63 ± 3.8
Cocaine Selective Severity Assessment (CSSA)	
CSSA – Anhedonia	0.70 ± 1.7
CSSA – Depression	0.39 ± 1.1

Note: Values are frequencies or means ± standard deviation (S.D.).

Table 2

Summary of Hierarchical Regression Analysis for Variables predicting RewP.

Variable	B	B-SE	β	t	p	R	R^2	ΔR^2	sig. ΔF
Model 1						0.15	0.02	0.02	0.607
Age	−0.08	0.10	−0.13	−0.84	0.405				
Gender	1.98	1.99	0.16	0.99	0.328				
Model 2						0.32	0.10	0.08	0.347
Severity of dependence score	0.28	0.18	0.23	1.50	0.141				
Length of abstinence of cocaine	0.00	0.01	−0.01	−0.05	0.964				
Cigarette smokers	0.51	1.41	0.06	0.36	0.719				
Model 3						0.49	0.24	0.14*	0.012
CSSA – Anhedonia	−0.89	0.43	−0.32	−2.06*	0.046				
Model 4						0.50	0.25	0.01	0.428
CSSA – Depression	−0.56	0.67	−0.14	−0.80	0.428				

* $p<0.05$