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A neurophysiological measure of reward sensitivity and its association with anhedonia in psychiatrically healthy adolescents and young adults

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Abstract

Anhedonia (i.e., the attenuated ability to enjoy pleasurable stimuli) characterizes multiple mood disorders, but its neurophysiological underpinnings are not yet clear. Here, we measured event-related potentials in 116 adolescents and young adults engaged in an asymmetric reinforcement procedure designed to objectively characterize the anhedonic phenotype. In line with previous studies, the behavioral results showed that approximately 35% of the sample did not develop a response bias towards the more frequently rewarded stimuli (a sign of low hedonic capacity). The event-related potentials (ERPs) evoked by the reward feedback stimuli delivered during the task showed that individuals that did not develop a response bias had less cortical positivity at Fz from 224 ms to 316 ms post feedback onset compared to those that developed a response bias during the task. However, further analyses showed that this between groups difference was relatively weak, as it disappeared when we controlled for response-locked ERPs. Furthermore, the response bias observed in the asymmetric reinforcement procedure was not strongly associated with self-reported ratings of hedonic capacity. We conclude that even though the asymmetric reinforcement procedure may be used as a reward sensitivity measure in neurotypical adolescents and young adults, this task may only be able to detect clinically significant levels of anhedonia in this particular population.

Keywords

Anhedonia; Feedback Related Negativity; Reward; ERP; Adolescent; Young Adult

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Introduction

Anhedonia, the attenuated ability to enjoy pleasurable stimuli (Chapman, Chapman, & Raulin, 1976), is associated with psychiatric disorders in adults, including major depressive disorder (Loas, 1996; Treadway & Zald, 2011), bipolar disorder (Pizzagalli, Goetz, Ostacher, Iosifescu, & Perlis, 2008), schizophrenia (Gard, Kring, Gard, Horan, & Green, 2007; Kwapil, 1998), and substance use disorder (Garfield, Lubman, & Yucel, 2014; Markou, Kosten, & Koob, 1998). In adolescents, anhedonia is associated with enhanced depression severity and longer time to remission (Bennik, Nederhof, Ormel, & Oldehinkel, 2014; Gabbay et al., 2015; McMakin et al., 2012). Given its clinical relevance, understanding the neurophysiological mechanisms underlying anhedonia is extremely significant as it can contribute to the improvement of diagnostic procedures and clinical interventions (Der-Avakian, Barnes, Markou, & Pizzagalli, 2015).

Anhedonia is generally measured using self-report questionnaires, but many of these questionnaires may not generalize to a large portion of the population. For instance, some anhedonia scales may be culturally biased and may not be relevant to all nationalities or age groups (Leventhal, Chasson, Tapia, Miller, & Pettit, 2006). The Snaith-Hamilton Pleasure Scale (SHAPS; Snaith et al., 1995) was specifically developed to overcome these limitations by including general statements reflecting the ability to experience pleasure during everyday events that do not depend on social class, gender, age, dietary habits, or nationality (e.g. “I would enjoy being with my family or close friends”). Due to these characteristics, the SHAPS is considered a reliable index of anhedonia in both adult (Gilbert, Allan, Brough, Melley, & Miles, 2002; Leventhal et al., 2006) and younger populations (Leventhal et al., 2015). However, self-report measures cannot provide information about the neurophysiological underpinnings that contribute to the manifestation of anhedonia.

To supplement self-reports, Pizzagalli and colleagues (2005) developed a behavioral task aimed at objectively measuring sensitivity to reward, a key feature of anhedonia. In this asymmetric reinforcement procedure, the participant differentiates between two perceptually similar stimuli (a line drawing of a face with either a long or short mouth). During the task, a portion of correct responses are immediately followed by a reward feedback indicating a monetary gain. However, unbeknownst to the participant, one response is rewarded more frequently than the other. Due to the difficult nature of the task (the mouth lengths are nearly identical), the participant operates under high perceptual uncertainty, therefore often “guessing” the answer. Under this asymmetric reinforcement ratio, individuals who are more sensitive to reward should be more likely to develop a response bias toward “guessing” the mouth length that is rewarded most often, while those who are less sensitive to rewards should be less likely to develop such a bias. Empirical findings indicate that individuals with high scores on self-report scales of anhedonia are less likely to develop a response bias towards the frequently rewarded stimulus compared to controls (Bogdan & Pizzagalli, 2006; Pizzagalli, Goetz, et al., 2008; Pizzagalli, Iosifescu, Hallett, Ratner, & Fava, 2008; Pizzagalli et al., 2005; Santesso, Dillon, et al., 2008).

One advantage of this asymmetric reinforcement procedure is that it allows researchers to record neurophysiological responses to the stimuli indicating monetary gains, specifically

the amplitude of the feedback related negativity (FRN; Cohen, Elger, & Ranganath, 2007). Typically, the FRN is described as a negative-going component of the event-related potential (ERP) that peaks between 200 and 400ms post-stimulus onset. This ERP component has been suggested to reflect performance monitoring, as it is generated when performance expectations are violated by feedback indicating unexpected outcomes (Hajcak, Holroyd, Moser, & Simons, 2005; Holroyd & Coles, 2008; Holroyd & Coles, 2002; Oliveira, McDonald, & Goodman, 2007). The results that Santesso et al. (2008) obtained recording ERPs during the asymmetric reinforcement procedure described above seem in line with this interpretation. Santesso et al. (2008) showed that the feedback stimuli signaling monetary gains evoke a larger FRN in individuals who do not develop a response bias (i.e. are less sensitive to rewards) relative to individuals who develop a response bias (i.e., are sensitive to rewards). The amplitude of the FRN also correlates with higher levels of anhedonia (Santesso, Dillon, et al., 2008), and is enhanced for individuals with major depressive disorder compared to controls (Mueller, Pechtel, Cohen, Douglas, & Pizzagalli, 2015; Santesso, Steele, et al., 2008). These FRN differences during the asymmetric reinforcement procedure may also be described as due to differences in the amplitude of the reward positivity (RewP), a positive going component that follows rewards (such as the feedback signaling a correct response in the asymmetric reinforcement procedure) and overlaps with the FRN (Foti, Weinberg, Dien, & Hajcak, 2011; Proudfit, 2015).

Taken together, these electrophysiological and behavioral results are promising because they provide objective measures of anhedonia that are not possible when solely relying on self-report measures. Additionally, measuring the ERPs offers the opportunity to investigate the neural mechanisms that underlie anhedonic symptomology. Thus, combining information from electrophysiological, behavioral, and self-report measures can provide a more accurate assessment and, ultimately, improve treatments for individuals with anhedonia.

While these studies provide insight into reward learning, they were conducted with college aged adults and it is unclear the extent to which they translate to younger individuals. Due to the association between anhedonia and both increased depression severity and longer time to remission in the adolescent population (Bennik et al., 2014; Gabbay et al., 2015; McMakin et al., 2012), it is critical that the assessment of anhedonia in adolescents is as accurate as possible. However, electrophysiological research in this population is limited. We thus sought to replicate the neurobehavioral results from Santesso and colleagues (2008) while also extending our focus towards younger individuals.

Here we collected self-report, behavioral, and electrophysiological data to assess the multiple components contributing to anhedonia in adolescents and young adults. After completing questionnaires, participants performed the asymmetric reinforcement procedure while we continuously collected electroencephalogram (EEG). We hypothesized that individuals with reduced reward sensitivity, (as measured by their performance on the asymmetric reinforcement procedure) would report greater anhedonia scores on the SHAPS and exhibit a less negative FRN to reward feedback stimuli delivered during the asymmetric reinforcement procedure.

Method

Participants

All study procedures were approved by the Institutional Review Board at the University of Oklahoma Health Sciences Center (OUHSC). A total of 122 participants were recruited at the OUHSC Tobacco Research Center. Due to technical problems, data from six participants were not usable, hence 116 subjects were included in the final data set. Participants were young individuals (14–21 years old, 17.2 avg.; 60 female/55 male) recruited using flyers distributed at local community centers and by contacting local high schools. Participants reported being in good health and free of any psychological disorders. Written consent was obtained from all participants. For participants under the age of 18 ($n=61$), we also obtained in-person consent from a legal guardian. In addition to the procedures described below, the participants also viewed a slideshow depicting various naturalistic scenes. Those data are being analyzed and will be published elsewhere.

Questionnaires

Before participating in the EEG session, participants completed the following questionnaires: the Barratt Impulsivity Scale (BIS; Patton, Stanford, & Barratt, 1995), Positive and Negative Affect Scale (PANAS; Watson, Clark, & Tellegen, 1988), and the Snaith-Hamilton Pleasure Schedule (SHAPS; Snaith et al., 1995). The BIS is designed to measure impulsiveness by including eight items related to impulsive or non-impulsive behaviors and preferences (e.g. “I concentrate easily”). The PANAS measures positive and negative affect where participants endorse a series of 20 items (e.g. “During the past week I felt upset”). The SHAPS was specifically designed to measure anhedonia across age and cultural groups and contains 16 items for participants to endorse (e.g., “I would get pleasure from helping others”). The SHAPS was coded from zero to three, with three denoting the highest level of anhedonia on each item and zero denoting no anhedonia (Leventhal et al., 2015). We decided to code the SHAPS in this manner, instead of the original 0–1 rating, to obtain a more continuous, and therefore sensitive, measure of anhedonia. Participant gender, age, and questionnaire scores are reported in Table 1. To assess the association between reward sensitivity and anhedonia, for each questionnaire we conducted a one-way ANOVA between learners and non-learners (see Reward bias and task performance, below) using the average score for each participant.

Asymmetric reinforcement procedure

Before starting, a research assistant described the experiment to the participant, and explained that the task offered the possibility to gain real money that would be paid at the end of the session. Eight practice trials were then completed (with the option to repeat the practice trials) to make sure that the participants understood the procedure. The asymmetric reinforcement procedure was implemented using E-prime software (version 2.0; Psychology Tools, Pittsburgh, PA) and the stimuli were presented on a LCD screen placed approximately 60 cm from the participant.

Participants completed three task blocks of at least 100 trials each, dependent on task performance (see controlled reinforcer procedure, below). For each trial (Fig. 1), a line-

drawn face with no mouth would appear on the screen for 500ms, followed by a long or short mouth superimposed for 100ms. The participant then had up to 1500ms to decide if they had seen a short or a long mouth by pressing the “f” or “j” key on the keyboard (key assignment was counterbalanced across participants). The key press was followed by a blank screen on 60% of trials (non-reinforced trials), while on 40% of trials the key press was followed by feedback indicating that the participant had won five cents (reinforced trials). Unbeknownst to the participant, one of the two faces (either to the long or to the short mouth, counterbalanced across participants) was rewarded three times more frequently than the other (90 out of 120 total feedback trials). To ensure that the 3:1 reinforcement ratio for “rich” (i.e., the condition rewarded more often) and “lean” (i.e., the condition rewarded less often) conditions would remain the same in every block for all participants, rather than relying on a fixed trial sequence, we implemented a controlled reinforcer procedure. The procedure was implemented as follows, if the participant chose the wrong response in a trial designated to be followed by feedback, that trial was immediately repeated and feedback was withheld until the participant answered correctly. This procedure ensures that all participants receive, in every block, 30 reinforcers in the rich condition and 10 in the lean condition. By ensuring that the 3:1 reinforcement ratio is maintained for every participant throughout the task (the pre-requisite to evaluate individual differences in response-bias development), this procedure eliminates the need of discarding individuals not achieving a critical threshold of reinforcers in the rich or lean conditions because of missed trials (e.g., a ratio of at least 2.5:1, supplementary materials Webb et al., 2016), while also preventing missed trials to accumulate at the end of each block (Pizzagalli, 2005). However, this procedure also has some potential disadvantages. One is that it might lead to an infinite loop if a participant perseverates in making the same error in a trial designated to be reinforced. This was not the case for any of our participants (supplementary Figure S4 shows the number of additional trials delivered in each block because of errors in the to-be-reinforced trials). **Another limitation of our procedure is that, by withholding the feedback until the participant choses the correct response in the trials designated to be reinforced, it increases the number of nonreinforced trials, hence reducing the probability of rich to lean reinforcement across the entire task (Please see Supplement for a detailed description of the drawbacks of the asymmetric reinforcement procedure).** The task included three blocks with a short break between blocks to allow the participant to relax. Each block included 40 reinforced trials (30 rich, 10 lean), 60 non-reinforced trials (30 rich and 30 lean), plus the additional non-reinforced trials due to the errors made in the trials designated to be reinforced (on average 9 in the lean and 18 in the rich condition, supplementary figure S4). Within each block, reinforced and non-reinforced trials were presented randomly within sequences of 10 trials each (4 reinforced and 6 non-reinforced). Each trial was preceded by a variable interval that lasted between 500 and 1500 ms. All trials with reaction times under 100 ms. and the additional trials following errors in the trials designated to be reinforced, were excluded from the analyses.

Reward bias and task performance

In order to determine individual performance and identify individuals that developed a bias towards the more frequently rewarded stimulus (i.e. either the long or the short mouth), for each block we calculated discrimination and bias index scores applying the formulas

reported in Figure 2 (Panels A and B). Our controlled reinforcer procedure ensured that all participants received the same number of reinforced trials in the rich and lean conditions (i.e., 90 and 30 respectively). Since all participants received the same number of reinforcers, by including these trials in the computations would have distorted the estimates for both bias and discrimination index because we would have added the same “tare” to the actual performance of each individual. Hence, all computations to calculate discrimination and bias measures excluded the reinforced trials and used exclusively non-reinforced trials, where responses reflect the bias that a participant develops as a consequence of the asymmetric schedule in the reinforced condition. To allow calculations if any cell in the formula matrix had a value of zero, we added 0.5 to every cell (Hautus, 1995; Pizzagalli, Iosifescu, et al., 2008; Snodgrass & Corwin, 1988). We subtracted the bias index score of block one from the bias index score of block three. As a result, scores greater than zero denote individuals that, during the task, develop a progressively stronger response bias toward the condition reinforced more often. We labeled these individuals as learners. Scores less than or equal to zero indicate individuals that do not develop a bias toward the more frequently reinforced condition. We labeled these individuals as non-learners. We also computed the discrimination index for each block in order to ensure that bias changes were not the consequence of changes in performance accuracy. In addition to dichotomizing the sample in learners and non-learners, we conducted supplementary analyses using the bias differences scores (block 3 minus block 1) as a continuous measure.

EEG acquisition and data reduction

We recorded continuous EEG using a 32-channel actiCAP system (Brain Products GmbH, Gilching, Germany) and sampled at 500 Hz with electrodes positioned according to the 10/20 system. We then referenced each pre-amplified electrode to Cz. We set software filters to a 100Hz high cutoff and a 60Hz notch, and re-referenced the data offline to the average reference and corrected eyeblinks using Brain Electrical Source Analysis software (BESA GmbH, Gräfelfing, Germany). We then exported the data to BrainVision Analyzer (Brain Products GmbH, Gilching, Germany), where the data were filtered using 40 Hz low-pass and 0.1 Hz high-pass cutoffs, segmented (300ms pre- to 800ms post-response onset), and baseline corrected from 200ms prior to the response. Because, in this task, the feedback appears immediately after the response, time locking the ERPs to the response is effectively the same as time locking the ERPs to the feedback onset. We marked each segment as contaminated by artifacts if the waveform had a voltage step greater than 10 $\mu\text{V}/\text{ms}$, a maximal voltage difference greater than 70 μV over 50ms, less than 0.5 μV over 100ms, or amplitudes above 100 μV or below $-100 \mu\text{V}$. We interpolated channels using their four nearest neighbors if greater than 40% of a channel's segments were contaminated by such artifacts.

ERP Analysis

We focused our analyses on the ERPs observed at channel Fz in response to feedback on the rich trials. We selected this channel because previous work (Santesso, Dillon, et al., 2008) indicates that Fz is the site where the difference in the amplitude of the ERPs evoked by feedback stimuli signaling rewards recorded in learners and non-learners is the largest. Furthermore, following Santesso and colleagues, we computed the ERPs including only

trials in the rich condition (i.e., the most frequently reinforced condition). To assess ERP differences between learners and non-learners, and to avoid biasing the ERP estimates by measuring peak differences within arbitrary time windows (Clayson, Baldwin, & Larson, 2013; Keil et al., 2014; Luck, 2005a; Luck & Gaspelin, 2017), we computed a one-way ANOVA at each time point, up to 800ms after feedback onset. To correct for multiple comparisons, we used a randomization approach (Maris, 2012).

During the asymmetric reinforcement procedure, the feedback appears immediately after the response. Hence, the electrocortical responses evoked by the feedback may be confounded with those evoked by the motor response. To isolate the electrocortical activity specifically evoked by the feedback stimuli, we took advantage of the fact that, during the task, 60% of the responses are not followed by a feedback stimulus. Hence, for each participant, we also calculated the ERPs evoked by the trials not followed by feedback stimuli and subtracted them from the ERPs evoked by the trials followed by the feedback stimuli. This resulted in a difference waveform corrected for motor response for every participant (Kappenman & Luck, 2011). To test for the presence of differences between learners and non-learners on these difference waves, we computed a one-way ANOVA at each time point up to 800 ms post feedback onset.

Age-related analysis

To determine how age influenced results, we divided participants into terciles. We calculated terciles to maximize the difference between age groups while maintaining a suitable number of participants with equal group sizes. The oldest tercile group consisted of 19, 20, and 21-year old participants. The youngest tercile group consisted of 14 and 15-year old participants. Each of these groups included 37 participants. We conducted supplementary analyses using age as a continuous variable.

Results

Behavioral paradigm

We first evaluated participant task performance across blocks. As seen in Figure 2c, participants' discrimination of the correct stimulus did not improve across the three blocks. It was critical that participants performed this way because a bias towards the more frequently reinforced stimulus can only develop when the participant is uncertain of the correct answer. In fact, on average, participants *did* develop a bias toward the more frequently rewarded stimulus (Fig. 2d). Furthermore, as expected, this trend was not present in all of the participants; after subtracting the bias scores of block one from block three, a total of 76 individuals showed a positive difference (learners) and 40 individuals showed a negative difference (non-learners; Fig. 2f). The discrimination score remained constant across the blocks and comparable in both groups (Fig. 2e). The supplement details the results of a series of post-hoc analyses aimed at evaluating the strength of the correlations between bias differences scores (block 3 minus block 1) and age, ERPs, and questionnaire measures. We found that only bias scores and age were somewhat correlated ($r=0.18$, $p=0.05$; supplementary figure S1). However, this trend was mainly driven by two outliers

that had scores exceeding three standard deviations from the mean. When we removed these two outliers, the trend was no longer statistically significant ($r=0.15$, $p=0.10$).

Questionnaires

We next tested the relationship between reward learning and self-reported anhedonia. While non learners had slightly higher anhedonia scores than learners on the SHAPS, this difference was not significant for neither SHAPS scored from zero to three (Fig. 3; $F_{(1,114)}=1.46$, $p=0.23$), nor from zero to one ($F_{(1,114)}=0.50$, $p=0.48$). This might be due to our sample consisting of healthy individuals with a relatively narrow range of self-reported anhedonia scores. We also found no group differences in scores on the BIS ($F_{(1,114)}=1.34$, $p=0.25$), PANAS positive ($F_{(1,114)}=0.63$, $p=0.43$), or PANAS negative ($F_{(1,114)}=0.12$, $p=0.73$). Therefore, in this particular pool of healthy participants, it appears that reward learning does not differentiate individuals with high versus low anhedonia, as measured by the SHAPS.

ERPs

Feedback trials.—In order to assess electrocortical differences between learners and non-learners, we conducted at channel Fz a point by point analysis from 300 ms before feedback onset to 800 ms post-feedback onset on rich trials. As shown in Figure 4a, the feedback stimuli prompted less positivity in the ERPs of non-learners than learners and this difference crossed the (uncorrected for multiple comparisons) statistical threshold of $p<.05$ at 224 ms and remained above this threshold until 316 ms. While the differences did not survive correction for multiple comparisons when using a $p=0.05$ cutoff created using randomization tests (10,000 random permutations run on all data points in the time series), an additional post-hoc t test indicated a difference between learners and non-learners within an averaged ERP window of 250–350ms post-feedback onset ($t_{(114)}=2.40$, $p=0.02$, two-tailed). To ensure that the difference between learners and non-learners (for frequent feedback trials) was maximal at channel Fz, we tested also electrodes Cz, and the average of FC1 and FC2 (to approximate voltage at FCz, the other electrode presented by Santesso et al (2008). Indeed, neither the difference observed at Cz ($t_{(114)}=0.45$), nor that observed by averaging FC1 and FC2 ($t_{(114)}=1.27$), approached significance. Notwithstanding fewer trials contributed to the averages, the FRN observed in the lean condition was similar to the FRN observed in the rich condition, however the difference between learners and non-learners was less reliable and did not reach statistical significance using the average 250–350ms window ($t_{(114)}=1.6$, $p=0.11$, two-tailed; see supplementary Figure S2a). Furthermore, notwithstanding the lower number of trials in the lean condition, these results are remarkably similar to those reported in the rich condition (supplementary Figure S2a). We think that the lack of differences between ERPs in the rich and lean conditions is to be expected because rich and lean trials are perceptually identical and are followed by identical monetary rewards. No significant correlations were found between the 250–350ms ERP window and age, bias, or SHAPS scores (supplementary Figure S3abc).

Non-feedback trials.—In order to determine the effect of motor response on the ERPs, we also analyzed the between-groups differences in the waveforms prompted by rich trials not followed by feedback (Fig. 4b). Similarly to what we observed at channel Fz when

responses were followed by feedback, non-learners showed less positivity than learners and this difference crossed the (uncorrected for multiple comparisons) statistical threshold of $p < .05$ at 206 ms and remained above this threshold (for the most part) until 290 ms. When comparing the ERP using the average amplitude from 250 to 350ms, a difference between learners and non-learners was only found for a one tailed t test ($t_{(114)}=1.79$, $p=0.04$). No significant differences were found in the lean conditions ($t_{(114)}=0.92$, $p=0.36$, two-tailed; see supplementary Figure S2b)

Feedback minus non-feedback trials—To isolate the electrocortical activity specifically evoked by the feedback stimuli, we conducted an analysis subtracting the voltage observed in non-feedback from the voltage observed in the feedback trials. Figure 4c shows that after computing the difference waves, the voltage difference between the two groups shrank and it was no longer statistically significant, neither when we considered the point-by-point ANOVAs, nor when we considered the 250–350ms window ($t_{(114)}=1.31$, $p=0.19$, two-tailed). The supplementary Figure S2c shows that the between group differences disappeared also when the difference scores were computed on the waveforms recorded in the lean condition.

Age-related and gender effects

To determine the extent to which age influenced the results, we divided the whole sample into terciles and compared the oldest (19, 20, and 21 years old) and youngest (14 and 15 years old) terciles. The proportion of learners to non-learners was not statistically different between the upper and the lower tercile ($X^2=0.668$, $p=0.41$; Table 2). We found that older participants endorsed lower scores of anhedonia on the SHAPS than the younger participants ($F_{(1,72)}=14.20$, $p<0.001$). The ERP analyses conducted on each age group replicated the results observed in the whole sample: while feedback stimuli evoked slightly more positivity in learners than non-learners, this difference never approached significance. Furthermore, no difference in bias scores was found between males and females ($F_{(1,114)}=1.33$; $p=0.25$). While, our post-hoc correlational analysis (see supplementary Figure S1 panel E) indicated that age and bias were correlated at a marginally significant level ($r=0.18$, $p=0.05$), this effect disappeared ($r=0.15$, $p=0.10$) after removal of two outliers with bias scores outside three standard deviations from the mean. We did, however, find a negative correlation between age and SHAPS score, such that older individuals endorsed lower levels of anhedonia ($r=-0.31$, $p<0.001$).

Discussion

Here we sought to replicate and extend previous work supporting the use of ERPs as an electrocortical index of anhedonia during an asymmetric reinforcement procedure. We successfully used the asymmetric reinforcement procedure to identify differences in reward sensitivity in a group of young participants. However, unlike previous studies Santesso, Dillon, et al. (2008), those who were relatively insensitive to reward did not report significantly lower anhedonia scores compared to their reward sensitive peers. We successfully replicated previous results showing that reward feedback evoked less positive ERPs in non-learners relative to learners. However, we also showed that a similar difference

was present in trials not followed by reward feedback. When we disentangled the feedback-related effects from the response-related effects by computing a difference wave, the voltage difference between learners and non-learners almost disappeared and did not approach statistical significance (Fig. 4c).

ERPs

We implemented the asymmetric reinforcement procedure following established procedures (Pizzagalli et al., 2005; Santesso, Dillon, et al., 2008) and the feedback stimuli were presented as soon as the participant pushed the response button. As a consequence, the ERPs evoked by the feedback stimuli are confounded with the ERPs evoked by the responses. To remove the contribution of the motor response from the ERPs generated by the feedback stimuli, we computed difference waves. By isolating the ERP components evoked exclusively after feedback presentation, we expected to magnify the electrocortical differences between learners and non-learners. However, upon conducting this subtraction, the electrocortical differences between learners and non-learners no longer approached statistical significance, even when no correction for multiple comparisons was applied. While this outcome was unexpected, similar findings have been presented by others (Bismark, Hajcak, Whitworth, & Allen, 2013; Weinberg, Luhmann, Bress, & Hajcak, 2012). Weinberg and colleagues (2012), for instance, implemented a task in which participants had to make a decision and received feedback either one second after their motor response or six seconds after their motor response. They found that the FRN was present after one second, but eliminated after six seconds. The authors suggested that the elimination of the FRN after an extended delay may be due to interference between maintaining response-feedback contingencies. On the other hand, the results from Bismark et al. (2013) suggest that if the feedback is delivered before the subject has a chance to develop an expectation about the outcome, the feedback might not generate an FRN. Our results indicate that the individuals that develop a response bias towards the trials more often reinforced, tend to have ERPs that are more positive than in individuals not developing a response bias even when no feedback is provided (see figure 4C). Hence, the FRN differences observed when feedback stimuli are delivered immediately after the response seem to depend on a contribution of both feedback-related and response-related processes.

Although beyond the scope of the current work, we should also mention that in the past few years researchers proposed a different interpretation of ERPs evoked by feedback stimuli. Initially, the FRN was described as a negative-going component that followed feedback stimuli indicating negative outcomes such as errors or losses (Luck, 2005b; Miltner, Braun, & Coles, 1997). However, the results from more recent studies focusing on how gains affect the FRN (Holroyd, Pakzad-Vaezi, & Krigolson, 2008; Proudfit, 2015) suggest that rewards generate a positive wave component, called the RewP, rather than losses generating a negative-going component (Foti et al., 2011; Liu et al., 2014). The authors reached this conclusion by considering another component that is generated by task-relevant stimuli (i.e., both gain and loss feedback stimuli): the N200. The N200 is a negative-going component that has a similar temporal evolution and spatial distribution as the FRN (Baker & Holroyd, 2008; Baker & Holroyd, 2011; Gehring & Willoughby, 2002). Applying PCA analyses on the ERPs evoked by both losses and gains, Foti and colleagues (2011) demonstrated that

while both gains and losses evoke an N200, only gains evoke the RewP. However, due to temporal and spatial overlap, the RewP is masked by the N200. The characteristics of the asymmetric reinforcement procedure used here, where participants only received feedback stimuli signaling positive outcomes, seems more compatible with this interpretation. Hence, these results could be interpreted as showing that rewarding stimuli evoke more positive ERPs in individuals more sensitive to rewards than in individuals less sensitive to rewards. This hypothesis could be tested in future studies by introducing negative feedback trials to the asymmetric reinforcement procedure that we used. If the results observed here are due to larger RewP evoked by individuals sensitive to rewards, then the FRN (or, rather, the N200) to the negative outcomes should be similar in both groups.

Given the importance of maintaining the 3:1 ratio between rich and lean reinforced trials to appropriately evaluate individual differences in response bias, we did not rely on fixed trial sequences within task blocks. Instead, we applied a controlled reinforcer procedure that aimed at eliminating the need of excluding participants not achieving an appropriate ratio between rich and lean trials (e.g., 2.5:1 as see supplementary materials in Webb et al., 2016). Furthermore, it does not allow the missed reinforced trials to accumulate at the end of each task block Pizzagalli (2005). Thus, implementing this controlled reinforcer procedure aimed at maximizing the efficiency of our recruitment efforts because it allowed us to retain in the analyses more participants than those that a fixed trial sequence would have allowed.

However, while our procedure guaranteed that all participants saw the reinforced trials with a 3:1 ratio between rich and lean conditions, by withholding the feedback and repeating the incorrect trials designated for reinforcement, it varied the proportion of rich and lean trials across the whole task. Counterintuitively, this approach resulted in a weaker overall asymmetrical reinforcement schedule. It is possible that this contributed to the reduction of power to detect a difference in SHAPS scores between learners and non-learners (see next section), as the distribution of bias scores could have been different with a stronger asymmetric reinforcement ratio. We refer the reader to the supplementary materials for specific examples of reinforcement schedules produced by the controlled reinforcer procedure.

Anhedonia

Contrary to our initial hypothesis, we did not find differences in reward sensitivity, as measured by the asymmetric reinforcement procedure, between individuals who endorsed high versus low anhedonia scores on the SHAPS. This was surprising because enhanced FRN amplitude (i.e. more negativity) has been found both in individuals with depression (Foti, Carlson, Sauder, & Proudfit, 2014; Liu et al., 2014) and in healthy individuals endorsing higher depression scores than their peers (Foti & Hajcak, 2009). However this is not always the case, as work by Chen and colleagues (2018) recently found no differences in FRN amplitude between anhedonic (determined using the Temporal Experience of Pleasure Scale; Gard, Gard, Kring, & John, 2006) and healthy control participants for either reward or punishment contexts, although they did not employ the asymmetric reinforcement procedure. It is also possible that, for healthy adolescents, the questionnaire (and self-report assessments of anhedonia in general) may not be sensitive enough to correlate with the subtle differences in reward sensitivity evinced by the asymmetric reinforcement procedure.

For instance, Whitton and colleagues (2016) used the asymmetric reinforcement procedure to assess reward learning in individuals with fully remitted major depressive disorder (rMDD) and control participants. They found that individuals with rMDD exhibited reduced reward learning and a reduced RewP, compared to controls, while controlling for Beck Depression Inventory II scores (BDI-II; Beck, Steer, & Brown, 1996). This would suggest increased sensitivity of behavioral measures and supports the value of neurological biomarkers, as compared to self-report measures. As these kind of behavioral and neurological measures are inherently agnostic to cognitive bias, they may be the best approach to detecting sub-clinical levels of a psychiatric illness, and even predicting potential future psychological illness. For example, Kujawa and colleagues (2014) demonstrated that the RewP is reduced among children (without depression) with mothers who endorse more severe MDD symptoms. In another study, the RewP was used to predict future depression in never-depressed individuals (Bress, Foti, Kotov, Klein, & Hajcak, 2013).

Conclusion

In sum, given our relatively large sample size, we were able to closely replicate the results found in adults by Santesso and colleagues (2008); individuals that did not develop a bias during the asymmetric reinforcement procedure had less positive ERPs within a time window compatible with the FRN, compared to people who did develop a bias. However, these ERP differences were relatively weak and only met the conventional $p < 0.05$ threshold when no correction for multiple comparisons was applied. Furthermore, when we removed the confound due to the overlapping motor response, to exclusively examine the effects due to the feedback, the ERP negativity difference between groups essentially disappeared. This was surprising, as we expected more robust differences to emerge from the ERPs between groups when both removing potential confounds and including a large sample size. This outcome underscores the potential need of modifying the task by introducing a delay between response and feedback to record a pure feedback response without the need of computing a difference wave. However, regardless of the contribution of the motor response, the asymmetric reinforcement procedure was successful in differentiating hedonic capacity in young adults. In fact, it is plausible that the asymmetric reinforcement procedure is more sensitive in detecting hedonic capacity in healthy young adults than self-report measures (e.g. the SHAPS).

The rates of major depressive disorder are high among adolescents (Hankin et al., 1998; Oldehinkel, Wittchen, & Schuster, 1999) and anhedonia is a distinct predictor of this disorder (Bennik et al., 2014; Gabbay et al., 2015; McMakin et al., 2012), which also predicts higher rates of substance use among the adolescent population (Luby et al., 2018). It is therefore of critical importance to understand the neurophysiological underpinnings of anhedonia and to continue to develop markers of depressive mood disorders. Although the difference between groups that we observed here were weak, it is still possible that the asymmetric reinforcement procedure may be successfully implemented in young individuals to objectively assess individual differences in hedonic capacity. Including a delay between the response and the feedback onset will facilitate the interpretation of ERP results collected during the task. As mentioned above, our study only included healthy adolescents, and the

asymmetric reinforcement procedure may yield better results when comparing healthy controls to individuals with a clinically significant depressive mood disorder. This task may be additionally useful as it is an objective measure of reward sensitivity and may therefore be used to measure a distinct endophenotype associated with depression (Hasler, Drevets, Manji, & Charney, 2004). Thus, future studies investigating anhedonia among adolescent populations should continue to explore the utility of the asymmetric reinforcement procedure while incorporating electrophysiological data collection to better define the elements of anhedonia not captured by self-reports.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

- Baker TE, & Holroyd CB (2008). Which way do I go? Neural activation in response to feedback and spatial processing in a virtual T-maze. *Cerebral Cortex*, 19(8), 1708–1722. [PubMed: 19073622]
- Baker TE, & Holroyd CB (2011). Dissociated roles of the anterior cingulate cortex in reward and conflict processing as revealed by the feedback error-related negativity and N200. *Biological Psychology*, 87(1), 25–34. 10.1016/j.biopsycho.2011.01.010 [PubMed: 21295109]
- Beck A, Steer R, & Brown G (1996). Beck depression inventory manual. 2nd. San Antonio, TX: Psychological Corporation.
- Bennik EC, Nederhof E, Ormel J, & Oldehinkel AJ (2014). Anhedonia and depressed mood in adolescence: course, stability, and reciprocal relation in the TRAILS study. *Eur Child Adolesc Psychiatry*, 23(7), 579–586. 10.1007/s00787-013-0481-z [PubMed: 24154568]
- Bismark AW, Hajcak G, Whitworth NM, & Allen JJ (2013). The role of outcome expectations in the generation of the feedback-related negativity. *Psychophysiology*, 50(2), 125–133. 10.1111/j.1469-8986.2012.01490.x [PubMed: 23153354]
- Bogdan R, & Pizzagalli DA (2006). Acute stress reduces reward responsiveness: implications for depression. *Biol Psychiatry*, 60(10), 1147–1154. 10.1016/j.biopsych.2006.03.037 [PubMed: 16806107]
- Bress JN, Foti D, Kotov R, Klein DN, & Hajcak G (2013). Blunted neural response to rewards prospectively predicts depression in adolescent girls. *Psychophysiology*, 50(1), 74–81. 10.1111/j.1469-8986.2012.01485.x [PubMed: 23252717]
- Chapman LJ, Chapman JP, & Raulin ML (1976). Scales for physical and social anhedonia. *J Abnorm Psychol*, 85(4), 374–382. [PubMed: 956504]
- Chen Y, Xu J, Zhou L, & Zheng Y (2018). The time course of incentive processing in anticipatory and consummatory anhedonia. *J Affect Disord*, 238, 442–450. 10.1016/j.jad.2018.05.053 [PubMed: 29913381]
- Clayson PE, Baldwin SA, & Larson MJ (2013). How does noise affect amplitude and latency measurement of event-related potentials (ERPs)? A methodological critique and simulation study. *Psychophysiology*, 50(2), 174–186. [PubMed: 23216521]
- Cohen MX, Elger CE, & Ranganath C (2007). Reward expectation modulates feedback-related negativity and EEG spectra. *Neuroimage*, 35(2), 968–978. 10.1016/j.neuroimage.2006.11.056 [PubMed: 17257860]

- Der-Avakian A, Barnes SA, Markou A, & Pizzagalli DA (2015). Translational assessment of reward and motivational deficits in psychiatric disorders In *Translational Neuropsychopharmacology* (pp. 231–262): Springer.
- Foti D, Carlson JM, Sauder CL, & Proudfit GH (2014). Reward dysfunction in major depression: multimodal neuroimaging evidence for refining the melancholic phenotype. *Neuroimage*, 101, 50–58. 10.1016/j.neuroimage.2014.06.058 [PubMed: 24996119]
- Foti D, & Hajcak G (2009). Depression and reduced sensitivity to non-rewards versus rewards: Evidence from event-related potentials. *Biol Psychol*, 81(1), 1–8. 10.1016/j.biopsycho.2008.12.004 [PubMed: 19162124]
- Foti D, Weinberg A, Dien J, & Hajcak G (2011). Event-related potential activity in the basal ganglia differentiates rewards from nonrewards: temporospatial principal components analysis and source localization of the feedback negativity. *Hum Brain Mapp*, 32(12), 2207–2216. 10.1002/hbm.21182 [PubMed: 21305664]
- Gabbay V, Johnson AR, Alonso CM, Evans LK, Babb JS, & Klein RG (2015). Anhedonia, but not irritability, is associated with illness severity outcomes in adolescent major depression. *Journal of child and adolescent psychopharmacology*, 25(3), 194–200. [PubMed: 25802984]
- Gard DE, Gard MG, Kring AM, & John OP (2006). Anticipatory and consummatory components of the experience of pleasure: A scale development study. *Journal of Research in Personality*, 40(6), 1086–1102. 10.1016/j.jrp.2005.11.001
- Gard DE, Kring AM, Gard MG, Horan WP, & Green MF (2007). Anhedonia in schizophrenia: Distinctions between anticipatory and consummatory pleasure. *Schizophrenia Research*, 93(1–3), 253–260. 10.1016/j.schres.2007.03.008 [PubMed: 17490858]
- Garfield JBB, Lubman DI, & Yucel M (2014). Anhedonia in substance use disorders: A systematic review of its nature, course and clinical correlates. *Australian and New Zealand Journal of Psychiatry*, 48(1), 36–51. 10.1177/0004867413508455 [PubMed: 24270310]
- Gehring WJ, & Willoughby AR (2002). The medial frontal cortex and the rapid processing of monetary gains and losses. *Science*, 295(5563), 2279–2282. 10.1126/science.1066893 [PubMed: 11910116]
- Gilbert P, Allan S, Brough S, Melley S, & Miles JN (2002). Relationship of anhedonia and anxiety to social rank, defeat and entrapment. *J Affect Disord*, 71(1–3), 141–151. [PubMed: 12167510]
- Hajcak G, Holroyd CB, Moser JS, & Simons RF (2005). Brain potentials associated with expected and unexpected good and bad outcomes. *Psychophysiology*, 42(2), 161–170. 10.1111/j.1469-8986.2005.00278.x [PubMed: 15787853]
- Hankin BL, Abramson LY, Moffitt TE, Silva PA, McGee R, & Angell KE (1998). Development of depression from preadolescence to young adulthood: emerging gender differences in a 10-year longitudinal study. *J Abnorm Psychol*, 107(1), 128–140. [PubMed: 9505045]
- Hasler G, Drevets WC, Manji HK, & Charney DS (2004). Discovering endophenotypes for major depression. *Neuropsychopharmacology*, 29(10), 1765–1781. 10.1038/sj.npp.1300506 [PubMed: 15213704]
- Hautus MJ (1995). Corrections for extreme proportions and their biasing effects on estimated values of d' . *Behavior Research Methods, Instruments, & Computers*, 27(1), 46–51.
- Holroyd CB, & Coles MG (2008). Dorsal anterior cingulate cortex integrates reinforcement history to guide voluntary behavior. *Cortex*, 44(5), 548–559. 10.1016/j.cortex.2007.08.013 [PubMed: 18387587]
- Holroyd CB, & Coles MGH (2002). The neural basis of human error processing: reinforcement learning, dopamine, and the error-related negativity. *Psychol Rev*, 109(4), 679–709. 10.1037/0033-295X.109.4.679 [PubMed: 12374324]
- Holroyd CB, Pakzad-Vaezi KL, & Krigolson OE (2008). The feedback correct-related positivity: sensitivity of the event-related brain potential to unexpected positive feedback. *Psychophysiology*, 45(5), 688–697. 10.1111/j.1469-8986.2008.00668.x [PubMed: 18513364]
- Kappenman ES, & Luck SJ (2011). Manipulation of orthogonal neural systems together in electrophysiological recordings: the MONSTER approach to simultaneous assessment of multiple neurocognitive dimensions. *Schizophrenia bulletin*, 38(1), 92–102. [PubMed: 22080495]

- Keil A, Debener S, Gratton G, Junghofer M, Kappenman ES, Luck SJ, ... Yee CM (2014). Committee report: Publication guidelines and recommendations for studies using electroencephalography and magnetoencephalography. *Psychophysiology*, 51(1), 1–21. 10.1111/psyp.12147 [PubMed: 24147581]
- Kujawa A, Proudfit GH, & Klein DN (2014). Neural reactivity to rewards and losses in offspring of mothers and fathers with histories of depressive and anxiety disorders. *J Abnorm Psychol*, 123(2), 287–297. 10.1037/a0036285 [PubMed: 24886003]
- Kwapil TR (1998). Social anhedonia as a predictor of the development of schizophrenia-spectrum disorders. *Journal of Abnormal Psychology*, 107(4), 558–565. [PubMed: 9830243]
- Leventhal AM, Chasson GS, Tapia E, Miller EK, & Pettit JW (2006). Measuring hedonic capacity in depression: a psychometric analysis of three anhedonia scales. *J Clin Psychol*, 62(12), 1545–1558. 10.1002/jclp.20327 [PubMed: 17019674]
- Leventhal AM, Unger JB, Audrain-McGovern J, Sussman S, Volk HE, & Strong DR (2015). Measuring Anhedonia in Adolescents: A Psychometric Analysis. *J Pers Assess*, 97(5), 506–514. 10.1080/00223891.2015.1029072 [PubMed: 25893676]
- Liu WH, Wang LZ, Shang HR, Shen Y, Li Z, Cheung EF, & Chan RC (2014). The influence of anhedonia on feedback negativity in major depressive disorder. *Neuropsychologia*, 53, 213–220. 10.1016/j.neuropsychologia.2013.11.023 [PubMed: 24316199]
- Loas G (1996). Vulnerability to depression: a model centered on anhedonia. *J Affect Disord*, 41(1), 39–53. [PubMed: 8938204]
- Luby JL, Agrawal A, Belden A, Whalen D, Tillman R, & Barch DM (2018). Developmental Trajectories of the Orbitofrontal Cortex and Anhedonia in Middle Childhood and Risk for Substance Use in Adolescence in a Longitudinal Sample of Depressed and Healthy Preschoolers. *American Journal of Psychiatry*, 175(10), 1010–1021. 10.1176/appi.ajp.2018.17070777 [PubMed: 29558817]
- Luck SJ (2005a). Measuring ERP Amplitudes In Gazzaniga MS (Ed.), *An Introduction to the Event-Related Potential Technique* (pp. 230–234). Cambridge, MA: MIT Press.
- Luck SJ (2005b). A Summary of Major ERP Components In Luck SJ (Ed.), *An Introduction to the Event-related Potential Technique* (pp. 46–47). Cambridge, MA: The MIT Press.
- Luck SJ, & Gaspelin N (2017). How to get statistically significant effects in any ERP experiment (and why you shouldn't). *Psychophysiology*, 54(1), 146–157. [PubMed: 28000253]
- Maris E (2012). Statistical testing in electrophysiological studies. *Psychophysiology*, 49(4), 549–565. [PubMed: 22176204]
- Markou A, Kosten TR, & Koob GF (1998). Neurobiological similarities in depression and drug dependence: a self-medication hypothesis. *Neuropsychopharmacology*, 18(3), 135–174. 10.1016/S0893-133X(97)00113-9 [PubMed: 9471114]
- McMakin DL, Olino TM, Porta G, Dietz LJ, Emslie G, Clarke G, Brent DA (2012). Anhedonia Predicts Poorer Recovery Among Youth With Selective Serotonin Reuptake Inhibitor Treatment-Resistant Depression. *Journal of the American Academy of Child and Adolescent Psychiatry*, 51(4), 404–411. 10.1016/j.jaac.2012.01.011 [PubMed: 22449646]
- Miltner WH, Braun CH, & Coles MG (1997). Event-related brain potentials following incorrect feedback in a time-estimation task: evidence for a “generic” neural system for error detection. *J Cogn Neurosci*, 9(6), 788–798. 10.1162/jocn.1997.9.6.788 [PubMed: 23964600]
- Mueller EM, Pechtel P, Cohen AL, Douglas SR, & Pizzagalli DA (2015). Potentiated Processing of Negative Feedback in Depression Is Attenuated by Anhedonia. *Depression and Anxiety*, 32(4), 296–305. 10.1002/da.22338 [PubMed: 25620272]
- Oldehinkel AJ, Wittchen HU, & Schuster P (1999). Prevalence, 20-month incidence and outcome of unipolar depressive disorders in a community sample of adolescents. *Psychol Med*, 29(3), 655–668. [PubMed: 10405087]
- Oliveira FT, McDonald JJ, & Goodman D (2007). Performance monitoring in the anterior cingulate is not all error related: expectancy deviation and the representation of action-outcome associations. *Journal of Cognitive Neuroscience*, 19(12), 1994–2004. [PubMed: 17892382]
- Patton JH, Stanford MS, & Barratt ES (1995). Factor structure of the Barratt impulsiveness scale. *J Clin Psychol*, 51(6), 768–774. [PubMed: 8778124]

- Pizzagalli DA, Goetz E, Ostacher M, Iosifescu DV, & Perlis RH (2008). Euthymic patients with bipolar disorder show decreased reward learning in a probabilistic reward task. *Biological Psychiatry*, 64(2), 162–168. 10.1016/j.biopsych.2007.12.001 [PubMed: 18242583]
- Pizzagalli DA, Iosifescu D, Hallett LA, Ratner KG, & Fava M (2008). Reduced hedonic capacity in major depressive disorder: evidence from a probabilistic reward task. *J Psychiatr Res*, 43(1), 76–87. 10.1016/j.jpsychires.2008.03.001 [PubMed: 18433774]
- Pizzagalli DA, Jahn AL, & O'Shea JP (2005). Toward an objective characterization of an anhedonic phenotype: a signal-detection approach. *Biol Psychiatry*, 57(4), 319–327. 10.1016/j.biopsych.2004.11.026 [PubMed: 15705346]
- Proudfit GH (2015). The reward positivity: from basic research on reward to a biomarker for depression. *Psychophysiology*, 52(4), 449–459. 10.1111/psyp.12370 [PubMed: 25327938]
- Santesso DL, Dillon DG, Birk JL, Holmes AJ, Goetz E, Bogdan R, & Pizzagalli DA (2008). Individual differences in reinforcement learning: behavioral, electrophysiological, and neuroimaging correlates. *Neuroimage*, 42(2), 807–816. 10.1016/j.neuroimage.2008.05.032 [PubMed: 18595740]
- Santesso DL, Steele KT, Bogdan R, Holmes AJ, Deveney CM, Meites TM, & Pizzagalli DA (2008). Enhanced negative feedback responses in remitted depression. *Neuroreport*, 19(10), 1045–1048. 10.1097/WNR.0b013e3283036e73 [PubMed: 18580576]
- Snaith RP, Hamilton M, Morley S, Humayan A, Hargreaves D, & Trigwell P (1995). A scale for the assessment of hedonic tone the Snaith-Hamilton Pleasure Scale. *Br J Psychiatry*, 167(1), 99–103. [PubMed: 7551619]
- Snodgrass JG, & Corwin J (1988). Pragmatics of measuring recognition memory: applications to dementia and amnesia. *Journal of Experimental Psychology: General*, 117(1), 34. [PubMed: 2966230]
- Treadway MT, & Zald DH (2011). Reconsidering anhedonia in depression: lessons from translational neuroscience. *Neurosci Biobehav Rev*, 35(3), 537–555. 10.1016/j.neubiorev.2010.06.006 [PubMed: 20603146]
- Watson D, Clark LA, & Tellegen A (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol*, 54(6), 1063–1070. [PubMed: 3397865]
- Webb CA, Dillon DG, Pechtel P, Goer FK, Murray L, Huys QJ, Parsey R (2016). Neural correlates of three promising endophenotypes of depression: evidence from the EMBARC study. *Neuropsychopharmacology*, 41(2), 454. [PubMed: 26068725]
- Weinberg A, Luhmann CC, Bress JN, & Hajcak G (2012). Better late than never? The effect of feedback delay on ERP indices of reward processing. *Cognitive, Affective, & Behavioral Neuroscience*, 12(4), 671–677.
- Whitton AE, Kakani P, Foti D, Van't Veer A, Haile A, Crowley DJ, & Pizzagalli DA (2016). Blunted neural responses to reward in remitted major depression: A high-density event-related potential study. *Biol Psychiatry Cogn Neurosci Neuroimaging*, 1(1), 87–95. 10.1016/j.bpsc.2015.09.007 [PubMed: 26858994]

Highlights

- In a signal detection task, we measured behavioral and brain responses to rewards
- Rewards biased responses and evoked cortical positivity at fronto-central sites
- Rewards evoked more cortical positivity in individuals with stronger response bias
- The same individuals also had more cortical positivity after non-rewarded trials
- Response bias was not strongly associated with self-report ratings of anhedonia

Figure 1:

Asymmetric reinforcement procedure. In each trial, a line-drawn face missing the mouth would appear on the screen for 500ms, followed by a long or short mouth presented for 100ms. The participant then had up to 1500ms to decide if they had seen a short or long mouth by pressing the “f” or “j” key on the keyboard. On 40% of trials the correct key press was followed by a feedback (shown here) indicating that the participant had won 5 cents. Note that difference in mouth lengths depicted in the top left of the figure are amplified for illustration purposes; the actual mouth lengths during the task were nearly perceptually identical. Adapted from Pizzagalli et al., 2005.

Discrimination

Bias

Figure 2:

Using discrimination and bias formulas (A & B, respectively), we showed that, on average, participants did not improve performance during the task (C), but developed a response bias towards the more frequently rewarded condition (D). Participants were labeled as learners if they scored greater than zero when the bias value of block one was subtracted from block three, while those who scored less than or equal to zero were labeled as non-learners. These difference scores are plotted for both discrimination (E) and bias (F). Calculations included the number of correct (corr) and incorrect (incorr) responses to frequent (freq) and infrequent (infreq) mouth lengths that were not followed by feedback stimuli. Error bars denote 95% confidence intervals.

Figure 3: Learners (individuals that developed a response bias towards the more frequently rewarded stimuli) show no statistically significant difference on the SHAPS from non-learners (individuals who did not develop a bias; $F_{(1,114)}=1.46$, $p=0.23$). Error bars denote 95% confidence intervals.

Figure 4:

Average waveform at Fz for learners and non-learners in response to frequently rewarded (rich) trials. Grand averaged waveforms are plotted for learners and non-learners for trials in which they received the reward feedback (A), they received no feedback (B), and when waveforms following no feedback trials are subtracted from those following feedback trials (C). The solid black line at the bottom of each panel represents the pairwise one-way ANOVA conducted at each time point. ERP amplitudes and F-values of the point by point analysis are labeled on the left and right y-axes, respectively. The $p=.05$ threshold ($F=3.9$),

uncorrected for multiple comparisons, is denoted by the dotted horizontal black line. The dashed horizontal black line denotes the $p=.05$ threshold corrected using randomization tests (10,000 random permutations run on all data points in the time series); this was not used during statistical analysis, but is provided for reference. Shaded areas around the mean ERPs denote 95% confidence intervals.

Table 1.

Participant gender, age, and questionnaire scores

	Total participants (n=116)	Learners (n=76)	Non-Learners (n=40)
Gender	60 F / 56 M	42 F / 34 M	18 F / 22M
Age (years)	17.22 (± 0.22)	17.32 (± 0.27)	16.80 (± 0.37)
SHAPS	12.43 (± 0.47)	12.01 (± 0.56)	13.23 (± 0.85)
BIS	16.37 (± 0.35)	16.66 (± 0.45)	15.83 (± 0.57)
PANAS positive	47.15 (± 0.95)	46.49 (± 1.12)	48.40 (± 1.75)
PANAS negative	27.68 (± 0.85)	27.45 (± 1.04)	28.13 (± 1.50)

Table 1: Gender, age, and questionnaire average scores listed by the total sample of participants and by learners and non-learners (i.e. those who did or did not develop a response bias, respectively). Numbers in parenthesis denote the standard error of the mean. No significant differences (at $\alpha=0.05$) were found between learners and non-learners on any measure. SHAPS: Snaith Hamilton Pleasure Scale; BIS: Barratt Impulsivity Scale; PANAS: Positive and Negative Affect Schedule.

Table 2.

Number of participants in the oldest and youngest tercile groups.

Tercile (age)	Learners	Non-Learners	Total
Young (14–15)	21	15	36
Old (19–21)	25	12	37
Total	46	27	73

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