

Post-print version of Landes, Bakos, Kohls, Bartling, Schulte-Körne & Greimel (2018). Altered neural processing of reward and punishment in adolescents with Major Depressive Disorder, Journal of Affective Disorders, DOI 10.1016/j.jad.2018.01.017 (Publisher version available at: [http://www.jad-journal.com/article/S0165-0327\(16\)31969-3/fulltext](http://www.jad-journal.com/article/S0165-0327(16)31969-3/fulltext)).

## **Altered neural processing of reward and punishment in adolescents with Major Depressive Disorder**

Landes, I.<sup>1</sup>, Bakos, S.<sup>1</sup>, Kohls, G.<sup>2</sup>, Bartling, J.<sup>1</sup>, Schulte-Körne, G.<sup>1</sup> & Greimel, E.<sup>1\*</sup>

<sup>1</sup>Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University Hospital Munich, Munich, Germany

<sup>2</sup>Child Neuropsychology Section, Department of Child and Adolescent Psychiatry, Psychosomatics, and Psychotherapy, Medical Faculty, RWTH Aachen University Hospital, Aachen, Germany

### **\*Address for reprints or correspondence:**

Ellen Greimel, Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University Hospital Munich, Munich, Germany  
E-mail: [Ellen.Greimel@med.uni-muenchen.de](mailto:Ellen.Greimel@med.uni-muenchen.de), Phone: +4989440056952, Fax: +4989440055902

**Abbreviations:** Monetary Incentive Delay Task (MIDT), Cue-P3 (cP3), Feedback-P3 (fP3), Reward Positivity (RewP)



## **Abstract**

**Background:** Altered reward and punishment function has been suggested as an important vulnerability factor for the development of Major Depressive Disorder (MDD). Prior ERP studies found evidence for neurophysiological dysfunctions in reinforcement processes in adults with MDD. To date, only few ERP studies have examined the neural underpinnings of reinforcement processing in adolescents diagnosed with MDD. The present event-related potential (ERP) study aimed to investigate neurophysiological mechanisms of anticipation and consumption of reward and punishment in adolescents with MDD in one comprehensive paradigm.

**Method:** During ERP recording, 25 adolescents with MDD and 29 healthy controls (12-17 years) completed a Monetary Incentive Delay Task comprising both a monetary reward and a monetary punishment condition. During anticipation, the cue-P3 signaling attentional allocation was recorded. During consumption, the feedback-P3 and Reward Positivity (RewP) were recorded to capture attentional allocation and outcome evaluation, respectively.

**Results:** Compared to controls, adolescents with MDD showed prolonged cue-P3 latencies to reward cues. Furthermore, unlike controls, adolescents with MDD displayed shorter feedback-P3 latencies in the reward versus punishment condition. RewPs did not differ between groups.

**Limitations:** It remains unanswered whether the observed alterations in adolescent MDD represent a state or trait.

**Conclusions:** Delayed neural processing of reward cues corresponds to the clinical presentation of adolescent MDD with reduced motivational tendencies to obtain rewards. Relatively shorter feedback-P3 latencies in the reward versus punishment condition could indicate a high salience of performance-contingent reward. Frequent exposure of negatively biased adolescents with MDD to performance-contingent rewards might constitute a promising intervention approach.

**Keywords:** Adolescents; Major Depressive Disorder; Reward; Punishment; Event-related potentials

## **Introduction**

Major Depressive Disorder (MDD) is a severe mental disorder, which is characterized by debilitating symptoms including sustained negative affect and diminished experience of pleasure or reward (“anhedonia”) (American Psychiatric Association, 2000). Prevalence rates of MDD significantly increase up to 10% during adolescence and adolescent MDD is associated with a significant suicidal risk and particularly severe functional and psychosocial impairments (Rao and Chen, 2009).

The reasons for the increased prevalence of MDD during adolescence have not been sufficiently explored yet (Bress et al., 2013). However, it has been suggested that adolescents might be particularly prone to MDD because of the major physical and socio-affective maturation processes that take place during the adolescent period (Greimel, 2011; Davey et al. 2008). These maturation processes include dramatic biological changes within the brain, which considerably affect the neural bases of reinforcement processing (Rubia, 2013). In this context, neural dysfunction in reinforcement processing has been suggested to act as a main vulnerability factor for the development of a first MDD episode (see Kerestes et al., 2014, for details) and might especially characterize early-onset, adolescent MDD (Forbes and Dahl, 2012). Thus, insight into this field of research is important for a detailed understanding of the pathophysiology of adolescent MDD.

Experimental approaches to study the neural bases of reinforcement processing in MDD and healthy individuals typically differentiate between an anticipatory and a consummatory phase (e.g. Knutson et al., 2008; Liu et al., 2011). As each phase reflects a different psychological state and separately shapes human behavior, a distinct investigation of both phases is needed for a thorough understanding of the neural substrates underlying reward and punishment processing (Pizzagalli et al., 2009). A further relevant distinction concerns the stimulus valence, i.e. whether reward or punishment processes are studied (e.g. Dillon et al., 2008; Broyd et al., 2012). In this context, rewards are defined as stimuli an individual is willing to work for and that increase the frequency of a behavior upon which the stimulus is contingent. By contrast, punishments are defined as stimuli an individual is actively trying to

avoid and which decrease the frequency of a behavior. Punishment stimuli can consist of the presentation of aversive stimuli or the removal of appetitive stimuli (often operationalized as monetary loss) in response to a certain behavior (Lutz and Widmer, 2014). As prior research suggests that reward vs. punishment function might in part be distinctively altered in adolescent MDD (Kerestes et al., 2014), a separate investigation of both processes seems to be relevant.

So far, research on neural mechanisms of reinforcement processing in adolescent MDD is mainly dominated by functional magnetic resonance imaging (fMRI) studies, which have particularly focused on reward processing (e.g. Forbes et al., 2009; Forbes et al., 2010; Stringaris et al., 2015). These studies indicate disturbed neural activation patterns in areas of the reinforcement circuitry, including diminished striatal activation during both reward anticipation and consumption (for reviews see Forbes and Dahl, 2012; Kerestes et al., 2014). The results are largely in line with findings in adult samples (Kerestes et al., 2014) and presumably reflect a hyporesponsiveness to reward stimuli and a dysfunction in regions mediating hedonic impact and reinforcement (Pizzagalli et al., 2009).

Compared to reward processing, the neural bases of punishment processing have been far less studied in adolescent MDD (Luking et al., 2016; Kujawa and Burkhouse, 2017). The only fMRI study investigating response to punishment (operationalized as monetary loss) in adolescents diagnosed with MDD reported a blunted neural response in several brain regions including the striatum and anterior cingulate cortex (ACC) but increased activity in the amygdala (Forbes et al., 2006). Adolescents at high risk for MDD have also been found to exhibit less striatal activation to monetary loss compared to peers at lower risk for depression (Gotlib et al., 2010). However, contrasting the findings in clinically depressed adolescents (Forbes et al., 2006), adolescents at high risk for depression have been shown to exhibit increased activation in the ACC, which might reflect increased learning of outcome contingencies for this kind of stimuli (Gotlib et al., 2010). Taken together, the few fMRI studies in adolescent populations point to altered neural correlates of punishment processing in adolescent MDD, which can be brought in line with findings from adult MDD studies on

altered sensitivity and neural reactivity to punishment (see Eshel and Roiser, 2010, for a review). However, as evidence is scarce and mixed, future studies in adolescent MDD are clearly needed to draw more comprehensive conclusions.

In contrast to fMRI, event-related potentials (ERPs) provide millisecond temporal resolution, which allows for a chronological delineation of direct, reward-related neural activity (Goldstein et al., 2006; Banaschewski and Brandeis, 2007) by decomposing the neural responses of reinforcement anticipation and consumption in a very precise manner (Novak and Foti, 2015; Broyd et al., 2012). Despite clear restraints regarding spatial resolution, ERP approaches are very well-suited to investigate even subtle abnormalities in the temporal dynamics of reinforcement function (Hopfinger et al., 2005). ERP studies on reinforcement anticipation often focus on the P3, which is elicited after a (potential) positive or negative feedback has been announced by a relevant cue (Broyd et al., 2012). To investigate reward consumption, the P3 (e.g. Foti and Hajcak, 2009) and the Reward Positivity (RewP; e.g. Novak et al., 2016) are frequently assessed, which are both elicited after feedback presentation. Thus, recording the P3 component allows investigating reinforcement anticipation (cue-P3/cP3) and consumption (feedback-P3/fP3; Novak and Foti, 2015). The P3 shows its maximum over parietal regions between 300–500ms after stimulus onset, and is generally larger for stimuli with high salience, emotional value or informative content (Polich and Kok, 1995). The P3 is linked to the allocation of attentional resources to a stimulus (Polich and Kok, 1995), context updating (Venables et al., 2011), and the confirmation of subjective expectations (Verleger, 1988). It has been suggested that the P3 is particularly relevant to reinforcement processing (Wu and Zhou, 2009) and previous research has relied on both amplitude and latency parameters of this component to investigate reward and punishment function (e.g. Ramsey and Finn, 1997; Goldstein et al., 2006; Pfabigan et al., 2011; De Pascalis et al., 2004). Whereas the amplitude of an ERP component indicates the extent to which neural resources are assigned to a particular process, the latency tracks the time course of processing activity, i.e., the speed of information processing (Hansenne, 2006; Duncan et al., 2009). The latency of the P3 is

supposed to provide a temporal measure of the neural activity underlying attentional allocation and immediate memory, with longer P3 latencies interpreted as delays in stimulus processing/classification speed (Polich, 2003; Polich, 2007). Moreover, P3 latency has been linked to response selection (Verleger, 1997). Thus, in the context of reinforcement processing, the P3 amplitude reflects (among other processes) the amount of attentional resources allocated to incentive stimuli, whereas the P3 latency reflects the speed of this cognitive process.

The RewP (also known as Feedback Negativity (FN)/Feedback-Related Negativity (FRN))<sup>1</sup> is an ERP that differentiates favorable from unfavorable feedback and is relatively more positive for favorable outcomes. It appears as relative positivity peaking ~300ms after stimulus presentation at fronto-central recording sites. It has initially been suggested that this component is insensitive to absolute outcome values but instead reflects an evaluation of binary outcome valences (Gehring et al., 2012), thus representing a measure for neural sensitivity to outcome valence (Foti et al., 2011; Proudfit, 2015). However, more recent evidence supports the view that the RewP is also sensitive to variations in outcome magnitude (for a meta-analysis, see Sambrook and Goslin, 2015).

The Monetary Incentive Delay Task (MIDT; Knutson et al., 2000) is a very well-established paradigm and allows examining the neurophysiological bases of anticipation and consumption of reward and punishment within one experimental paradigm (Novak and Foti, 2015). This simple button-press task requires a quick response to a target announced by a cue. Dependent on the response, a performance-specific feedback is delivered.

To our knowledge, no ERP study in MDD patients has yet decomposed both anticipatory and consummatory phases of reward and punishment processing within the framework of the MIDT. Regarding the anticipatory phase, two ERP studies applied the MIDT in healthy adults

---

<sup>1</sup> The RewP difference wave is calculated as gain minus loss difference, resulting in a fronto-central positivity (e.g. Novak et al., 2016). In studies that apply the FN/FRN conceptualization, the loss minus gain difference is calculated instead, resulting in a fronto-central negativity. There is growing evidence that primarily reward-related activity following favorable outcomes elicits a relative positivity, supporting the RewP conceptualization. Following the emphasis current literature puts on the link between this component and reward sensitivity, we refer to the RewP conceptualization here (for details, see Proudfit, 2015). The magnitude of the valence effect (win vs. loss) is the same in each case.

to explore a potential link between elevated negative emotionality/depressive symptoms and reward or punishment function (Santesso et al., 2012; Novak et al., 2016). Both studies investigated the P3 (besides other components) but did not find a relationship between this component and negative emotionality/depressive symptoms during reward or punishment anticipation. However, it remains unclear whether the results can be generalized to MDD patients. Regarding the consummatory phase (for a recent review, see Proudfit, 2015), ERP studies (mainly using gambling tasks) revealed blunted RewPs in adults with MDD indicating reduced sensitivity for rewards (Foti et al., 2014; Liu et al., 2014). The link between adult depression and blunted RewPs is also supported by findings in non-clinical samples (e.g. Foti and Hajcak, 2009; but see Santesso et al., 2012)

Regarding adolescent MDD, our understanding of the neurophysiological bases underlying reward and punishment processes is particularly limited due to only few ERP studies in the field. Moreover, these studies have mainly been conducted in non-clinical adolescent samples and have focused on the consummatory phase of reinforcement processing.

In non-clinical and at-risk samples, blunted RewPs during monetary reward consumption were linked to increased depressive symptoms and prospectively predicted adolescent MDD (Bress et al., 2012; Bress et al., 2013; Bress et al., 2015; Nelson et al., 2016; Kujawa et al., 2014). However, it remains unclear whether these findings can be transferred to adolescent samples with acute clinical depression, as the stability of depression-related ERP findings over the course of the disease and from non-clinical to clinical stages is yet to be determined (Bress et al., 2015). One factor that complicates a transfer is that non-clinical populations differ from clinical samples regarding, e.g., the severity and constellations of MDD symptoms (Coyne and Whiffen, 1995; Novak et al., 2016). This aspect might result in differential ERP findings in non-clinical and clinical MDD study populations. Furthermore, in contrast to adolescent samples with clinically manifest depression, at-risk samples include participants that will remain healthy or develop either adult- or adolescent-onset depression, with the latter two conditions differing from each other with respect to symptomatology,



neurobiological underpinnings and/or vulnerability factors (e.g. Kaufman et al., 2001; Fernando et al., 2011; Jaffee et al., 2002).

To date, only one ERP study investigated reinforcement processing in adolescents with a current clinical MDD diagnosis (Webb et al., 2017). This study applied a gambling task and reported a potentiated RewP in adolescents with MDD, presumably driven by increased loss-related activity (for results in preschool-age children with MDD, see Belden et al., 2016). While this study provides important insights, further ERP studies on anticipatory and consummatory reinforcement processes in adolescents diagnosed with MDD are needed.

A detailed understanding of the neural bases of reinforcement processing in adolescents with MDD is important for at least three reasons. First, although adolescence is a period of increased risk for depression and adolescent MDD is particularly severe (Rao and Chen, 2009), core biological mechanisms which are thought to act as vulnerability factors for the disorder remain poorly understood. Second, developmental maturation processes affecting the neurobiological bases of depression (Rao and Chen, 2009) might limit the generalizability of adult findings to adolescent populations. Third, in adolescents with MDD, the interpretation of results is not complicated by a long illness history (Houston et al., 2004) and might thus provide additional insight.

Given the importance of the topic and the scarcity of ERP research in the field, our ERP study aimed to investigate the neurophysiological mechanisms underlying anticipation and consumption of reward and punishment in adolescents with MDD. Our study extends previous ERP research in clinical samples by investigating the neural underpinnings of reward and punishment function based on a stage-specific approach, thereby including anticipatory and consummatory phases. Unlike previous approaches in clinical MDD populations, we focused on performance-contingent feedback. This feedback type has been suggested to be characteristically different from arbitrary outcomes (Foti and Hajcak, 2009; Murphy et al., 2003) and might be particularly relevant in respect of depression as feedback on the own performance is delivered (Novak et al., 2016; Knutson et al., 2008).

We therefore applied the MIDT and included a separate punishment and reward condition. We focused on the cP3 to examine anticipatory processes and on the fP3 and RewP to examine consummatory processes. Based on previous ERP and fMRI studies on MDD indicating reduced neural responsivity to reward (e.g. Liu et al., 2014; Foti et al., 2014; Pizzagalli et al., 2009), we expected blunted ERP components (cP3/fP3/RewP) during reward anticipation and consumption in adolescent MDD compared to controls. Regarding punishment consumption, we expected potentiated RewPs based on prior ERP findings in adolescent MDD (Webb et al., 2017). We did not expect group differences during punishment anticipation (cP3), as a prior study showed that cP3 parameters were not linked to depressive symptoms during punishment anticipation (Santesso et al., 2012; for similar results from related lines of research also see McFarland and Klein, 2009).

## **Method**

### **Participants**

25 adolescents with MDD and 29 controls, aged 12-17 years, were included in the sample. All participants had IQs  $\geq 85$  (Culture Fair Intelligence Test 20-R; CFT 20-R; Weiss, 2006) and groups were comparable regarding age, IQ, handedness and gender (see Table 1).

MDD participants were recruited from the Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy at the University of Munich. The Kinder-DIPS (Diagnostisches Interview bei psychischen Störungen im Kindes- und Jugendalter [„Diagnostic Interview for Mental Disorders for Children and Adolescents“]; Unnewehr et al., 1995) was administered to all participants by trained clinicians and served as diagnostic instrument to extensively screen for/record all major current and former psychiatric disorders. The Kinder-DIPS is a well-established, semi-structured German diagnostic interview with a high retest-reliability for all DSM-IV diagnoses (Adornetto et al., 2008). According to the Kinder-DIPS, all MDD participants were diagnosed with a current MDD episode (for information on comorbidities and further clinical characteristics see S1/supporting material). Four of the MDD participants received antidepressants (n=3 SSRI, n=1 tricyclic-

antidepressant). Since their inclusion did not change the pattern of results, findings are reported for the full sample. Control participants had no parental history of affective disorders and were free of any past or current psychiatric disorder according to the Kinder-DIPS. All participants completed the Beck Depression Inventory-II (BDI-II; Beck et al., 1996) to assess the severity of present depressive symptoms. Moreover, we applied the Behavior Inhibition System/Behavior Approach System scales (BIS/BAS-scales; Carver and White, 1994; German version: Strobel et al., 2001) to assess individual differences in personality qualities that reflect the sensitivity of two self-regulatory systems: The BAS modulating approach motivation (Carver and White, 1994) and the BIS supporting the identification of goal-conflict and serving to inhibit ongoing behavior (Wacker et al., 2010). BDI-II-scores and BIS-scores, but not BAS-scores, were significantly higher in the MDD group compared to controls<sup>2</sup> (see Table 1).

To ensure that the sample size was sufficiently large to detect group differences in ERPs, we conducted a power analysis based on previous reports on reward/punishment processing in clinical MDD populations (Liu et al., 2014; Foti et al., 2014; Webb et al., 2017). These investigations revealed effect sizes (Cohen's *d*) ranging between 0.42-1.66 for group differences in ERP components including the RewP. Based on the conservative assumption of an effect size in the lower range of these values ( $d=0.8$ ), calculation of the minimal required sample size to detect a significant group difference (MDD vs. healthy controls) in reward-related ERPs revealed a required sample size of  $N=52$  (independent *t*-test; alpha level=.05; power=.8). Thus, based on this estimation, the sample size of  $N=54$  was appropriate to examine the research question.

The study was approved by the institutional review board and was performed in accordance with the latest version of the Declaration of Helsinki and national legislation. All participants were explicitly informed about the experimental procedures and study aims, and informed written consent (parents) and assent (adolescents) was obtained from all participants.

---

<sup>2</sup> Regarding both questionnaires, higher scores represent higher levels of the respective attribute being measured.

## Experimental procedure

The trial structure and the time line of the MIDT are illustrated in Figure 1 and are based on prior reports (e.g. Broyd et al., 2012). We applied the MIDT across two blocks: One with potential monetary rewards (monetary reward condition) and one with potential monetary punishments (monetary punishment condition), counterbalanced in presentation-order across participants<sup>3</sup>. Each block comprised 80 experimental trials, specific for one of the two conditions, as well as 40 control trials serving as baseline condition. Each experimental trial offered two possible outcomes (monetary reward condition: "reward" vs. "no-reward"/monetary punishment condition: "punishment" vs. "no-punishment"). A relatively positive feedback was presented (reward/no-punishment outcome) if the participant managed to hit a target symbol in time. Each target was preceded by a condition-specific cue stimulus. Regarding the response time window of the target, we applied an online response algorithm (see S3/supporting material). This algorithm adjusted the presentation duration of the cued target individually to the reaction times of the participant, aiming at a hit ratio of ~50%. Depending on performance, the specific feedback was presented at the end of each trial. Control trials were randomly intermixed with experimental trials, and differed in two aspects: First, the control feedback was non-informative (meaningless patterns) and irrespective of the individual performance. Second, the control cue informed participants of a non-informative feedback within the current trial. Thereby, an informative function of experimental cues was induced, enabling to investigate reward/punishment anticipation.

---

<sup>3</sup> Exploratory analyses showed that there was no significant interaction of block order with group for any of the ERP parameters investigated (all  $p \geq .12$ ).

Additional information on the task and stimuli is given in S2-4/supporting material. For an illustration of different stimuli presented as cue and feedback within the monetary reward, monetary punishment and control trials, see Figure 1A.

A practice session (19 trials) and extensive visually animated verbal task instructions were administered before each experimental block. The participants were informed that all monetary feedback stimuli were also represented by real money: In the monetary reward condition, each positive feedback (reward outcome; +0.20€) resulted in monetary gain, each negative feedback (no-reward outcome) meant a missed opportunity to gain 0.20€. Likewise, in the monetary punishment condition, each negative feedback (punishment outcome; -0.20€) resulted in monetary loss, each positive feedback (no-punishment outcome) meant avoiding the loss of 0.20€ (for a similar approach, see Broyd et al., 2012). Participants received a starting value of 8€ and were instructed that better performance would result in a higher total win. A manipulation check at the end of the experiment confirmed that all participants perceived the feedback as performance-contingent within each trial. At the end of the testing session, a bonus of 10€ was paid to each participant. Response collection and stimulus presentation was controlled by the software E-prime2.0 (Psychology Software Tools, Pittsburgh, PA; Schneider et al., 2012).

### **EEG recording and processing**

During the experiment, EEG was recorded using an Electrical Geodesic Inc.-128-channel system with a sampling rate of 500Hz, and Cz as reference electrode (see S5/supporting material). The impedance was kept below 50kΩ during recording.

Further processing steps were performed with Brainvision Analyzer (Brain Products GmbH, Gilching, Germany). After visual inspection of the data and offline filtering with a 0.53 (time constant 0.3) to 30Hz band-pass (Butterworth zero phase, 12dB/Oct) and 50Hz notch filter, independent component analysis was run to remove electroocular (EOG) artefacts. Subsequently, all electrodes were re-referenced to the averaged mastoids (Electrode 57LM/100RM, see S5/supporting material). Artefacts apart from EOG artefacts were defined

as i) amplitudes exceeding  $\pm 100\mu\text{V}$ , ii) bursts of electromyographic activity (maximal allowed voltage step:  $50\mu\text{V/ms}$ , max-min:  $100\mu\text{V}$ ) and iii) any activity lower than  $0.5\mu\text{V}$  in intervals of  $100\text{ms}$ . These artefacts were excluded from further processing.

## Data analysis

### ERP data

Positive feedback trials were defined as trials with button presses within the presentation duration of the target. Negative feedback trials were defined as trials with responses after the target had disappeared from screen. Anticipatory and missed button presses were excluded. For the cP3, fP3 and RewP, the data were segmented into epochs ( $-200\text{ms}$  to  $1000\text{ms}$  related to the cue/feedback onset; stimulus-locked ERPs), baseline-corrected ( $200\text{ms}$  pre-stimulus interval for baseline correction) and averaged separately for each participant and condition (monetary reward/monetary punishment) for the cP3 or outcome valence (negative/positive feedback trials per condition) for the fP3/RewP. For the analysis of the RewP, we computed a RewP difference wave (Foti and Hajcak, 2009; Novak and Foti, 2015) by subtracting negative from positive feedback trials (monetary reward condition: reward – no-reward; monetary punishment condition: no-punishment – punishment).

According to relevant P3 literature, which reports highest P3 amplitudes over parietal regions (Novak and Foti, 2015) and based on visual data inspection, the ROIs for both the fP3 and the cP3 were defined around the electrode Pz, spanning six electrodes (61,62[Pz],67,72,77,78, see S5/supporting material). For the RewP, we defined a frontal and a central ROI based on data inspection and previous literature (Novak et al., 2016). The frontal ROI was defined around Fz and the central ROI around Cz, spanning the electrodes 4,5,10,11[Fz],12,16,18,19 and 7,31,55,80,106,129[Cz], respectively (see S5/supporting material).

Inclusion criterion for analyses was a minimum of  $\geq 20$  artefact-free trials per condition/outcome for each ROI electrode. All participants included in the final sample (see “Participants”) met this criterion. Regarding the cP3 and RewP analyses, group means were

$\geq 75.0$  (cP3)/ $\geq 66.5$  (RewP) trials for each of the two conditions (monetary reward/monetary punishment). Regarding fP3 analyses, group means were  $\geq 31.0$  trials for each of the four outcomes. Groups did not differ in mean trial numbers (all  $p > .05$ ).

Within the ROIs, ERPs from single electrodes were averaged for statistical analysis. Grand averages were computed separately for the control/MDD group. Based on visual inspection of the grand averages and on previous reports, the cP3 was scored as the mean amplitude from 200-340ms after cue onset and the fP3 as the mean amplitude from 220-400ms after feedback onset (Broyd et al., 2012). The RewP was scored as the mean amplitude from 260-360ms after feedback onset (Bress et al., 2012). Furthermore, to evaluate potential alterations regarding the speed of attentional allocation and cue/feedback stimulus classification (Polich, 2007), cP3/fP3 peak latencies were measured within the interval of 200ms to 400ms after stimulus onset (Goldstein et al., 2006). Peak latency measures were based on local ( $\pm 10$  data points) instead of absolute peaks (Luck, 2005). We favored peak latency measures over other less frequently applied latency measures, as peak latency is considered an appropriate parameter when late and comparatively large P3 components are studied (Luck, 2005; Handy, 2005). We took several precautions to ensure that noise was unlikely to bias peak latency findings (Clayson et al., 2013) and to ensure the appropriateness of peak latency measures (Luck, 2005). In particular for all experimental conditions, noise level estimates (Kappenman and Luck, 2010) were comparable between groups (see S9/supporting material).

Mean amplitudes of the cP3/fP3 and the RewP as well as cP3 and fP3 peak latencies were each analyzed using repeated-measures ANOVAs with group as between-subjects factor (controls/MDD), and feedback modality (reward/punishment) as within-subjects factor. For the fP3, the factor outcome valence (positive/negative), and for the RewP, the factor ROI (frontal/central) was included as a further within-subjects factor.

As cP3/fP3 components for control trials were characteristically different from those for monetary reward/monetary punishment trials, the control condition was not included in the main analyses described here. However, we conducted an additional analysis including the

control condition to examine incentive effects of meaningful vs. meaningless cue/feedback presentation on cP3/fP3 amplitudes (see supporting material S6).

For the cP3, fP3 and RewP, further post-hoc comparisons were conducted if ANOVAs revealed a significant interaction. As the present study focuses on group differences, significant interaction effects are only reported if they involve the factor group. In case of significant group differences in ERP parameters, we further investigated brain-behavior relationships by examining correlations with the severity of depressive symptoms (BDI-II-score) and behavioral inhibition tendencies (BIS-scale) across both groups (for details see data analysis).

### Behavioral data

Reaction times (RTs) of the experimental trials were entered into a 2(group)x2(feedback modality: reward/punishment) repeated-measures ANOVA with group as between-subjects factor and feedback modality as within-subjects factor. Regarding control trials, RTs in each of the two conditions (monetary reward/monetary punishment) were compared between the two groups using independent t-tests. RTs between experimental and control trials within each group and condition were compared using paired samples t-tests to examine motivational speed effects depending on which trial (control/experimental) was presented.

Statistical analyses of the ERP data and behavioral data were conducted with IBM SPSS Statistics22. For all analyses the significance level was set to  $p=.05$  (two-tailed). Greenhouse-Geisser's correction was applied to all ANOVAs in case of violation of sphericity (Mauchly's test).

## Results

### **Behavioral data**

The descriptive behavioral data are summarized in Table 2. The 2(group)x2(feedback modality) repeated measures ANOVA for RTs revealed no significant main effect of feedback modality ( $F(1,52)=2.77;p=.10;\eta^2_p=.05$ ), group ( $F(1,52)=3.23;p=.08;\eta^2_p=.06$ ), and no



significant interaction involving the factor group ( $F(1,52)=.68;p=.41;\eta^2_p=.01$ ).

RTs for control trials in both conditions (monetary reward/monetary punishment) did not differ significantly between groups (all  $p>=.25$ ). RTs between experimental and control trials differed significantly within both conditions for the MDD (all  $p\leq .001$ ) and the control group (all  $p<.001$ ): RTs for experimental trials were significantly shorter than for control trials.

\_\_\_\_\_insert Table 2 \_\_\_\_\_

### **ERP data**

Group means of cP3, fP3 and RewP mean amplitudes and cP3/fP3 peak latencies are summarized in Table 3.

\_\_\_\_\_insert Table 3 \_\_\_\_\_

### Cue-P3

For cP3 mean amplitudes, neither the main effect of group ( $F(1,52)=.76;p=.39;\eta^2_p=.01$ ) nor the main effect of feedback modality ( $F(1,52)=3.53;p=.07;\eta^2_p=.06$ ) was significant. The interaction between group and feedback modality also failed to be significant ( $F(1,52)=.31;p=.58;\eta^2_p=.01$ ).

For cP3 peak latencies, there was a significant interaction of group x feedback modality ( $F(1,52)=4.30;p=.04;\eta^2_p=.08$ ). Further post-hoc comparisons revealed a significant group difference ( $p=.04$ ) in cP3 latencies in the monetary reward, but not monetary punishment condition ( $p=.97$ ; see S8/supporting material). In the monetary reward condition, MDD participants showed longer cP3 latencies compared to the control group (see Figure 2). No main effects were significant (all  $p>=.24$ ).

\_\_\_\_\_insert Figure 2 \_\_\_\_\_

### Feedback-P3

fP3 mean amplitudes were comparable across groups ( $F(1,52)=.47; p=.50; \eta^2_p=.01$ ). There was a significant main effect of feedback modality ( $F(1,52)=15.69; p<.001; \eta^2_p=.23$ ) and outcome valence ( $F(1,52)=47.16; p<.001; \eta^2_p=.48$ ). Amplitudes were significantly higher for the monetary reward than monetary punishment condition ( $p<.001$ ), and also for positive compared to negative outcome valence ( $p<.001$ ). None of the interactions involving the factor group reached significance (all  $p\geq.48$ ).

For fP3 peak latencies, there was a significant interaction between feedback modality and group ( $F(1,52)=6.52; p=.01; \eta^2_p=.11$ ). Post-hoc paired t-tests showed that the MDD group exhibited significantly longer fP3 latencies in the monetary punishment compared to the monetary reward condition ( $p<.001$ ; Figure 3). By contrast, fP3 latencies in the control group were comparable in both conditions ( $p=.44$ ). No other interaction involving the factor group reached significance (all  $p\geq.34$ ). A main effect of feedback modality was also significant ( $F(1,52)=13.36; p=.001; \eta^2_p=.20$ ). There was no main effect of outcome valence ( $F(1,52)=1.71; p=.20; \eta^2_p=.03$ ) or group ( $F(1,52)=.07; p=.80; \eta^2_p=.001$ ).

\_\_\_\_\_insert Figure 3\_\_\_\_\_

### Reward Positivity

A one-sample t-Test revealed the RewP mean amplitudes (monetary reward condition: difference between no-reward and reward/monetary punishment condition: difference between punishment and no-punishment) to be significantly greater than zero (all  $p\leq.002$ ). This indicates that the MIDT used in the present study reliably elicited an enhanced RewP in both the monetary reward and punishment condition (for a similar approach see Foti and Hajcak, 2009; see S7/supporting material). RewP amplitudes were comparable across

groups ( $F(1,52)=.18;p=.67;\eta^2_p=.003$ )<sup>4</sup>. There was no significant main effect of feedback modality ( $F(1,52)=.16;p=.68;\eta^2_p=.003$ ). There was a significant main effect of ROI ( $F(1,52)=4.46;p=.04;\eta^2_p=.08$ ), with higher RewP mean amplitudes for the central than the frontal ROI ( $p=.04$ ). None of the interactions involving the factor group reached significance (all  $p>=.26$ ).

### **Correlations between ERP components and the severity of depressed symptoms (BDI-II-score) and behavioral inhibition (BIS-score)**

Regarding the fP3, we computed a difference score in fP3 latencies to the monetary punishment minus monetary reward condition (averaged across positive and negative outcome valences) as fP3 latency analyses revealed within-group differences between the monetary reward and punishment condition.

In both groups, non-significant correlations were found between BDI-II-scores/BIS-scores and i) the cP3 latency in the monetary reward condition and ii) the fP3 latency difference score (all  $p>=.09$ ). The correlation between the cP3 latency in the monetary reward condition and the BIS-score in MDD participants reached marginal significance ( $p=.09$ ).

## **Discussion**

The present study aimed to investigate neurophysiological correlates of reinforcement anticipation and consumption in adolescent MDD. During anticipation, adolescents with MDD displayed delayed neural processing of reward cues (prolonged cP3 latencies) compared to controls. During consumption, adolescents with MDD displayed shorter fP3 latencies in the reward versus punishment condition, which was not the case in controls. No group differences emerged for RewPs or behavioral responses.

### **Behavioral data**

---

<sup>4</sup> Exploratory analysis showed that the absence of group differences in RewP mean amplitude was not due to differences in RewP peak latency, which did not significantly differ between groups.

For both groups, our behavioral data clearly revealed motivational effects as RTs significantly decreased following cues signaling potential punishment or reward compared to the control condition. This supports that the paradigm was suited to engage effortful response processes to achieve a better performance (Broyd et al., 2012). Consistent with prior reports on adults with MDD (Pizzagalli et al., 2009), we did not find differences in behavioral performance between adolescents with MDD and controls, suggesting that our ERP findings on group differences cannot be dismissed as artefacts related to a differing task performance.

## **ERP data**

### Cue-P3

Compared to healthy controls, the MDD group exhibited delayed cP3 latencies during the anticipation of potential monetary reward. This is in line with our hypotheses of disturbed processes during reward anticipation in MDD. Our result is also in accordance with McFarland and Klein (2009), who reported reduced emotional reactivity in adults with MDD, in particular regarding reward anticipation. Disturbed reward anticipation concurs with the clinical pattern of adolescent depression, which is characterized by low motivational tendencies to obtain rewards (Forbes and Dahl, 2012) and an underestimation of the probability of positive future events (Thimm et al., 2013).

Consistent with the notion that the P3 reflects the allocation of attentional resources (Polich and Kok, 1995) and that disturbances during this process represent a central deficit in MDD (Whitton et al., 2015), our results suggest a delayed allocation of attentional resources and a slowing in stimulus classification (Polich, 2007) towards reward predicting cues in adolescent MDD. Previous research that has studied P3 latency in the context of reward/punishment function has found shorter P3 latencies towards target stimuli in an incentive compared to a neutral condition in healthy individuals (Ramsey and Finn, 1997), indicating that a higher motivational value of a stimulus is linked to a faster allocation of attentional resources. With respect to our findings, this might suggest that for adolescents with MDD, the anticipated monetary reward was less motivationally relevant and thus led to a slowed attentional

allocation compared to controls.

In line with this suggestion, longer P3 latencies towards stimuli signaling reward (low-intensity happy faces) have previously been reported in depressed individuals (Cavanagh and Geisler, 2006). Our results of a slower stimulus classification speed for reward cues in adolescents with MDD can also be brought in line with previous research reporting longer P3 latencies to rare events in individuals with reduced novelty seeking, which describes a reduced behavioral tendency towards potential rewards (Kim et al., 2002). As the reward cue displayed in the present study provided salient information about the subsequent behavior-outcome contingency, a disruption in cP3 processing may indicate an abnormal processing of reward salience (Novak and Foti, 2015).

Disruptions in the neural system underlying positive affect constitute a core feature of adolescent MDD (Forbes and Dahl, 2005), and the signaling of a potentially pleasurable outcome is supposedly a mood-incongruent event for individuals with MDD. In this regard, an fMRI study found increased activation of the dorsal ACC (dACC) during reward anticipation in adult MDD (Knutson et al., 2008), which was suggested to reflect elevated affective conflict. As the ACC is associated with the generation of the P3 (Mulert et al., 2004), delayed cP3 latencies might also point to an elevated affective conflict with delayed stimulus classification speed regarding reward cues in individuals with MDD during reward anticipation.

Consistent with the literature (Mellick et al., 2014), BIS-scores in the MDD group were significantly higher compared to controls. Increased behavioral inhibition is discussed as a potential vulnerability factor for MDD (Johnson et al., 2003). In adolescents at risk for depression, higher behavioral inhibition has been linked to altered brain connectivity in regions supporting reward prediction (Frost Bellgowan et al., 2015). As in the MDD group higher BIS-scores marginally correlated with longer cP3 latencies in the monetary reward condition, it would be interesting to follow up this tendency in future studies including larger adolescent MDD samples.

### Feedback-P3

MDD participants displayed longer fP3 latencies in the monetary punishment compared to the monetary reward condition. By contrast, the control group showed comparable fP3 latencies across both conditions. These findings suggest a slowed attentional allocation and stimulus classification in adolescents with MDD when feedback about their own performance was delivered within a punishment (compared to a reward) context. Previous research suggests that a higher motivational value of a stimulus is linked to a faster allocation of attentional resources (Ramsey and Finn, 1997). Based on these findings, shorter P3 latencies in the reward compared to the punishment condition might reflect that adolescents with MDD attributed a higher motivational relevance to reward-related (compared to punishment-related) performance-dependent feedback.

Within the MDD group, the difference in fP3 latencies emerged between the experimental conditions, regardless of the outcome valence. Therefore, the mindset of MDD participants during reward and punishment processing seems predominantly relevant for the observed findings. Our experimental set-up was based on an artificially set ~50% hit rate, which could have differentially influenced the mind-set of the two groups. In participants with MDD, negative cognitive biases, including negative self-concepts (Beauchaine and Hinshaw, 2010), might have resulted in expectations of performance-dependent reward rates lower than 50% (Foti and Hajcak, 2009). Reward rates of ~50% in the MR condition then likely constituted an infrequent, unfamiliar and thus highly salient setting for the MDD group. This might have accelerated feedback processing in the MDD group and might also explain why, against our hypotheses, we did not find blunted fP3s in the monetary reward condition in adolescent MDD. In line, a recent ERP study in healthy adults reported the fP3 to be primarily influenced by stimulus salience (Novak and Foti, 2015). The brain's salience network (including the ACC and insula) segregates the most relevant stimuli for future behavioral guidance, focuses attention and enhances access to cognitive resources (Menon, 2015). The present findings add evidence to the notion that this network is disrupted in MDD (Hamilton et al., 2013; Goodkind et al., 2015) and that it plays a crucial role in disturbed

reinforcement processing in adolescent MDD.

Our results suggest that during the consummatory phase, reinforcement is not generally less salient for adolescents with MDD but may even be processed in a prioritized manner in situations where it is scarce and inconsistent with negative cognitive biases. In the long run, our findings might have important clinical implications as they point towards the possibility that frequently delivering performance-contingent reward might constitute a promising intervention approach in adolescents with depression. An essential next step would be to systematically study the (long-term) effects of performance-contingent rewards on depressive symptoms in adolescent MDD.

### Reward Positivity

Consistent with previous literature (Proudfit, 2015), the RewP was observed as a positive deflection in the ERP difference following positive compared to negative feedback. This pattern was evident in both the MDD and the control group (for similar results, see, e.g., Foti et al., 2014). Our finding of comparable RewP amplitudes across groups is in contrast to our hypotheses, which were based on reports of altered RewPs during reinforcement processing in clinical MDD (Liu et al., 2014; Foti et al., 2014; Webb et al., 2017) and non-clinical samples (Bress et al., 2012; Foti and Hajcak, 2009). The differential results can be explained by several reasons relating to the methodological approach and the sample of the present study: First, due to the block-wise presentation of the monetary reward/monetary punishment condition in the present study, the RewP difference wave was calculated based on reward minus no-reward trials and no-punishment minus punishment trials. This approach allows decomposing neurophysiological processes associated with reward vs. punishment in a fine-grained manner (e.g. Novak and Foti, 2015). However, it might well result in different findings than an event-related presentation of reward and punishment and a direct subtraction of reward minus punishment trials (e.g. Bress et al., 2012; Liu et al., 2014). Second, evidence suggests that feedback processing is differentially altered in depression dependent on whether it is performance-contingent or not (Murphy et al., 2003). Therefore, reports of a link

between altered RewPs and depression from studies using a gambling task (e.g. Foti et al., 2014; Liu et al., 2014; Webb et al., 2017) might not be transferable to studies using performance-related feedback (Foti and Hajcak, 2009). Third, there is evidence that the RewP is particularly modulated within certain MDD subgroups: Foti et al. (2014) found RewP alterations in MDD to be specifically linked to impaired mood reactivity and Liu et al. (2014) reported an association of reduced RewP amplitude and low hedonic capacity. Both studies were based on adult samples. Compared to adult MDD samples, our adolescent MDD sample may have been characterized by higher mood reactivity/hedonic capacity (see Weiss and Garber, 2003; Carlson and Kashani, 1988; Rohde et al., 2009) and may thus have exhibited intact reward sensitivity as reflected by the RewP. In future studies it would be important to systematically investigate whether the discussed design and sample issues impact on RewP findings in depressed individuals.

### **Limitations and conclusions**

The present study has some limitations that should be taken into account. The balanced positive/negative feedback ratio of ~50/50 has many advantages (Dillon et al., 2008), however, ecological validity is limited. Furthermore, although the exclusion of medicated individuals did not change the pattern of results, future studies should explicitly investigate potential influences of medication on reinforcement processing in adolescent MDD. Moreover, it would be desirable to replicate our ERP findings in larger samples. Finally, pubertal status was not assessed in the study. In this regard, groups were comparable in age known to be highly correlated with pubertal development (Goddings, 2014). Furthermore, prior research (for a review see Galvao et al., 2014) has not revealed an association between pubertal timing and adolescent-onset depressive symptoms in girls (Gaysina et al., 2015). Thus, we did not expect group differences in pubertal development. Notwithstanding this issue, and given prior literature linking pubertal status and reward sensitivity (Urosevic et al., 2014), pubertal assessment would be beneficial in future ERP studies on adolescent MDD.



Despite these limitations, this study is one of the first ERP studies to explore neurophysiological mechanisms of reinforcement function in adolescents with a current diagnosis of MDD and the first to thereby examine both anticipatory and consummatory phases. Our findings demonstrate that youths with MDD show distinct disturbances in reinforcement processing, depending on the phase (anticipation/consumption) and feedback modality (reward/punishment) investigated. This clearly suggests that these aspects should be separately studied in future research on adolescent MDD (Novak and Foti, 2015). Future studies should investigate if our findings can be generalized to other age groups. The ERP approach taken provides a precise chronological delineation of disruptions in the temporal dynamics underlying reinforcement processing. However, future multimodal studies combining ERP and fMRI methods will allow to more comprehensively examine both the “when” and “where” of altered reinforcement processes in adolescents with MDD (see Foti et al., 2014). Moreover, as prior fMRI research reported group differences in activation patterns between adolescents with and without MDD depending on reinforcement magnitude (Forbes et al., 2006), it would be worthwhile to explore whether and how reward/punishment magnitude might impact on neurophysiological differences in adolescent MDD. Regarding clinical implications, it seems promising to investigate whether the repeated exposure to performance-contingent, frequent reward might result in beneficial changes including a normalization of reinforcement-related processes and a reduction of depressive symptoms in adolescent MDD.

## References

- Adornetto, C., In-Albon, T., Schneider, S., 2008. Diagnostik im Kindes- und Jugendalter anhand strukturierter Interviews: Anwendung und Durchfuehrung des Kinder-DIPS. (Diagnostics in childhood and adolescence using structured interviews: application and execution of the Kinder-DIPS.). *Klin. Diagnostik u. Evaluation* 1, pp. 363-377.
- American Psychiatric Association, 2000. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR). APA, Washington, DC.
- Banaschewski, T., Brandeis, D., 2007. Annotation: what electrical brain activity tells us about brain function that other techniques cannot tell us - a child psychiatric perspective. *J. Child Psychol. Psychiatry* 48, 415-435.
- Beauchaine, T.P., Hinshaw, S.P., 2010. *Child and Adolescent Psychopathology*. John Wiley & Sons, Hoboken, N.J. USA.
- Beck, A.T., Steer, R.A., Brown, G.K., 1996. *Manual for the Beck Depression Inventory-II*. San Antonio, TX: Psychological Corporation.
- Belden, A.C., Irvin, K., Hajcak, G., Kappenman, E.S., Kelly, D., Karlow, S., Luby, J.L., Barch, D.M., 2016. Neural correlates of reward processing in depressed and healthy preschool-age children. *J. Am. Acad. Child Adolesc. Psychiatry* 55, 1081-1089.
- Bress, J.N., Meyer, A., Proudfit, G.H., 2015. The stability of the feedback negativity and its relationship with depression during childhood and adolescence. *Dev. Psychopathol.* 27, 1285-1294.
- Bress, J.N., Foti, D., Kotov, R., Klein, D.N., Hajcak, G., 2013. Blunted neural response to rewards prospectively predicts depression in adolescent girls. *Psychophysiology* 50, 74-81.
- Bress, J.N., Smith, E., Foti, D., Klein, D.N., Hajcak, G., 2012. Neural response to reward and depressive symptoms in late childhood to early adolescence. *Biol. Psychol.* 89, 156-162.
- Broyd, S.J., Richards, H.J., Helps, S.K., Chronaki, G., Bamford, S., Sonuga-Barke, E.J., 2012. An electrophysiological monetary incentive delay (e-MID) task: a way to decompose the different components of neural response to positive and negative monetary reinforcement. *J. Neurosci. Methods* 209, 40-49.
- Carlson, G.A., Kashani, J.H., 1988. Phenomenology of major depression from childhood through adulthood: analysis of three studies. *Am J Psychiatry* 145, 1222-1225.
- Carver, C.S., White, T.L., 1994. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS scales. *J. Pers. Soc. Psychol.* 67, 319-333.
- Cavanagh, J. & Geisler, M. W., 2006. Mood effects on the ERP processing of emotional intensity in faces: A P3 investigation with depressed students. *Int. J. Psychophysiology* 60, 27-33.
- Clayson, P.E., Baldwin, S.A., Larson, M.J., 2013. How does noise affect amplitude and latency measurement of event-related potentials (ERPs)? A methodological critique and simulation study. *Psychophysiology* 50, 174-186.
- Coyne, J.C., Whiffen, V.E., 1995. Issues in personality as diathesis for depression: The case of sociotropy-dependency and autonomy-self-criticism. *Psychol. Bull.* 118, 358-378.
- Davey, C.G., Yucel, M., Allen, N.B., 2008. The emergence of depression in adolescence: development of the prefrontal cortex and the representation of reward. *Neurosci. Biobehav. Rev.* 32, 1-19.
- De Pascalis, V., Strippoli, E., Riccardi, P., Vergari, F., 2004. Personality, event-related potential (ERP) and heart rate (HR) in emotional word processing. *Personality and Individual Differences* 36, 873-891.
- Dillon, D.G., Holmes, A.J., Jahn, A.L., Bogdan, R., Wald, L.L., Pizzagalli, D.A., 2008. Dissociation of neural regions associated with anticipatory versus consummatory phases of incentive processing. *Psychophysiology* 45, 36-49.
- Duncan, C.C., Barry, R.J., Connolly, J.F., Fischer, C., Michie, P.T., Näätänen, R., Polich, J., Reinvang, I., Van Petten, C., 2009. Event-related potentials in clinical research: guidelines for eliciting, recording, and quantifying mismatch negativity, P300, and N400. *Clin Neurophysiol.* 120, 1883-1908.
- Eshel, N., Roiser, J.P., 2010. Reward and punishment processing in depression. *Biol. Psychiatry* 68, 118-124.
- Fernando, K., Carter, J.D., Frampton, C.M.A., Luty, S.E., McKenzie, J., Mulder, R.T., Joyce, P.R., 2011. Childhood-, teenage-, and adult-onset depression: diagnostic and individual characteristics in a clinical sample. *Comprehensive Psychiatry* 52, 623-629.
- Forbes, E.E., Dahl, R.E., 2012. Research Review: altered reward function in adolescent depression: what, when and how? *J. Child Psychol. Psychiatry* 53, 3-15.
- Forbes, E.E., Olino, T.M., Ryan, N.D., Birmaher, B., Axelson, D., Moyles, D.L., Dahl, R.E., 2010. Reward-related brain function as a predictor of treatment response in adolescents with major depressive disorder. *Cogn. Affect. Behav. Neurosci.* 10, 107-118.

- Forbes, E.E., Hariri, A.R., Martin, S.L., Silk, J.S., Moyses, D.L., Fisher, P.M., Brown, S.M., Ryan, N.D., Birmaher, B., Axelson, D.A., Dahl, R.E., 2009. Altered striatal activation predicting real-world positive affect in adolescent major depressive disorder. *Am. J. Psychiatry* 166, 64-73.
- Forbes, E.E., Christopher May, J., Siegle, G.J., Ladouceur, C.D., Ryan, N.D., Carter, C.S., Birmaher, B., Axelson, D.A., Dahl, R.E., 2006. Reward-related decision-making in pediatric major depressive disorder: an fMRI study. *J. Child Psychol. Psychiatry* 47, 1031-1040.
- Forbes, E.E., Dahl, R.E., 2005. Neural systems of positive affect: relevance to understanding child and adolescent depression? *Dev. Psychopathol.* 17, 827-850.
- Foti, D., Carlson, J.M., Sauder, C.L., Proudfit, G.H., 2014. Reward dysfunction in major depression: multimodal neuroimaging evidence for refining the melancholic phenotype. *Neuroimage* 101, 50-58.
- Foti, D., Weinberg, A., Dien, J., & Hajcak, G., 2011. Event-related potential activity in the basal ganglia differentiates rewards from non-rewards: temporospatial principal components analysis and source localization of the feedback negativity. *Hum. Brain Mapp.* 32, 2207-2216.
- Foti, D., Hajcak, G., 2009. Depression and reduced sensitivity to non-rewards versus rewards: Evidence from event-related potentials. *Biol. Psychol.* 81, 1-8.
- Frost Bellgowan, J., Molfese, P., Marx, M., Thomason, M., Glen, D., Santiago, J., Gotlib, I.H., Drevets, W.C., Hamilton, J.P., 2015. A neural substrate for behavioral inhibition in the risk for major depressive disorder. *J. Am. Acad. Child Adolesc. Psychiatry* 54, 841-848.
- Galvao, T.F., Silva, M.T., Zimmermann, I.R., Souza, K.M., Martins, S.S., Pereira, M.G., 2014. Pubertal timing in girls and depression: a systematic review. *J. Affect. Disord.* 155, 13-19.
- Gaysina, D., Richards, M., Kuh, D., Hardy, R., 2015. Pubertal maturation and affective symptoms in adolescence and adulthood: Evidence from a prospective birth cohort. *Dev. Psychopathol.* 27, 1331-1340.
- Gehring, W.J., Liu, Y., Orr, J.M., Carp, J. 2012. The error-related negativity (ERN/Ne), in: Luck, S.J., Kappenman, E.S. (Eds), *The Oxford Handbook of Event-Related Potential Components*. Oxford University Press, New York, pp. 231-291.
- Goddings, A.-L., 2014. The role of puberty in human adolescent brain development, in: Bourgoignon, J.P., Carel, J.-C., Christen, Y. (Eds.), *Brain Crosstalk in Puberty and Adolescence*. Springer, pp. 75-83.
- Goldstein, R.Z., Cottone, L.A., Jia, Z., Maloney, T., Volkow, N.D., Squires, N.K., 2006. The effect of graded monetary reward on cognitive event-related potentials and behavior in young healthy adults. *Int. J. Psychophysiol.* 62, 272-279.
- Goodkind, M., Eickhoff, S.B., Oathes, D.J., Jiang, Y., Chang, A., Jones-Hagata, L.B., Ortega, B.N., Zaiko, Y.V., Roach, E.L., Korgaonkar, M.S., Grieve, S.M., Galatzer-Levy, I., Fox, P.T., Etkin, A., 2015. Identification of a common neurobiological substrate for mental illness. *JAMA psychiatry* 72, 305-315.
- Gotlib, I. H., Hamilton, J. P., Cooney, R. E., Singh, M. K., Henry, M. L., & Joormann, J. (2010). Neural processing of reward and loss in girls at risk for major depression. *Arch. Gen. Psychiatry* 67, 380-387.
- Greimel, E., 2011. Sozial-affektive Entwicklung im Jugendalter, in: Uhlhaas, P.J., Konrad, K. (Eds.), *Das adoleszente Gehirn*. Kohlhammer, Stuttgart, pp. 158-172.
- Hamilton, J.P., Chen, M.C., Gotlib, I.H., 2013. Neural systems approaches to understanding major depressive disorder: an intrinsic functional organization perspective. *Neurobiol. Dis.* 52, 4-11.
- Handy, T.C., 2005. Basic principles of ERP quantification, in: Handy, T.C. (Ed.), *Event-Related Potentials: A Methods Handbook*. MIT Press, Cambridge, pp. 33-55.
- Hansenne, M., 2006. Event-related brain potentials in psychopathology: Clinical and cognitive perspectives. *Psychologica Belgica* 46, 5-36.
- Hopfinger, J.B., Khoe, W., Song, A., 2005. Combining Electrophysiology with Structural and Functional Neuroimaging: ERPs, PET, MRI and fMRI, in: Handy, T.C. (Ed.), *Event-Related Potentials: A Methods Handbook*. MIT Press, Cambridge, M.A, pp. 345-380.
- Houston, R.J., Bauer, L.O., Hesselbrock, V.M., 2004. P300 evidence of cognitive inflexibility in female adolescents at risk for recurrent depression. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 28, 529-536.
- Jaffee, S.R., Moffitt, T.E., Caspi, A., Fombonne, E., Poulton, R., Martin, J., 2002. Differences in early childhood risk factors for juvenile-onset and adult-onset depression. *Arch. Gen. Psychiatry* 59, 215-222.
- Johnson, S.L., Turner, R.J., Iwata, N., 2003. BIS/BAS levels and psychiatric disorder: an epidemiological study. *J. Psychopath. Behav. Assess.* 25, 25-36.
- Kappenman, E.S., Luck, S.J., 2010. The effects of electrode impedance on data quality and statistical significance in ERP recordings. *Psychophysiology* 47, 888-904.

- Kaufman, J., Martin, A., King, R.A., Charney, D., 2001, Are child-, adolescent-, and adult-onset depression one and the same disorder? *Biol. Psychiatry* 12, 980-1001.
- Kerestes, R., Davey, C.G., Stephanou, K., Whittle, S., Harrison, B.J., 2014. Functional brain imaging studies of youth depression: a systematic review. *NeuroImage. Clin.* 4, 209-231.
- Kim, M.-S., Cho, S.-S., Kang, K.-W., Hwang, J.-L., Kwon, J.S., 2002. Electrophysiological correlates of personality dimensions measured by Temperament and Character Inventory. *Psychiatry Clin. Neurosci.* 56, 631–635.
- Knutson, B., Bhanji, J.P., Cooney, R.E., Atlas, L.Y., Gotlib, I.H., 2008. Neural responses to monetary incentives in major depression. *Biol. Psychiatry* 63, 686-692.
- Knutson, B., Westdorp, A., Kaiser, E., Hommer, D., 2000. fMRI visualization of brain activity during a monetary incentive delay task. *NeuroImage* 12, 20-27.
- Kujawa, A., Burkhouse, K.L., 2017. Vulnerability to depression in youth: Advances from affective neuroscience. *Biol. Psychiatry Cogn. Neurosci. Neuroimaging* 2, 28-37.
- Kujawa, A., Proudfit, G.H., Klein, D.N., 2014. Neural reactivity to rewards and losses in offspring of mothers and fathers with histories of depressive and anxiety disorders. *J. Abnorm. Psychol.* 123, 287-297.
- Liu, Hairston, J., Schrier, M., Fan, J., 2011. Common and distinct networks underlying reward valence and processing stages: a meta-analysis of functional neuroimaging studies. *Neurosci. Biobehav. Rev.* 35, 1219-1236.
- Liu, Wang, L.Z., Shang, H.R., Shen, Y., Li, Z., Cheung, E.F., Chan, R.C., 2014. The influence of anhedonia on feedback negativity in major depressive disorder. *Neuropsychologia* 53, 213-220.
- Luck, S.J., 2005. An Introduction to Event-Related Potential Technique, in: Luck, S.J. (Ed.), *An Introduction to Event-Related Potential Technique*. The Massachusetts Institute of Technology Press Cambridge, Massachusetts, pp. 7-50.
- Luking, K.R., Pagliaccio, D., Luby, J.L., Barch, D.M., 2016. Depression risk predicts blunted neural responses to gains and enhanced responses to losses in healthy children. *J. Am. Acad. Child Adolesc. Psychiatry* 55, 328-337.
- Lutz, K., Widmer, M., 2014. What can the monetary incentive delay task tell us about the neural processing of reward and punishment? *Neurosci. Neuroecon.* 3, 33-45.
- McFarland, B.R., Klein, D.N., 2009. Emotional reactivity in depression: diminished responsiveness to anticipated reward but not to anticipated punishment or to nonreward or avoidance. *Depress. Anxiety* 26, 117-122.
- Mellick, W., Sharp, C., Alfano, C., 2014. The role of BIS/BAS in the vulnerability for depression in adolescent girls. *Personal. Individ. Differ.* 69, 17-21.
- Menon, V., 2015. Salience Network, in: Toga, A.W. (Ed.), *Brain Mapping: An Encyclopedic Reference*. Academic Press: Elsevier, pp. 597-611.
- Mulert, C., Pogarell, O., Juckel, G., Rujescu, D., Giegling, I., Rupp, D., Mavrogiorgou, P., Bussfeld, P., Gallinat, J., Moller, H.J., Hegerl, U., 2004. The neural basis of the P300 potential. Focus on the time-course of the underlying cortical generators. *Eur. Arch. Psychiatry Clin. Neurosci.* 254, 190-198.
- Murphy, F.C., Michael, A., Robbins, T.W., Sahakian, B.J., 2003. Neuropsychological impairment in patients with major depressive disorder: The effects of feedback on task performance. *Psychological Medicine* 33, 455–467.
- Nelson, B.D., Perlman, G., Klein, D.N., Kotov, R., Hajcak, G., 2016. Blunted neural response to rewards as a prospective predictor of the development of depression in adolescent girls. *Am. J. Psychiatry* 173, 1223-1230.
- Novak, B.K., Novak, K.D., Lynam, D.R., Foti, D., 2016. Individual differences in the time course of reward processing: Stage-specific links with depression and impulsivity. *Biol. Psychol.* 119, 79-90.
- Novak, K.D., Foti, D., 2015. Teasing apart the anticipatory and consummatory processing of monetary incentives: An event-related potential study of reward dynamics. *Psychophysiology* 52, 1470-1482.
- Pfabigan, D.M., Alexopoulos, J., Bauer, H., Lamm, C., Sailer, U., 2011. All about the money – external performance monitoring is affected by monetary, but not by socially conveyed feedback cues in more antisocial individuals. *Front. Hum. Neurosci.* 100.
- Pizzagalli, D.A., Holmes, A.J., Dillon, D.G., Goetz, E.L., Birk, J.L., Bogdan, R., Dougherty, D.D., Iosifescu, D.V., Rauch, S.L., Fava, M., 2009. Reduced caudate and nucleus accumbens response to rewards in unmedicated individuals with major depressive disorder. *Am. J. Psychiatry* 166, 702-710.
- Polich, J., 2007. Updating P300: an integrative theory of P3a and P3b. *Clin. Neurophysiol.* 118, 2128-2148

- Polich, J., 2003. Theoretical overview of P3a and P3b, in: Polich, J. (Ed.) *Detection of change: Event-related potential and fMRI findings*. Kluwer Academic; Boston, MA: 2003. pp. 83-98.
- Polich, J., Kok, A., 1995. Cognitive and biological determinants of P300: an integrative review. *Biol. Psychol.* 41, 103-146.
- Proudfit, G.H., 2015. The reward positivity: from basic research on reward to a biomarker for depression. *Psychophysiology* 52, 449-459.
- Ramsey, S.E., Finn, P.R., 1997. P300 from men with a family history of alcoholism under different incentive conditions. *J. Stud. Alcohol.* 58, 606-616.
- Rao, U., Chen, L.A., 2009. Characteristics, correlates, and outcomes of childhood and adolescent depressive disorders. *Dialogues Clin. Neurosci.* 11, 45-62.
- Rohde, P., Beavers, C.G., Stice, E., O'Neil, K., 2009. Major and minor depression in female adolescents: onset, course, symptom presentation, and demographic associations. *J. Clin. Psychol.* 65, 1339-1349.
- Rubia, K., 2013. Functional brain imaging across development. *Eur. Child Adolesc. Psychiatry* 22, 719-731.
- Sambrook, T.D., Goslin, J., 2015. A neural reward prediction error revealed by a meta-analysis of ERPs using great grand averages. *Psychol. Bull.* 141, 213-235.
- Santesso, D.L., Bogdan, R., Birk, J.L., Goetz, E.L., Holmes, A.J., Pizzagalli, D.A., 2012. Neural responses to negative feedback are related to negative emotionality in healthy adults. *Soc. Cogn. Affect. Neurosci.* 7, 794-803.
- Schneider, W., Eschman, A., Zuccolotto, A., 2012. *E-Prime User's Guide*. Psychology Software Tools, Inc., Pittsburgh.
- Stringaris, A., Vidal-Ribas Belil, P., Artiges, E., Lemaitre, H., Gollier-Briant, F., Wolke, S., Vulser, H., Miranda, R., Penttilä, J., Struve, M., Fadai, T., Kappel, V., Grimmer, Y., Goodman, R., Poustka, L., Conrod, P., Cattrell, A., Banaschewski, T., Bokde, A.L., Bromberg, U., Buchel, C., Flor, H., Frouin, V., Gallinat, J., Garavan, H., Gowland, P., Heinz, A., Ittermann, B., Nees, F., Papadopoulos, D., Paus, T., Smolka, M.N., Walter, H., Whelan, R., Martinot, J.L., Schumann, G., Paillere-Martinot, M.L., Consortium, I., 2015. The brain's response to reward anticipation and depression in adolescence: dimensionality, specificity, and longitudinal predictions in a community-based sample. *Am. J. Psychiatry* 172, 1215-1223.
- Strobel, A., Beauducel, A., Debener, S., Brocke, B., 2001. Eine deutschsprachige Version des BIS/BAS-Fragebogens von Carver und White (A German version of Carver and White's BIS/BAS scales). *Z. Diff. und Diagnost. Psychol.* 22, 216-227.
- Thimm, J.C., Holte, A., Brennen, T., Wang, C.E., 2013. Hope and expectancies for future events in depression. *Front. Psychol.* 4, 470.
- Unnewehr, S., Schneider, S., Margraf, J. (Eds.), 1995. *Diagnostisches Interview bei psychischen Störungen im Kindes und Jugendalter (Kinder-DIPS)*, first ed. Springer, Berlin.
- Urosevic, S., Collins, P., Muetzel, R., Lim, K.O., Luciana, M., 2014. Pubertal status associations with reward and threat sensitivities and subcortical brain volumes during adolescence. *Brain and Cogn.* 89, 15-26.
- Venables, N.C., Patrick, C.J., Hall, J.R., Bernat, E.M., 2011. Clarifying relations between dispositional aggression and brain potential response: overlapping and distinct contributions of impulsivity and stress reactivity. *Biol. Psychol.* 86, 279-288.
- Verleger, R., 1997. On the utility of P3 latency as an index of mental chronometry. *Psychophysiol.* 34, 131-56.
- Verleger, R., 1988. Event-related potentials and cognition: A critique of the context updating hypothesis and an alternative interpretation of P3. *Behav. Brain Sci.* 11, 343-356.
- Wacker, J., Chavanon, M.-L., Leue, A., Stemmler, G., 2010. Trait BIS predicts alpha asymmetry and P300 in a Go/No-Go task. *Eur. J. Pers.* 24, 85-105.
- Webb, C.A., Auerbach, R.P., Bondy, E., Stanton, C.H., Foti, D., Pizzagalli, D.A., 2017. Abnormal neural responses to feedback in depressed adolescents. *J. Abnorm. Psychol.* 126, 19-31.
- Weiss, B., Garber, J., 2003. Developmental differences in the phenomenology of depression. *Dev. Psychopathol.* 15, 403-430.
- Weiss, R.H., 2006. *Grundintelligenztest Skala 2- Revision*. CFT 20-R. Hogrefe, Goettingen.
- Whitton, A.E., Treadway, M.T., Pizzagalli, D.A., 2015. Reward processing dysfunction in major depression, bipolar disorder and schizophrenia. *Curr. Opin. Psychiatry* 28, 7-12.
- Wu, Y., Zhou, X., 2009. The P300 and reward valence, magnitude, and expectancy in outcome evaluation. *Brain Res.* 1286, 114-122.

## **Tables**

**Table 1.** Demographic and clinical characteristics for the Major Depressive Disorder (MDD) and control group.

	<b>MDD (n=25)</b>	<b>Controls (n=29)</b>	<b><i>p</i></b>
<b>Mean Age</b> <b>(years)</b>	15.20 (1.50)	15.46 (1.46)	.51
<b>Age range</b> <b>(years; Min-Max)</b>	12.3–17.7	12.3–17.5	
<b>Mean IQ (CFT 20-R)</b>	111.46 (11.87)	107.79 (9.84)	.22
<b>Handedness</b> <b>(right/left)</b>	23/2	27/2	.88
<b>Gender</b> <b>(female/male)</b>	21/4	23/6	.89
<b>Mean score Beck</b> <b>Depression</b> <b>Inventory-II</b>	25.27 (12.22)	3.00 (3.55)	<.01 *
<b>Mean BAS drive</b> <b>score</b>	27.00 (2.13)	26.24 (1.75)	.16
<b>Mean BAS fun</b> <b>score</b>	25.71 (2.12)	25.17 (1.81)	.33
<b>Mean BAS</b> <b>reward score</b>	24.58 (3.11)	25.07 (1.67)	.50
<b>Mean BIS Score</b>	20.75 (3.54)	17.93 (2.19)	.002 *

\*significant at alpha=.05; standard deviations in brackets. BAS = Behavioral Approach System; BIS = Behavioral Inhibition System; CFT 20-R = Culture Fair Intelligence Test 20-R

**Table 2.** Group means and standard deviations (in brackets) of reaction times (RTs) for the Major Depressive Disorder (MDD) and control group

	<b>MDD (n=25)</b>	<b>Controls (n=29)</b>	<b>p</b>
<b>RTs MR trials</b>	221.32 (18.20)	231.59 (27.41)	.12
<b>RTs MP trials</b>	223.08 (22.57)	236.79 (31.04)	.07
<b>RTs control trials-MR block</b>	242.12 (34.20)	253.14 (38.23)	.27
<b>RTs control trials-MP block</b>	244.56 (46.08)	257.86 (36.15)	.26

Abbreviations: MR=monetary reward; MP=monetary punishment

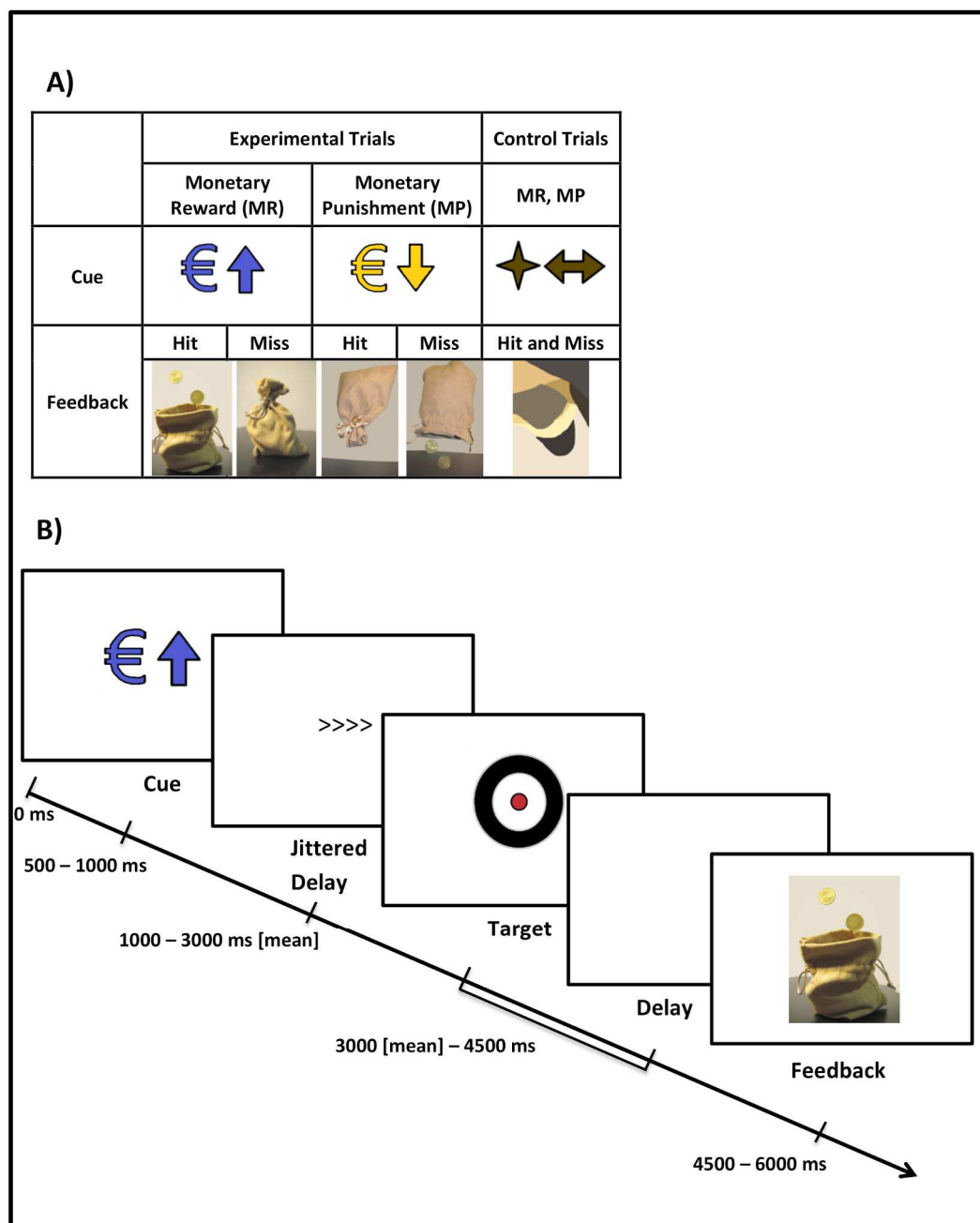
**Table 3.** Group means of event-related potential parameters (amplitude in  $\mu\text{V}$ /latency in ms)

	Major Depressive Disorder (n=25)	Controls (n=29)
<b>Cue-P3 mean amplitude MR</b>	3.81 (3.05)	3.98 (2.86)
<b>Cue-P3 mean amplitude MP</b>	2.48 (3.18)	3.25 (2.18)
<b>Cue-P3 peak latency MR</b>	282.12 (38.01)	260.48 (36.14)
<b>Cue-P3 peak latency MP</b>	266.08 (38.44)	266.49 (41.02)
<b>Feedback-P3 mean amplitude MR</b>	8.83 (4.72)	9.69 (4.65)
<b>Feedback-P3 mean amplitude MP</b>	7.19 (4.19)	8.82 (5.41)
<b>Feedback-P3 peak latency MR</b>	285.58 (23.52)	293.29 (32.22)
<b>Feedback-P3 peak latency MP</b>	308.82 (27.35)	297.42 (33.89)
<b>RewP mean amplitude MR – central ROI</b>	3.09 (3.05)	3.29 (2.60)
<b>RewP mean amplitude MR – frontal ROI</b>	1.15 (3.52)	1.68 (2.83)
<b>RewP mean amplitude MP – central ROI</b>	2.30 (2.79)	1.32 (3.94)
<b>RewP mean amplitude MP – frontal ROI</b>	2.71 (3.79)	2.02 (2.22)

Abbreviations: MR=monetary reward; MP=monetary punishment; RewP=Reward Positivity (difference wave); standard deviations in brackets.



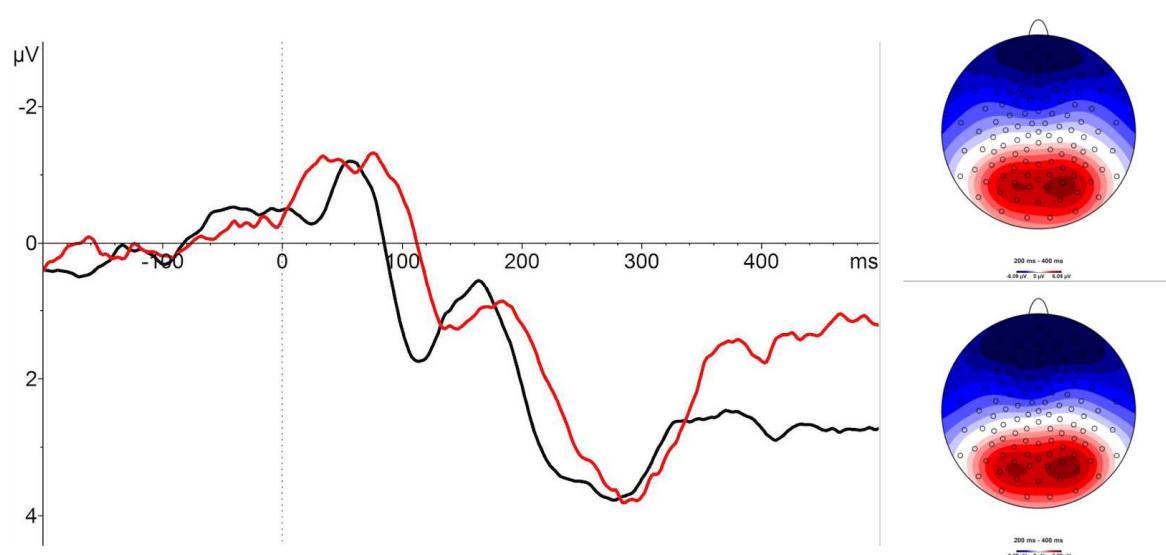
## Figures



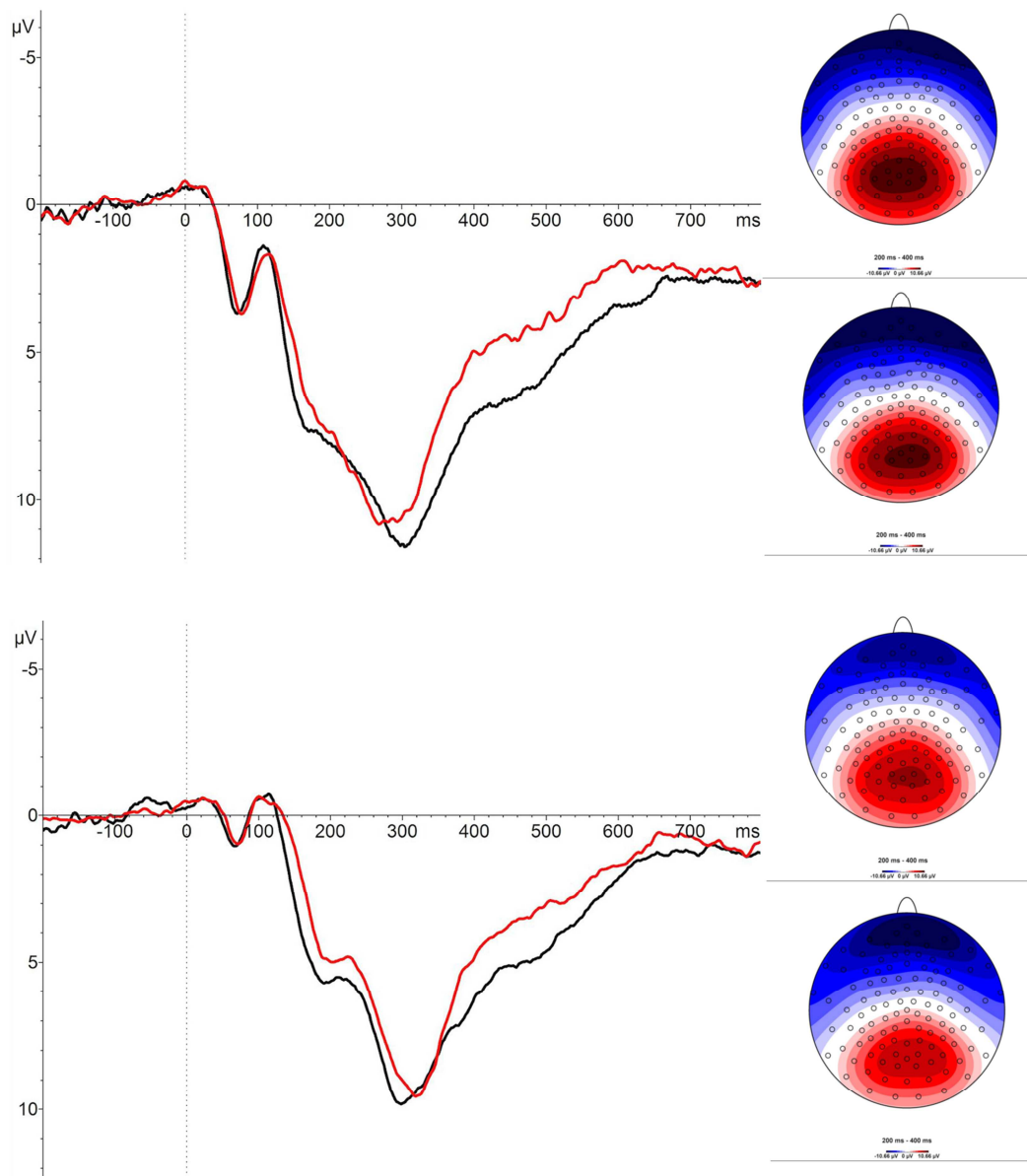
**Figure 1.**

A) MIDT design and stimuli (cue/feedback) of the experimental and control trials

B) MIDT trial structure (example: Monetary reward condition, positive feedback)



**Figure 2.** Left: Stimulus-locked event-related potentials to cues in the monetary reward condition for the Major Depressive Disorder (MDD; red) and control group (black) at sample electrode site 61. Right: Scalp distribution for the cP3 (time window: 200-400ms) for the control (top) and MDD group (bottom).



**Figure 3.** Left: Stimulus-locked event-related potentials to feedback for the Major Depressive Disorder (MDD; red) and control group (black) within the monetary reward (top) or monetary punishment condition (bottom) averaged across positive and negative outcome valences at electrode site 62 (Pz). Right: Scalp distribution for the fP3 (time window: 200-400ms) for the control (top) and MDD group (bottom) for each condition, respectively.

## **Role of Funding**

This work was supported by the Faculty of Medicine, University of Munich (Foerderprogramm für Forschung & Lehre to E. Greimel, 776). The funding source had no involvement in the study design, the collection, analysis and interpretation of data or the writing of the manuscript.

## **Acknowledgements**

We wish to thank all our participants and families as well as Carolina Silberbauer, Petra Wagenbüchler & Julia Stiegert for assistance in data collection.

## Supporting Material

**S1** – Information on comorbidities and further clinical characteristics within the Major Depressive Disorder group

**S2** – Detailed trial structure of the Monetary Incentive Delay Task used in this study

**S3** – Online response algorithm of the Monetary Incentive Delay Task used in this study

**S4** – Stimuli of the Monetary Incentive Delay Task used in this study

**S5** – **Figure A.** Radial projection of the electrode montage: Illustration of the 128-channel arrangement and electrode position

**S6** – Incentive effects of cue/feedback presentation on cP3/fP3 mean amplitude

**S6** – **Figure B & C.** Stimulus-locked event-related potentials to experimental and control feedback

**S7** – **Figure D.** Reward Positivity (RewP) difference wave: Stimulus locked event-related potentials to positive and negative outcomes as well as the difference wave between both within the monetary reward and monetary punishment condition

**S8** – **Figure E.** Stimulus-locked event-related potentials to cues in the monetary punishment condition for the Major Depressive Disorder and control group at sample electrode site 61 & and scalp distributions for the cP3.

**S9** – Information on noise level estimates

**S9** – **Table A.** Noise level estimates for the cP3 and fP3 for the monetary reward and monetary punishment condition, separately for the Major Depressive Disorder (MDD) and control group

## References Supporting Material

*S1 - Information on comorbidities and further clinical characteristics within the Major Depressive Disorder (MDD) group:*

In regard of psychiatric comorbidities, MDD participants who met the criteria of a current or past diagnosis in terms of attention deficit [and hyperactivity] disorder (AD[H]S), obsessive-compulsive disorder, substance abuse or dependence, bipolar disorder, schizophrenic disorder or social phobia were not included in the present study. MDD patients comorbid with other than the above listed disorders were included, if MDD was the main psychiatric condition. Two MDD participants were diagnosed with a comorbid eating disorder (one with Bulimia nervosa, one with Anorexia nervosa [BMI>10<sup>th</sup> percentile at time of assessment]), two participants met the criteria of a comorbid

posttraumatic stress disorder, three participants were diagnosed with a comorbid episode of dysthymia (one with an additional diagnosis of a past conduct disorder and one with an additional diagnosis of specific phobia, see below), and three participants fulfilled the criteria for a specific phobia (one with an additional diagnosis of dysthymia, see above). Of note, none of the MDD participants met the criteria of a comorbid general anxiety disorder, panic disorder or agoraphobia. This was presumably due to the fact that MDD was requested to be the main psychiatric condition and patients presenting with MDD that was secondary to an anxiety disorder or patients for whom MDD as the primary diagnosis could not reliably be confirmed based on the Kinder-DIPS were not included in the study. Regarding the course of depression, 15 out of 25 participants were diagnosed with a first episode of depression at the time of study assessment, the remaining 10 participants were diagnosed with a recurrent depressive disorder. The mean age of onset of MDD was 13.24 years (SD 2.13), ranging from 7 years to 17 years. A parental/sibling history of depression was reported for seven participants of the MDD group (mother: 1; father: 6, one with additionally 1 sibling affected by depression).

#### *S2 - Detailed trial structure of the Monetary Incentive Delay Task (MIDT) used in this study:*

Each trial started with a cue (500ms), informing the participant of a possible reward or punishment, depending on the specific experimental condition (monetary reward/monetary punishment) or the occurrence of a control trial. After the presentation of the cue, an anticipation phase followed, with a duration jittered between 1750–2250ms (mean: 2000ms) in order to prevent an automated response and to ensure that the participants' attention was focused on the upcoming target. Thereafter, the target was presented and remained on screen for an individually set period of time, which was defined through our adaptive online response algorithm (see S3). The participants were instructed to press the left mouse button with the index finger of the dominant hand as fast and as precisely as possible (i.e., avoiding anticipatory responses or misses) in order to hit the target while it was presented on screen. 1500ms after target onset, the condition-specific feedback stimulus or the control feedback was presented and remained on screen for 1500ms. If the participant managed to press the response button in time in experimental trials, a positive feedback occurred (reward outcome within the monetary reward condition or likewise no-punishment outcome within the monetary punishment condition) whereas late responses (when the target had already disappeared from screen) led to negative feedback (no-reward outcome within the monetary reward condition or likewise punishment

outcome within the monetary punishment condition). Note that also missing responses and anticipatory responses were followed by negative feedback. In control trials, a non-informative stimulus was presented as feedback regardless of the participant's reaction. After feedback presentation, an Inter-Trial-Interval (ITI) of 500ms followed displaying a blank screen. Given that the feedback onset was presented 1500ms after target onset (independent of the individual RTs) trial duration was kept constant across participants.

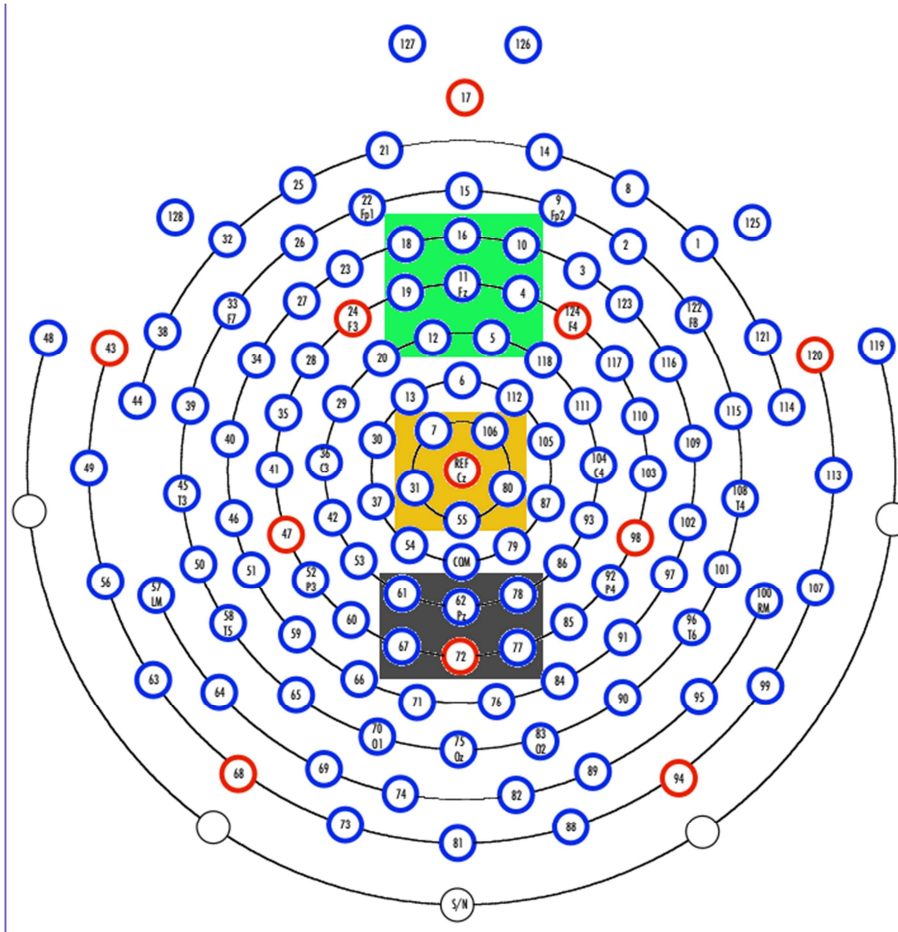
### *S3 - Online response algorithm of the Monetary Incentive Delay Task (MIDT) used in this study:*

The individual response window, namely the period of time while the target remained on screen, was defined through an online response algorithm (for a similar approach see, e.g. Kohls et al., 2013). In detail, the target duration was adjusted online based on the reaction times of the two previous experimental trials to achieve an accuracy rate of ~50%. Aligning all participants to an accuracy rate – and thus positive feedback rate – of approximately 50% has been shown to be optimal with regard to the motivational value (Martens & White, 1975) and also guarantees that positive and negative feedback is presented in the same frequency. The online algorithm furthermore promoted task believability as outcomes were clearly linked to the specific individual reaction within each trial. In this study, the hit rate of the participants across groups was on average  $45.20\% \pm 6.65\%$  in monetary reward trials and  $45.31\% \pm 6.27\%$  in monetary punishment trials (both approximating the targeted 50%). Notably, groups did not differ in hit rates in both experimental conditions (all  $p > .22$ ). The initial target durations for both conditions (monetary reward, monetary punishment) were based on the individual mean reaction times in a condition-specific practice session.

### *S4 – Stimuli of the Monetary Incentive Delay Task (MIDT) used in this study:*

The feedback stimuli of the MIDT were designed to concur with the themes of monetary reward (“reward” vs. “no-reward”) and punishment (“punishment” vs. “no-punishment”). Altogether 40 slightly varying photographs of money bags were presented (10 for each outcome type: reward/no-reward; punishment/no-punishment). The 40 control trials within each block consisted of 10 slightly varying scrambled patterns (designed with Adobe Photoshop7.0). Pictures were controlled in luminescence and design to match the stimuli of the experimental conditions. Likewise Adobe Photoshop7.0 was used to design the cue stimuli. The two condition specific cue stimuli as well as the control cue

stimulus each consisted of an array of a money/control symbol and an arrow (see Figure 1 in the main text). All stimuli were presented on a 17inches Dell monitor placed 70cm in front of the participants.



S5 – Figure A:

Illustration of the 128-channel arrangement and electrode position taken from Electrical Geodesic, Inc.

Black square: Parietal ROI for the cP3 and fP3 analyses, spanning electrodes 61,62[Pz],67,72,77&78;

Orange square: Central ROI for the RewP analyses, spanning electrodes 7,31,55,80,106,129[Cz];

Green square: Frontal ROI for the RewP analyses, spanning electrodes 4,5,10,11[Fz],12,16,18,19.

#### S6 - Incentive effects of cue/feedback presentation on cP3/fP3 mean amplitude:

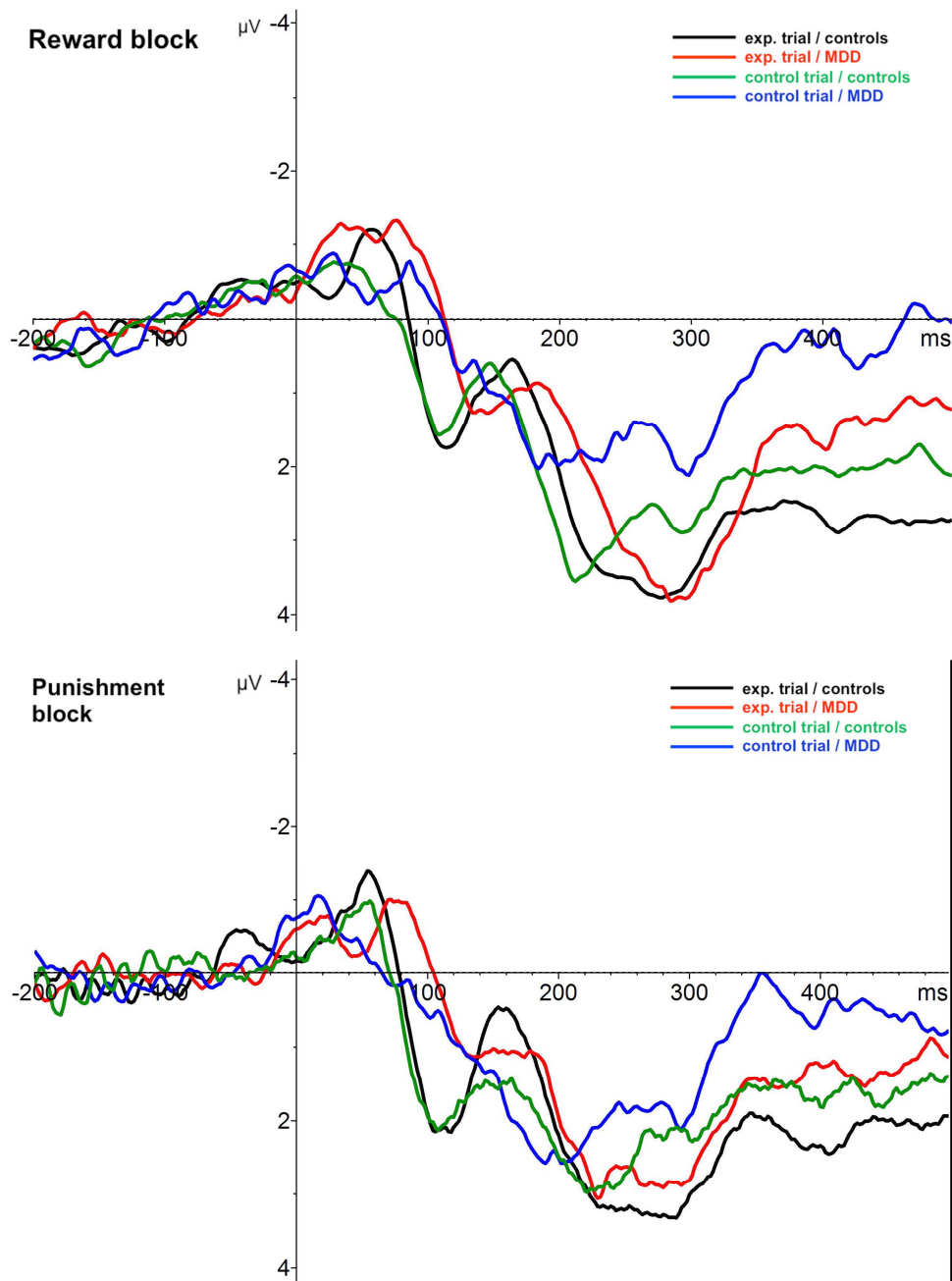
cP3 and fP3 components for control trials were characteristically different from those for monetary reward/monetary punishment trials. More precisely no clear peak of the components was evident for control trials. In order to nevertheless examine incentive effects of meaningful vs. meaningless cue/feedback presentation on cP3/fP3 amplitudes, we conducted additional analyses in which we



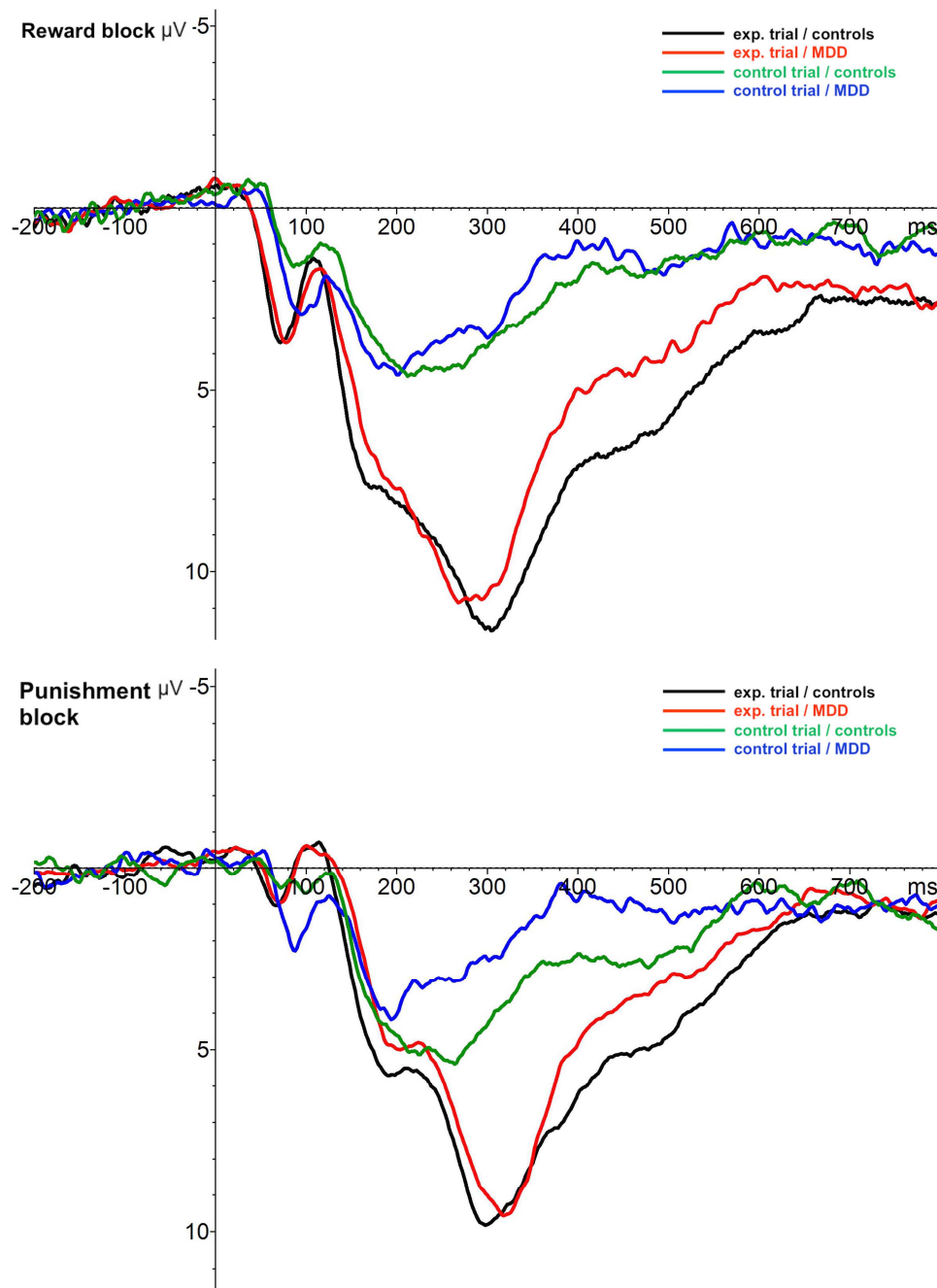
compared mean amplitudes for experimental and control trials, taking into account the factors block and group.

cP3 mean amplitudes were analyzed in the time window between 200-340ms at the parietal ROI (see S5 - Figure A) based on a 2(block: reward/punishment)x2(trial type: experimental trial/control trial)x2(group: MDD/control) repeated-measures ANOVA. This analysis revealed a significant main effect of block ( $F(1,52)=10.24; p=.002; \eta^2_p=.17$ ) and trial type ( $F(1,52)=4.61; p=.04; \eta^2_p=.08$ ) with smaller mean amplitudes for monetary reward trials (compared to monetary punishment trials) and higher mean amplitudes for experimental trials (compared to control trials; see S6 Figure B). Higher mean amplitudes to experimental compared to control cues indicate an elevated attentional effect of the reward/punishment-predicting cues on the cP3 component across all participants. Enhanced cP3 amplitudes are commonly interpreted as stronger allocation of attention towards the cue, which subsequently motivates incentive-seeking behavior (Novak & Foti, 2015).

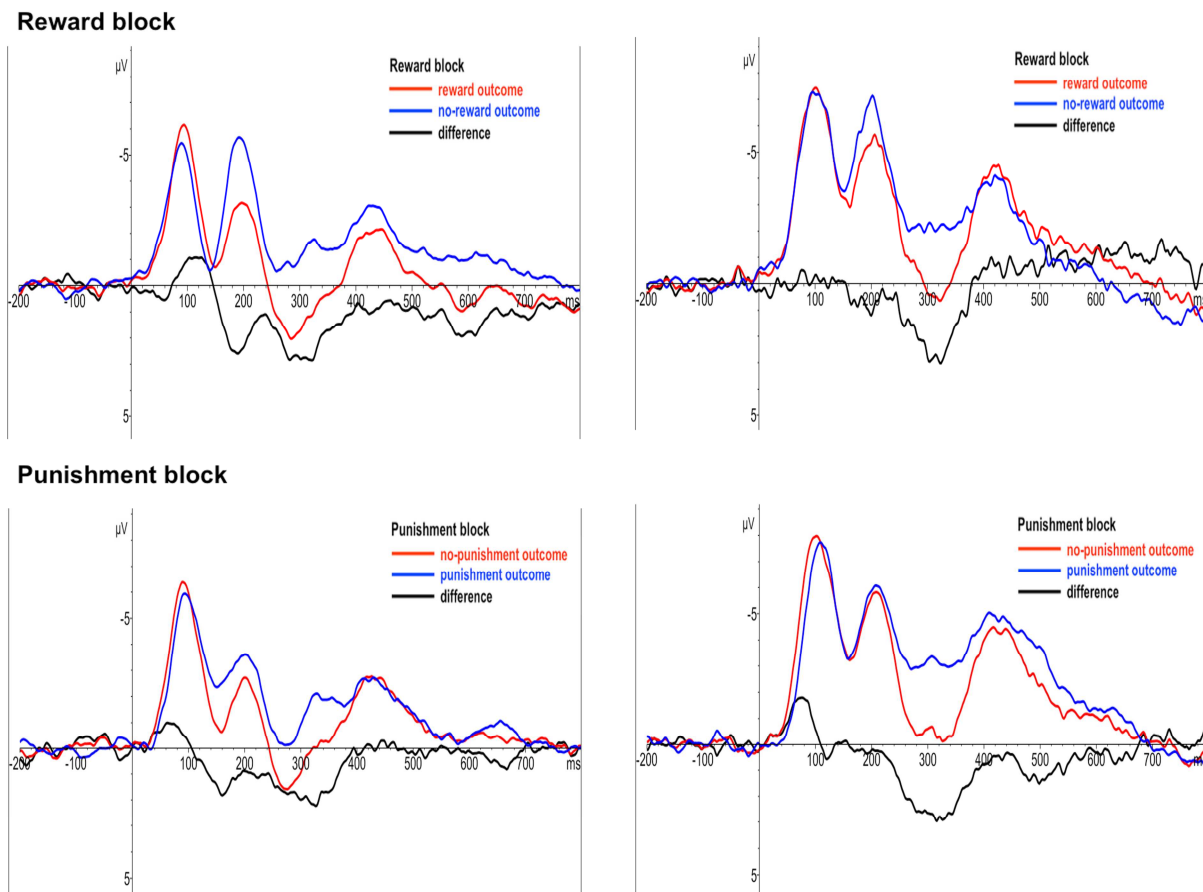
fP3 mean amplitudes were analyzed in the time window between 220-400ms at the parietal ROI (see S5 – Figure A) based on a 2(block: reward/punishment)x2(trial type: experimental trial/control trial)x2(group: MDD/control) repeated-measures ANOVA. This analysis revealed significant main effects of block ( $F(1,52)=6.83; p=.01; \eta^2_p=.12$ ) and trial type ( $F(1,52)=188.79; p<.001; \eta^2_p=.78$ ) with smaller mean amplitudes for monetary punishment trials (compared to monetary reward trials) and higher mean amplitudes for experimental trials (compared to control trials; see S6 Figure C). The latter result indicates elevated consummatory brain activity across all participants elicited by performance-based, incentive feedback as higher fP3 amplitudes are commonly interpreted as stronger allocation of attention towards the feedback stimuli (Novak&Foti, 2015).



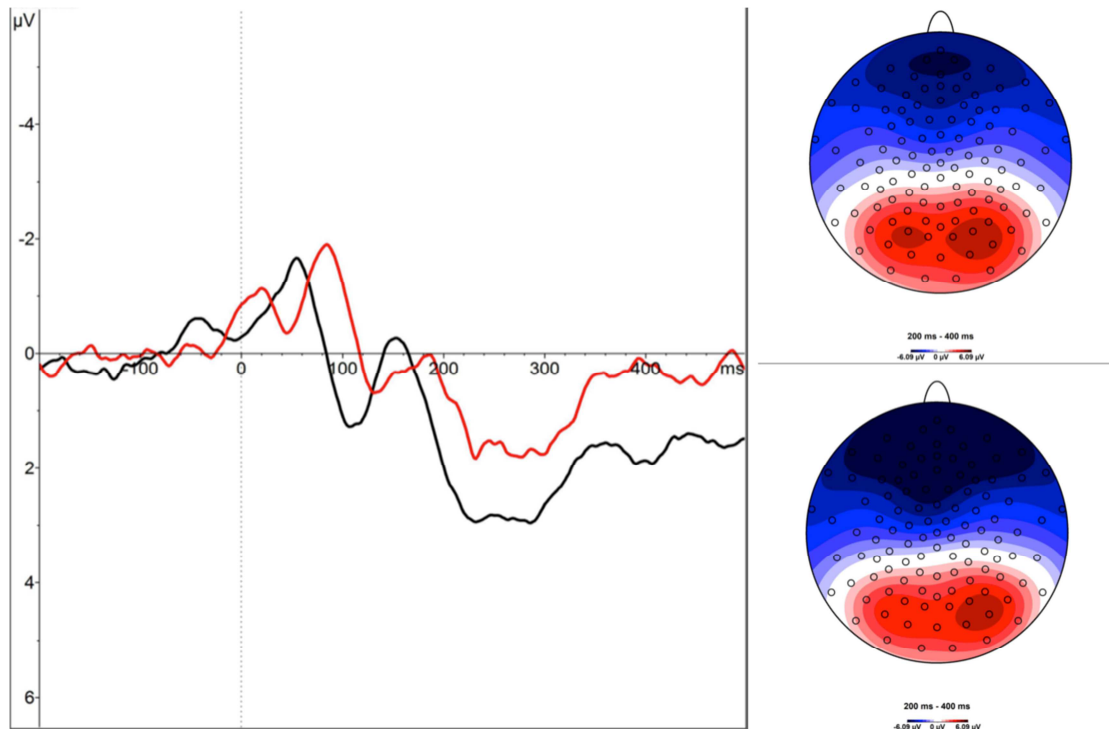
S6 – Figure B. Stimulus-locked event-related potentials for the Major Depressive Disorder (MDD) and controls to experimental cues (exp. trial) or control cues (control trial) in the reward block at sample electrode site 61 (top) and in the punishment block at sample electrode site 62 (bottom).



S6 – Figure C. Stimulus-locked event-related potentials for the Major Depressive Disorder group (MDD) and controls to experimental feedback (exp. trial) or control feedback (control trials) in the reward block (top) or punishment block (bottom) averaged across positive and negative outcome valences at electrode site 62 (Pz).



S7 – Figure D. RewP difference wave: Stimulus-locked event-related potentials for the Major Depressive Disorder group (right) and controls (left) to positive (reward block: reward; punishment block: no-punishment) and negative (reward block: no-reward; punishment block: punishment) outcomes as well as the difference wave between both outcome valences (positive minus negative outcomes) in the reward block (top) or punishment block (bottom) at a fronto-central electrode pooling of the frontal and central ROI (see S5 – Figure A).



S8 – *Figure E*. Left: Stimulus-locked event-related potentials to cues in the monetary punishment condition for the Major Depressive Disorder (red) and control group (black) at sample electrode site 61. Right: Scalp distribution for the cP3 (time window: 200-400ms) for the control (top) and MDD group (bottom).

#### S9 – *Information on noise level estimates*

Following recent recommendations (Clayson et al., 2013), we calculated noise level estimates (RMS (root mean square) amplitudes of the baseline period; see Kappenman and Luck, 2010) and compared them between groups for all experimental conditions to ensure the appropriateness of peak latency measures with respect to the cP3 and the fP3 component. The noise level of the prestimulus baseline period is generally considered a useful metric of the overall noise level of the data (Kappenman and Luck, 2010).

Noise levels for both components were comparable between groups (cP3: all  $p \geq .60$ ; fP3: all  $p \geq .47$ ; see S9 – Table A). Likewise, for both components, noise levels were comparable between the experimental conditions within both groups (all  $p \geq .35$ ).

*S9 –Table A. Noise level estimates for the cP3 and fP3 for the monetary reward and monetary punishment condition, separately for the Major Depressive Disorder (MDD) and control group*

	<b>MDD (n=25)</b>	<b>Controls (n=29)</b>	<b>p</b>
<b>Cue-P3, monetary reward</b>	.74 (.30)	.80 (.44)	.60
<b>Cue-P3, monetary punishment</b>	.75 (.48)	.74 (.37)	.96
<b>Feedback-P3, monetary reward – gain outcomes</b>	1.06 (.51)	1.16 (.59)	.52
<b>Feedback-P3, monetary reward – no-gain outcomes</b>	1.04 (.49)	1.12 (.64)	.63
<b>Feedback-P3, monetary punishment – loss outcomes</b>	1.00 (.43)	1.11 (.62)	.47
<b>Feedback-P3 monetary punishment – no-loss outcomes</b>	1.02 (.45)	1.12 (.60)	.51

Standard deviations in brackets; Noise levels were estimated based on RMS (root mean square) amplitude values of the baseline period (-200 to 0ms prestimulus; Kappenman and Luck, 2010).

### **References Supporting Material**

- Clayson, P.E., Baldwin, S.A., Larson, M.J., 2013. How does noise affect amplitude and latency measurement of event-related potentials (ERPs)? A methodological critique and simulation study. *Psychophysiology* 50, 174-186.
- Kappenman, E.S., Luck, S.J., 2010. The effects of electrode impedance on data quality and statistical significance in ERP recordings. *Psychophysiology* 47, 888-904.
- Kohls, G., Perino, M.T., Taylor, J.M., Madva, E.N., Cayless, S.J., Troiani, V., Price, E., Faja, S., Herrington, J.D., Schultz, R.T., 2013. The nucleus accumbens is involved in both the pursuit of social reward and the avoidance of social punishment. *Neuropsychologia* 51, 2062-2069.
- Martens, R., & White, V., 1975. Influence of win-loss ratio on performance, satisfaction and preference for opponents *Journal of Experimental Social Psychology* 11, 343-362.
- Novak, K.D., Foti, D., 2015. Teasing apart the anticipatory and consummatory processing of monetary incentives: An event-related potential study of reward dynamics. *Psychophysiology* 52, 1470-1482.

