



Published in final edited form as:

*Curr Opin Psychol.* 2015 August 1; 4: 110–113. doi:10.1016/j.copsyc.2014.12.018.

## Depression and Event-related Potentials: Emotional disengagement and reward insensitivity

Greg Hajcak Proudfit<sup>1</sup>, Jennifer N. Bress<sup>1</sup>, Dan Foti<sup>2</sup>, Autumn Kujawa<sup>1</sup>, and Daniel N. Klein<sup>1</sup>

<sup>1</sup>Stony Brook University

<sup>2</sup>Purdue University

### Overview

Event-related brain potentials (ERPs) are a cost-effective and direct measure of neural activity with excellent temporal resolution and are well-suited for understanding information processing abnormalities related to depression and risk for depression. We have examined ERPs among normative samples that vary in depressive symptom severity, individuals with diagnosed major depressive disorder (MDD), and children at high risk for depression based on maternal history of depression. In the current paper, we review recent ERP research on MDD and risk that focuses on deficits in emotion and motivation [1]. We emphasize ERPs elicited by emotional compared to neutral pictures, and the ERP differentiation between feedback indicating monetary gain and loss. By focusing on the processing of valenced stimuli, this review stands in contrast to previous work which has couched ERP abnormalities in MDD in terms of cognitive dysfunction [2]. The ERP work reviewed below suggests that MDD and risk for depression are characterized by deficits in emotional engagement and reward processing [3].

### ERP abnormalities in MDD: From cognition to motivation

A wealth of data suggests that MDD is characterized by a *reduced* P300 [2]. In a typical P300 task, participants listen to frequent standard sounds, and must count or respond to relatively infrequent target sounds; the P300 is evident 300 to 500 ms following infrequent target stimuli as an increased positive potential at parietal sites. Bruder and colleagues report a mean effect size (i.e., Cohen's *d*) of .85 across many studies documenting a reduced P300 in MDD and link this abnormality to cognitive deficits in depression: the increased P300 to targets has been postulated to reflect cognitive processes that include memory and related constructs such as context updating [4].

An increased P300 has also been observed following the presentation of emotional compared to neutral stimuli [5]-[7]. When participants view both pleasant and unpleasant

---

Correspondence concerning this article should be addressed to Greg Hajcak Proudfit, Ph.D., Department of Psychology, Stony Brook University, Stony Brook, NY, 11794-2500; greg.hajcak@stonybrook.edu.

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

compared to neutral stimuli, the ERP is also characterized by a *sustained* positivity at midline parietal sites that has been referred to as the late positive potential [LPP; 8]. We have argued that the P300 and LPP both reflect attentional engagement with salient environmental stimuli – and that salience can be determined by either task relevance (e.g., in an oddball task) or stimulus content (Proudfit, Jackson, Ferri, & Weinberg, in press). We focus on the LPP in this paper; our view is that the reduced LPP in MDD may reflect deficits in attentional engagement with salient environmental stimuli, and might best be understood in terms of emotional and motivational abnormalities.

Very early studies using emotional words reported that individuals with MDD had a reduced LPP to both pleasant and unpleasant emotional words—but the LPP did not differ in response to neutral words [9]. Using pictures of dermatological disease, Kayser and colleagues [10] found that patients with MDD were characterized by a reduced LPP to unpleasant pictures.

These early studies are supported by a growing body of literature indicating that both clinical diagnoses of depression and depressive symptoms are associated with reduced LPPs to positive and negative emotional stimuli in children and adults. For example, in a passive viewing paradigm, adults with MDD exhibited reduced LPPs to angry and fearful faces compared to healthy controls [11]. Relatedly, in clinical samples, depression predicted blunted LPPs to both unpleasant and pleasant emotional scenes (A MacNamara et al., in preparation; A Weinberg et al., in preparation). The effects of depression on the LPP appear to be most apparent for participants with an early onset depression (i.e., before age 18) or suicidality (A Weinberg et al., in preparation). Little work has evaluated the LPP and depression across development; however, there is evidence of similar patterns in youth, with greater depressive symptoms associated with a reduced LPP to threatening faces in children and adolescents (A Kujawa et al., under review).

Despite high comorbidity and shared etiological influences [12], depression and anxiety may be associated with distinct effects on the LPP. In one study, symptoms of generalized anxiety disorder (GAD) predicted an *increased* LPP to unpleasant images, but only when controlling for the blunting effect of depressive symptoms on the LPP (A MacNamara et al., in preparation). Relatedly, youth with anxiety disorders exhibited *enhanced* LPPs to threatening emotional faces compared to controls, while greater depressive symptoms predicted *reduced* LPP to angry faces across both groups (A Kujawa et al., under review). Lastly, in a very large sample of adolescents, reduced LPPs were related to low positive emotionality, a temperament trait thought to be specific to depression as opposed to anxiety [13], but negative emotionality, which characterizes both depression and anxiety, did not exhibit effects on the LPP (B Speed et al., under review). Thus, decreased attention towards motivationally salient information, as measured by the LPP, may be relatively specific to depression, highlighting the importance of identifying core disturbances in emotional reactivity underlying psychopathology [1].

Lastly, reduced LPPs to positive and negative emotional faces and scenes have been observed among never-depressed offspring of parents with histories of depression, even in children as young as six years old [14; Nelson B et al., under review], suggesting that the

LPP may be a vulnerability marker for depression. That is, reduced emotional reactivity is evident before the onset of depression in at-risk youth, and the LPP could be useful for identifying children most in need of prevention and early intervention.

## Reward dysfunction in anhedonia

A defining feature of MDD is anhedonia, defined as markedly diminished interest or pleasure in normally enjoyable activities. In recent years, there has been growing interest in translating findings from basic neuroscience to characterize anhedonia in terms of dysfunction in reward-related brain circuitry, and in anhedonia as a potential endophenotype for MDD [15]. ERP research in this area has focused primarily on the electrocortical differentiation at frontocentral electrode sites that occurs approximately 300 ms following feedback indicating monetary reward versus loss. After losses, the ERP is characterized by an N2-like negative deflection previously referred to as the feedback negativity, or FN; following reward, a relative positivity (the Reward Positivity or RewP) is observed [16]. The RewP amplitude captures sensitivity to reward outcomes, and is correlated with indicators across other units of analysis, including self-reported reward sensitivity and reward learning behavior [17]. Source localization and combined ERP/fMRI indicate that RewP amplitude reflects—either directly or indirectly—activation of the basal ganglia by reward delivery [18-21].

Recent studies consistently demonstrate that RewP amplitude is a neurophysiological indicator of diminished reward sensitivity in MDD. In non-clinical samples, RewP amplitude is blunted among individuals with depressive symptomatology [22], an effect which is driven specifically by reduced neural activity to monetary gains [23]. In clinical samples, RewP amplitude is blunted in patients with an MDD diagnosis compared to never-depressed controls [24,25]. These studies are consistent with fMRI findings of reduced activity in reward circuitry, including the dorsal/ventral striatum and orbitofrontal cortex [15]. Moreover, RewP amplitude is also associated with variability in reward functioning *within* MDD samples: In one study of patients with MDD, reduced RewP amplitude was associated with severity of self-reported anhedonia, even after adjusting for illness severity [24]. In a separate clinical study, the effect of MDD diagnosis on RewP amplitude was found to be driven by a subgroup of patients who reported impaired mood reactivity to positive life events, a core feature of melancholic MDD—but not the full, *DSM*-defined melancholic subtype [25]. These data suggest that reduced RewP amplitude may be a biomarker for an anhedonic/melancholic phenotype, accounting for heterogeneity within MDD populations that is not captured by the current diagnostic system.

## Depression and ERPs elicited by gain and loss in childhood and adolescence

As in adults, depressive symptoms relate to reduced reward-related neural activity in children and adolescents. Among unselected 8- to 13-year-olds, those with greater depressive symptomatology show a blunted neural response to monetary losses compared to gains [26]; this association has been reproduced in the same sample at a two-year follow-up [27]. Notably, despite high comorbidity between depression and anxiety, the RewP appears

to relate uniquely to depressive symptoms when controlling for the contribution of anxious symptoms [28].

The blunted RewP also relates to multiple measures of *risk* for depression. Low positive emotionality – a temperamental risk factor for depression [13, 29] – at age 3 is associated with a reduced RewP at age 9 [30]. At age 9, children with a maternal history of depression – the best-established predictor of later depression in offspring [31-33] – show less neural differentiation between losses and gains than peers, even when controlling for the child's depressive symptoms [34, 35]. This is particularly true if the mothers also exhibit low levels of positive parenting [35]. In addition to associations with established risk factors, the RewP has also been associated directly with subsequent depression in youth. A reduced RewP predicts subsequent depressive symptomatology in 8- to 13-year-olds [27] and subsequent first onset of major depressive episodes in 15- to 17-year-olds [36] over the course of two years. Thus, accumulating evidence suggests that a blunted RewP may precede depressive symptomatology.

Several of these studies have examined depression in relation to the difference between gains and losses (i.e., RewP); however, some studies have found that depression is specifically predicted by the RewP to monetary *gains*. In 8- to 13-year-olds, depressive symptoms relate both to the RewP and to the RewP to gains, but not to the N2 to losses [26]. Likewise, RewP to gains, but not N2 to losses, measured at baseline in both 8- to 13-year-olds and 15- to 17-year-olds predict subsequent depressive symptomatology [27, 36]. However, a contrasting effect has been found in 9-year-olds: maternal depression relates only to the RewP, and not the RewP to gain or N2 to loss separately [35]. It will be important for future studies to examine both the RewP and N2, as well as the difference between them, in studies of depression and risk—especially across development.

## Summary

ERPs provide economical neural indices of depression and depression-risk. Early ERP studies of depression focused on cognitive deficits; more recent studies have examined ERPs to emotionally and motivationally relevant stimuli. Both the LPP, a measure of sustained processing of motivationally salient stimuli, and the RewP, an index of reactivity to receipt of reward, appear to be diminished in individuals with MDD and depressive symptoms, suggesting that depression is associated with emotional disengagement and deficits in reward processing. Compared to the effect size reported by Bruder and colleagues [4], the average effect size in our studies relating LPP to depressive symptoms and MDD diagnosis is somewhat smaller ( $d = .60$ ); the association between RewP and depressive symptoms and MDD diagnosis is also moderate ( $r = .33$  and  $r = .40$  in adults and adolescents, respectively). One important area for future research may involve leveraging and combining multiple ERP measures (i.e., P300, LPP, and RewP) in the same studies of depression and risk—to examine potential combinations of biomarkers that may form biosignatures.

Interestingly, these findings are not observed in the anxiety disorders, despite their clinical and etiological overlap with depression. Moreover, among depressed individuals, blunted

RewP is specifically associated with anhedonia and lack of mood reactivity, suggesting that it may be useful in parsing the heterogeneity of MDD. Finally, the offspring of parents with MDD exhibit diminished LPP and RewP, and blunted RewP in adolescents predicts subsequent increases in depressive symptoms and the first onset of MDD. Thus ERPs to emotional and motivational stimuli may also serve as vulnerability markers, and may be useful for identifying at-risk youth for prevention and early intervention. Important future directions will be to determine whether ERPs can be used to guide treatment selection in depression and if they are modifiable biomarkers that can also serve as treatment targets.

## References

1. Tracy J, Klonsky ED, Proudfit GH. How Affective Science Can Inform Clinical Science An Introduction to the Special Series on Emotions and Psychopathology. *Clinical Psychological Science*. 2014; 2(4):371–386.
2. Bruder, G.; Kayser, J.; Tenke, C. Event-related brain potentials in depression: Clinical, cognitive and neurophysiologic implications. In: Luck, SJ.; Kappenman, ES., editors. *Oxford Handbook of Event-Related Potential Components*. New York: Oxford University Press; 2012. p. 563-592.
3. Rottenberg J, Gross J, Gotlib I. Emotion context insensitivity in major depressive disorder. *Journal of Abnormal Psychology*. 2005; 114(4):627–639. [PubMed: 16351385]
4. Polich J. Updating P300: an integrative theory of P3a and P3b. *Clinical Neurophysiology*. 2007; 118(10):2128–2148. [PubMed: 17573239]
5. Johnston V, Miller D, Burselen M. Multiple P3s to emotional stimuli and their theoretical significance. *Psychophysiology*. 1986; 23(6):684–694. [PubMed: 3823344]
6. Lifshitz K. The averaged evoked cortical response to complex visual stimuli. *Psychophysiology*. 1966; 3(1):55–68. [PubMed: 5942874]
7. Radilova J. The late positive component of visual evoked response sensitive to emotional factors. *Activitas Nervosa Superior*. 1982; Suppl(3):334–337. [PubMed: 7183099]
8. Cuthbert B, Schupp H, Bradley M. Brain potentials in affective picture processing: covariation with autonomic arousal and affective report. *Biological Psychology*. 2000; 52:95–111. [PubMed: 10699350]
9. Blackburn IM, Roxborough HM, Muir WJ, Glabus M, Blackwood DH. Perceptual and physiological dysfunction in depression. *Psychological Medicine*. 1990; 20(1):95–103. [PubMed: 2320702]
10. Kayser J, Bruder G, Tenke C. Event-related potentials (ERPs) to hemifield presentations of emotional stimuli: differences between depressed patients and healthy adults in P3 amplitude and asymmetry. *International Journal of Psychophysiology*. 2000; 36:211–236. [PubMed: 10754195]
11. Foti D, Olvet DM, Klein DN, Hajcak G. Reduced electrocortical response to threatening faces in major depressive disorder. *Depression and Anxiety*. 2010; 27:813–820. [PubMed: 20577985]
12. Goldberg DP, Krueger RF, Andrews G, Hobbs MJ. Emotional disorders: Cluster 4 of the proposed meta-structure for DSM-V and ICD-11. *Psychological Medicine*. 2009; 39:2043–2059. [PubMed: 19796429]
13. Clark LA, Watson D, Mineka S. Temperament, personality, and the mood and anxiety disorders. *Journal of Abnormal Psychology*. 1994; 103:103–116. [PubMed: 8040472]
- \*14. Kujawa A, Hajcak G, Torpey D, Kim J, Klein DN. Electrocortical reactivity to emotional faces in young children and associations with maternal and paternal depression. *Journal of Child Psychology and Psychiatry*. 2012; 53:207–215. This paper examined the LPP in 6-year-old offspring of parents with and without histories of depressive disorders. Children of mothers with histories of depression exhibited reduced LPPs for emotional compared to neutral faces. [PubMed: 21895650]
15. Pizzagalli DA. Depression, stress, and anhedonia: toward a synthesis and integrated model. *Annual Review of Clinical Psychology*. 2014; 10:393–423.

16. Proudfit GH. The reward positivity: From basic research on reward to a biomarker for depression. *Psychophysiology*. in press.
17. Bress JN, Hajcak G. Self-report and behavioral measures of reward sensitivity predict the feedback negativity. *Psychophysiology*. 2013; 50:610–616. [PubMed: 23656631]
- \*18. Becker MP, Nitsch AM, Miltner WH, Straube T. A Single-Trial Estimation of the Feedback-Related Negativity and Its Relation to BOLD Responses in a Time-Estimation Task. *Journal of Neuroscience*. 2014; 34:3005–3012. This is the first study to utilize simultaneous ERP/fMRI data to characterize reward processing in an unselected sample. This adds to a growing body of research characterizing the RewP as a reward-related ERP response that covaries with activation in the basal ganglia. [PubMed: 24553940]
19. Carlson JM, Foti D, Harmon-Jones E, Proudfit GH. Midbrain volume predicts fMRI and ERP measures of reward reactivity. *Brain Structure and Function*. in press.
20. Carlson JM, Foti D, Mujica-Parodi LR, Harmon-Jones E, Hajcak G. Ventral striatal and medial prefrontal BOLD activation is correlated with reward-related electrocortical activity: A combined ERP and fMRI study. *NeuroImage*. 2011; 57:1608–1616. [PubMed: 21624476]
21. Foti D, Weinberg A, Dien J, Hajcak G. Event-related potential activity in the basal ganglia differentiates rewards from non-rewards: Temporospatial principal components analysis and source localization of the feedback negativity. *Human Brain Mapping*. 2011; 32:2207–2216. [PubMed: 21305664]
22. Foti D, Hajcak G. Depression and reduced sensitivity to non-rewards versus rewards: Evidence from event-related potentials. *Biological Psychology*. 2009; 81:1–8. [PubMed: 19162124]
- \*23. Foti D, Weinberg A, Bernat E, Proudfit GH. Anterior cingulate activity to monetary loss and basal ganglia activity to monetary gain uniquely contribute to the feedback negativity. *Clinical Neurophysiology*. in press This is the first study to combine advanced data analytic techniques (principal components analysis, time-frequency signal decomposition, source localization) to reward-related ERPs. The RewP was characterized as a composite of dissociable gain- and loss-related signals, with distinct neural generators.
- \*24. Liu WH, Wang LZ, Shang HR, Shen Y, Li Z, Cheung EF, Chan RC. The influence of anhedonia on feedback negativity in major depressive disorder. *Neuropsychologia*. 2014; 53:213–220. This is the first study to isolate the RewP from other ERPs using principal components analysis within an MDD sample. [PubMed: 24316199]
- \*25. Foti D, Carlson JM, Sauder CL, Proudfit GH. Reward dysfunction in major depression: Multimodal neuroimaging evidence for refining the melancholic phenotype. *NeuroImage*. 2014; 101:50–58. This is the first study to combine ERP and fMRI measures of reward processing deficits within a single MDD sample. [PubMed: 24996119]
26. Bress JN, Smith E, Foti D, Klein DN, Hajcak G. Neural response to reward and depressive symptoms in late childhood to early adolescence. *Biological Psychology*. 2012; 89(1):156–162. [PubMed: 22015709]
27. Bress JN, Meyer A, Proudfit GH. The stability of the feedback negativity and its relationship with depression during childhood and adolescence. *Development and Psychopathology*. in press.
28. Bress JN, Meyer A, Hajcak G. Differentiating Anxiety and Depression in Children and Adolescents: Evidence From Event-Related Brain Potentials. *Journal of Clinical Child & Adolescent Psychology*. 2013:1–12.
29. Dougherty LR, Klein DN, Durbin CE, Hayden EP, Olino TM. Temperamental positive and negative emotionality and children's depressive symptoms: A longitudinal prospective study from age three to age ten. *Journal of Social and Clinical Psychology*. 2010; 29(4):462–488.
30. Kujawa A, Proudfit GH, Kessel EM, Dyson MW, Olino TM, Klein DN. Neural reactivity to monetary rewards and losses in childhood: Longitudinal and concurrent associations with observed and self-reported positive emotionality. *Biological Psychology*. in press.
31. Beardslee WR, Versage EM, Gladstone TR. Children of affectively ill parents: a review of the past 10 years. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1998; 37:1134–1141. [PubMed: 9808924]



32. Brennan PA, Hammen C, Katz AR, Le Brocque RM. Maternal depression, paternal psychopathology, and adolescent diagnostic outcomes. *Journal of Consulting and Clinical Psychology*. 2002; 70(5):1075–85. [PubMed: 12362958]
33. Klein DN, Lewinsohn PM, Rohde P, Seeley JR, Olino TM. Psychopathology in the adolescent and young adult offspring of a community sample of mothers and fathers with major depression. *Psychological Medicine*. 2005; 35(3):353–65. [PubMed: 15841871]
- \*34. Kujawa A, Proudfit GH, Klein DN. Neural reactivity to rewards and losses in offspring of mothers and fathers with histories of depressive and anxiety disorders. *Journal of Abnormal Psychology*. 2014; 123(2):287. This study examines associations between the RewP in 9-year-old children and parental depression and anxiety. The authors report a blunted RewP in offspring of mothers with depression, but only if the mother did not have anxiety. [PubMed: 24886003]
35. Kujawa A, Proudfit GH, Laptook R, Klein DN. Early parenting moderates the association between parental depression and neural reactivity to rewards and losses in offspring. *Clinical Psychological Science*. 2014
- \*36. Bress JN, Foti D, Kotov R, Klein DN, Hajcak G. Blunted neural response to rewards prospectively predicts depression in adolescent girls. *Psychophysiology*. 2013; 50(1):74–81. In this study, the RewP was measured in a group of never-depressed adolescent girls. Girls who developed a first-onset major depressive episode during the following two years had shown a smaller RewP at baseline, and a smaller RewP to gains at baseline was associated with subsequent depression severity. [PubMed: 23252717]

### Highlights

Event-related potentials (ERPs) can be used to understand core deficits in major depressive disorder (MDD) and risk.

Depression and risk for depression are associated with decreased ERP response to emotional stimuli.

Depression and risk for depression are associated with decreased neural response to monetary gain versus loss.

ERP work suggests emotional and motivational disengagement as core features of depression and risk.