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Can Understanding Reward Help Illuminate Anhedonia?

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Abstract

Purpose of Review The goal of this paper is to examine how reward processing might help us understand the symptom of anhedonia.

Recent Findings There are extensive reviews exploring the relationship between responses to rewarding stimuli and depression. These often include a discussion on anhedonia and how this might be underpinned in particular by dysfunctional reward processing. However, there is no specific consensus on whether studies to date have adequately examined the various sub-components of reward processing or how these might relate in turn to various aspects of anhedonia symptoms.

Summary The approach to understanding the symptom of anhedonia should be to examine all the sub-components of reward processing at the subjective and objective behavioural and neural levels, with well-validated tasks that can be replicated. Investigating real-life experiences of anhedonia and how these might be predicted by objective lab measures is also needed in future research.

Keywords Reward · Anhedonia · Depression · Ventral striatum · Mood disorders · Stress

Introduction

Depression is defined as a negative emotional state that affects daily life, ranging from unhappiness and displeasure to extreme sadness and pessimism. In accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria, the diagnosis of depression necessitates five or more symptoms within a 2-week period [1]. Anhedonia is the loss of interest and pleasure during depression and is one of the two main diagnostic criteria alongside low mood [1]. Even though anhedonia is one of the most important components of depression, the behavioural and neurobiological basis of anhedonia is not completely understood [2•, 3]. In this respect, the main purpose of this review is to discuss anhedonia in relation to reward processing as studies on the neurobiology of depression [4, 5] suggest that anhedonia is related to

dysfunction in the brain's reward pathways [6] which in turn, therefore, may be a potential target for treatment development.

Why Is It Important to Understand the Symptom of Anhedonia Better?

The term anhedonia was first used in 1896 to describe reduced hedonic capacity by Théodule-Armand Ribot [7]. Although historically anhedonia has been mainly described as a 'loss of pleasure', studies reveal other components such as reduced desire, expectation, motivation, and enjoyment of reward [8•]. Further, even though anhedonia is frequently considered as a specific symptom for depression [2•, 7], it is also a common symptom of many neuropsychological disorders [9•], such as schizophrenia [10], Parkinson's disease [11], and substance abuse [12]. In a recent meta-analysis [13], it has been emphasized that there is a strong relationship between anhedonia and suicidal thoughts, and studies suggest anhedonia increases the risk of suicide [14•, 15, 16]. Furthermore, in relation to treatment, anhedonia is the strongest predictor, among all depressive symptoms, of increased time to remission [17] and reduced response to serotonergic treatment [8•]. Therefore, it is imperative to increase our understanding of anhedonia so that we can not only alleviate depression

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symptoms and prevent relapse but also possibly help reduce suicide risk.

How Might Understanding Reward Illuminate the Symptom of Anhedonia?

There are many theories as to what might cause anhedonia, such as stress [18, 19], genetic variations [20••], and dysfunction in brain activity [21, 22]. The brain's response to reward during depression is of interest in relation to understanding the causes of anhedonia [23] as it is thought that anhedonia comes about by dysfunctional reward mechanisms in the brain [24]. Seeking out reward is vital for human survival, and eating, drinking, and mating are basic physiological needs [25, 26]. However, reward processing involves more than one neuropsychological component such as 'liking', defined as a hedonic sensation; there is also 'wanting', thought of as the motivation to get a reward, and there is also 'learning' how we learn and make decisions to get rewards. Each of these components plays an important adaptive role in initiating, maintaining, and modifying our behaviour [27]. The neurobiology of reward has already been widely reviewed [28]; in summary, neuroimaging and neural recording studies have found that rewards ranging from sweet taste to intravenous cocaine, winning money, or a smiling face activate many brain structures, including orbitofrontal cortex, anterior cingulate and insula, and subcortical structures such as nucleus accumbens, ventral pallidum, ventral tegmentum, and mesolimbic dopamine projections and the amygdala [29–37]. Thus, neural differences in these systems may be underpinned by variations in dopamine, and reviews suggest that anhedonia might be improved by modulating changes in the mesolimbic dopamine system, which in turn could increase motivation and reactivity to reward [38]. However, dopamine is not the only neurotransmitter involved in reward and pleasure and rather the opioid, endocannabinoid, and GABA-benzodiazepine neurotransmitter systems are important for generating pleasurable reactions [3, 4, 39]. As the symptom of anhedonia itself is also multidimensional with various components that each might be contributing to various aspects of the experience, more work is needed on a detailed examination of the sub-components of reward processing in relation to anhedonia and brain function. Whether it is the desire/expectation for reward or the effort to reach reward or the consummatory response upon receiving a reward that is the main dysfunction during anhedonia, is not yet clear [8•, 40, 41••].

It is suggested that stress can disrupt reward processing [19], and preclinical work shows that physical stress (e.g. foot shock) decreases consummatory behaviour in rats (decreased saccharine consumption) [42] and exploratory behaviour [43, 44]. Similarly, acute social stress by means of social defeat in rats leads to a decrease in reward-seeking behaviour [45]. In

humans, studies have found that an interaction between recent life stress and ventral striatal (VS) reactivity predicted self-reported positive affect (PA), such that higher levels of life stress were associated with lower PA for participants with relatively low, but not for those with high, VS reactivity. Interestingly, this work suggests that even in the face of stress, those with high VS activity may be protected against vulnerability to low positive mood precipitated by stressful life events [46]. Furthermore, Corral-Frias and colleagues [47] showed that individual differences in neural responses to reward may confer vulnerability to stress-related psychopathology. They found that as activation in the VS of individuals exposed to early life stress (ELS) decreased, the risk for anhedonia increased [47]. However, the authors point out that more work needs to be done to elucidate the relationship between stress and anhedonia in more detail; for example, it is not known which types of stress lead to changes in motivation and reward processing at the molecular and neural levels [19]. Further studies in humans have found that ELS is associated with reward dysfunction, as evidenced by blunted activation during both reward anticipation in the dorsal striatum [48, 49] and reward receipt in the ventral striatum [50–52]. Studies have also found that the stress of active military service, for example, was related to reduced VS activation during reward receipt [53] while the stress of a physical cold pressor has been found to decrease activation to monetary reward in the dorsal striatum and orbitofrontal cortex in healthy adults [54]. In an effort to examine patterns of reward function before and after acute stress, a study by Kumar and colleagues showed reduced activation in the putamen and caudate during reward receipt following stress relative to no stress, suggesting that stress can elicit anhedonic-like activation patterns [55]. Taken together, most studies to date have assessed reward processing in adults but have not always clearly differentiated the effects of stress on the sub-components of reward processing. Further, it is important for future work to investigate how stress and reward processing interact in young people at increased risk of depression, to identify risk factors early that might be targets for treatment.

Family and twin studies have been used to examine genetic links with symptoms such as anhedonia [56, 57]. For instance, Liu and colleagues [56] compared the reward sensitivity of a group of healthy individuals with no family history of depression and another group of first-degree relatives of depressed patients. Compared with the control group, relatives of patients with major depression who themselves had sub-clinical depressive symptoms displayed a blunted reward bias which was associated with anhedonia. Relatives without symptoms displayed largely intact motivational processing on both self-report and experimental measures [29]. In another study examining twins, responses to an objective behavioural measure of hedonic capacity (reward responsiveness), it was found that hedonic capacity and perceived stress are indeed

heritable with substantial shared additive genetic contributions [30]. The authors also pointed out that replications in larger samples are needed. Accumulating research suggests that genetic differences conferring relatively increased subcortical DA or reduced cortical DA signalling (via either receptor availability or synaptic clearance) are associated with enhanced reward-related neural activation and behaviour [58]. This supports the notion that anhedonia might therefore have a genetic component. Yet most research on the genetics of reward processing have yet to establish how the various *sub-components* (anticipation vs motivation vs consummation) of reward processing might confer genetic risk [58]. Therefore, more work needs to be done on how to examine if one sub-component or a combination of them confers risk differently, in different people. Taken together, it is possible that anhedonia might be precipitated by various factors such as stressful life events, genetic variations, and/or neural dysfunction. Knowing more about the mechanisms underpinning anhedonia could help us detect early signs and thus help us develop preventative strategies and improved treatments.

The Link Between Anhedonia and Reward Processing in Depression

To date, the neurobiology of reward deficits in depression have been well documented in adults [59, 60] and more recently in adolescents [61–64]. In summary, studies report mostly decreased responses to the anticipation and outcome of reward (money) in regions like the ventral striatum, caudate, the dorsolateral and medial prefrontal cortex (PFC), orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), and amygdala [61, 65]. Striatal regions are often reported as negatively correlating with anhedonia and subjective positive affect in depression [9, 66]. Yet as mentioned above, the sub-components of reward processing are not always explicitly examined in studies of reward and it has been argued that using the receipt of monetary rewards in tasks cannot capture adequately consummatory hedonic responses as the money is not actually received during the study (on each trial) and money is itself a secondary reinforcer [6, 41•]. In an attempt to examine the various sub-components of reward processing in relation to anhedonia, we have employed a task that uses both primary and secondary reinforcers. Our tasks also separate out anticipation from motivation using effort and anticipation from consummation using taste. We recently found using this that adolescents with depression symptoms have blunted neural responses during the anticipation, effort, and consummation of rewarding and aversive stimuli [67, 68]. This work is of interest as it shows how anhedonia is related to all the sub-components of reward processing but also to blunted aversion processing. This data is novel and interesting as it provides evidence for motivational deficits in those at increased risk of

clinical depression and that motivational deficits need not be just to reward but could affect how one acts to avoid aversion.

As mentioned above, learning about rewards is also important if we are to optimally direct our behaviour towards gaining rewards. Previous research suggests that anhedonia and depression are related to impaired reward learning, on both the behavioural and the neural levels [38, 69]. Computational models have been used to examine learning about rewards and specifically used to examine how prediction error signalling is related to reward learning deficits in depression. A prediction error (PE), in simple terms, is calculated by subtracting the prediction value (how strongly a given cue is associated with positive or negative outcomes) from the outcome value. Finally, the prediction value is updated by adding the prediction error, multiplied by a learning rate. Studies find that medicated depressed subjects have reduced reward PE encoding in the ventral and dorsal striatum, the midbrain, and the hippocampus [70]. Further studies find that self-reported depression scores in unmedicated individuals negatively correlate with decreased reward PE encoding in the ventral striatum [71]. Interestingly, not all studies measure anhedonia and of those that do, the sub-components are not always measured, e.g. anhedonia scores, using the Snaith Hamilton Pleasure Scale (SHAPS), in unmedicated depressed individuals were found to negatively correlate with reward PE signals in the medial OFC [72]. However, the SHAPS measures only hedonic tone and not anticipatory of motivational aspects of anhedonia. Further, most studies to date have not related their findings to real-life experiences of anhedonia. In an attempt to address this, we recently found that adults with high depression symptoms compared to those with low symptoms spend higher amounts of time in negatively perceived real-life situations and that this was predicted by lower learning rates in our social reward learning task (using Facebook likes as a reward) using computational modelling [73•]. These findings support the idea that deficits in learning may negatively affect the quality of everyday life experiences and that impaired ability to use reward feedback to appropriately update future actions may lead to suboptimal real-life experiences. It therefore would be of interest in future work to examine how we can use objective measures of the various sub-components of reward processing, i.e. reward learning, reward anticipation, motivation, and consummation, to predict real-life rewarding interactions and therefore risk of anhedonia in young people. As it has been suggested that anhedonia may be a possible biomarker for depression [57] as it seems to predate depression and persist into recovery [74], examining young people before they have clinical depression and how they respond to reward in a dimensional fashion across the spectrum would be beneficial [24, 67].

Further understanding of the neural functions underlying reward could then allow the testing of the effects of antidepressant treatments on reward function in line with

anhedonia's potential as a biomarker tool [75]. In this context, a recent qualitative analysis by Cao and colleagues [76] examined the therapeutic efficacy of pharmacological treatments on measures of anhedonia in adults with MDD. They reported that a significant number of antidepressants do have beneficial effects on anhedonic symptoms as well as depressive symptoms [5, 76]. Interestingly, the authors also state that therapies targeting melatonergic receptors and circadian rhythm imbalances are more direct targets for treating anhedonia while drugs like ketamine may be faster acting on anhedonia due to their direct effect on mitochondrial energy metabolism. The authors also point out that future studies should aim to evaluate the comparative efficacy of different pharmacological agents on measures of anhedonia and that measures of function and quality of life should also be investigated.

Although perhaps less often studied, there is also growing evidence for the effects of psychological treatments on anhedonia. Behavioural activation (BA), for example, works by increasing engagement with reinforcers within the environment and overcoming avoidance [5]. Recent promising findings in adults show that greater pre-treatment anhedonia severity in a monetary reward processing task [77] and decreased neural functional connectivity, in a positive emotion upregulation task [78], are predictive of response to BA treatment. Further, BA is thought to be more cost effective and more acceptable to young people who are depressed than other psychotherapies [79], but it is still not effective for everyone. Therefore, increased understanding of reward processing and how it underpins the symptom of anhedonia could also allow the development of more effective psychological treatments for depression.

Conclusion

Studies to date have elucidated the reward system in both animal and human neural systems and behaviours. Reviews have described the role of the reward system in depression and those at risk of depression. However, there is still not a clear understanding of how the sub-components of reward processing might underpin the symptom of anhedonia in depression or in those at risk of depression. Further, it is still not clear how the everyday experiences of anhedonia relate back to the objective measures of reward processing used in lab experiments. Therefore, going forward, more needs to be done to map the subjective experience of anhedonia with the behavioural and neural measures of reward processing if we are to find new targets for intervention and treatment strategies.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. APA. Diagnostic and statistical manual of mental disorders (DSM-V). 2013.
2. Cooper JA, Arulpragasam AR, Treadway MT. Anhedonia in depression: biological mechanisms and computational models. *Curr Opin Behav Sci* [Internet]. Elsevier Ltd; 2018;22:128–35. Available from: <https://doi.org/10.1016/j.cobeha.2018.01.024>. **This review describes (1) advances in behavioral and computational methods of assessing reward processing and motivation and (2) the development of new self-report, neurological, and biological methods of subtyping that may be useful in future pursuits to expand our understanding of the neurobiology of anhedonia in depression.**
3. Keller J, Young CB, Kelley E, Prater K, Levitin DJ, Menon V. Trait anhedonia is associated with reduced reactivity and connectivity of mesolimbic and paralimbic reward pathways. *J Psychiatr Res* [Internet]. Elsevier; 2013(10):1319–28. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0022395613001556>.
4. Treadway MT. The neurobiology of motivational deficits in depression—an update on candidate pathomechanisms. *Behav Neurosci Motiv* [Internet]. Springer; 2015:337–55. Available from: http://link.springer.com/10.1007/7854_2015_400
5. Dimidjian S, Barrera M, Martell C, Muñoz RF, Lewinsohn PM. The origins and current status of behavioral activation treatments for depression. *Annu rev Clin Psychol* [internet] *Annual Reviews*; 2011;7:1–38. Available from: <http://www.annualreviews.org/doi/10.1146/annurev-clinpsy-032210-104535>.
6. Argyropoulos SV, Nutt DJ. Anhedonia revisited: is there a role for dopamine-targeting drugs for depression? *J Psychopharmacol* [Internet]. Sage Publications sage UK: London England; 2013;27: 869–77. Available from: <http://journals.sagepub.com/doi/10.1177/0269881113494104>
7. Naguy A, Alwetayan S, AlKhadhari S. Anhedonia as a transdiagnostic construct. *Asian J Psychiatr* [Internet]. Elsevier. 2019;35:1. <https://doi.org/10.1016/j.ajp.2019.01.001>.
8. Rizvi SJ, Pizzagalli DA, Sproule BA, Kennedy SH. Assessing anhedonia in depression: potentials and pitfalls. *Neurosci Biobehav Rev* [Internet]. Elsevier Ltd; 2016;65:21–35. Available from: <https://doi.org/10.1016/j.neubiorev.2016.03.004>. **This review assesses the current methodology to measure anhedonia, with a focus on scales and behavioural tasks in humans. Limitations of current work and recommendations for future studies are discussed.**

9. Husain M, Roiser JP. Neuroscience of apathy and anhedonia: a transdiagnostic approach. *Nat Rev Neurosci* [Internet]. Springer US; 2018;19:470–84. Available from: <https://doi.org/10.1038/s41583-018-0029-9>. **This review discusses The neurobiological mechanisms underpinning effort-based decisions in individuals with apathy or anhedonia, providing an important foundation for developing new treatments. The findings suggest that there might be some shared mechanisms between both syndromes. A transdiagnostic approach that cuts across traditional disease boundaries provides a potentially useful means for understanding these conditions.**
10. Yang ZY, Zhang RT, Li Y, Wang Y, Wang YM, Wang SK, et al. Functional connectivity of the default mode network is associated with prospection in schizophrenia patients and individuals with social anhedonia. *Prog neuro-psychopharmacology biol psychiatry* [internet]. Elsevier; 2019;92:412–20 Available from: <https://doi.org/10.1016/j.pnpbp.2019.02.008>.
11. Nagayama H, Maeda T, Uchiyama T, Hashimoto M, Nomoto N, Kano O, et al. Anhedonia and its correlation with clinical aspects in Parkinson's disease. *J Neurol Sci* [Internet]. Elsevier B.V.; 2017;372:403–7. Available from: <https://doi.org/10.1016/j.jns.2016.10.051>
12. Lubman DI, Garfield JBB, Gwini SM, Cheetham A, Cotton SM, Yücel M, et al. Dynamic associations between opioid use and anhedonia: a longitudinal study in opioid dependence. *J Psychopharmacol*. 2018;32:957–64.
13. Ducasse D, Loas G, Dassa D, Gramaglia C, Zeppegno P, Guillaume S, et al. Anhedonia is associated with suicidal ideation independently of depression: a meta-analysis. *Depress Anxiety*. 2018;35:382–92. <https://doi.org/10.1002/da.22709>.
14. Daghigh A, Daghigh V, Niazi M, Nadorff MR. The association between anhedonia, suicide ideation and suicide attempts: a replication in a Persian student sample. *Suicide Life Threat Behav*. 2018;1–6. <https://doi.org/10.1111/sltb.12469>. **This study replicated a recent anhedonia and suicide study (conducted in a western culture) in a Persian sample using the Specific Loss of Interest and Pleasure Scale, Persian version. Participants consisted of 404 students who were recruited from a Persian university. Surprisingly, the results indicated that anhedonia levels were more than double those found in similar American student sample. Despite this marked difference in anhedonia symptoms, they found that anhedonia was associated with suicide risk, even when it was statistically accounting for other depressive symptoms.**
15. Winer ES, Nadorff MR, Ellis TE, Allen JG, Herrera S, Salem T. Anhedonia predicts suicidal ideation in a large psychiatric inpatient sample. *Psychiatry Res* [Internet]. Elsevier; 2014;218:124–8 Available from: <https://doi.org/10.1016/j.psychres.2014.04.016>.
16. Winer ES, Drapeau CW, Veilleux JC, Nadorff MR. The association between anhedonia, suicidal ideation, and suicide attempts in a large student sample. *Arch Suicide Res* [Internet]. Taylor & Francis; 2016;20:265–72. Available from: <https://www.tandfonline.com/doi/full/10.1080/13811118.2015.1025119>.
17. McMakin DL, Olino TM, Porta G, Dietz LJ, Emslie G, Clarke G, et al. Anhedonia predicts poorer recovery among youth with selective serotonin reuptake inhibitor treatment-resistant depression. *Elsevier*; 2012;51:404–11. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0890856712000469>.
18. Pizzagalli DA. Depression, stress, and anhedonia: toward a synthesis and integrated model. *Annu rev Clin Psychol* [internet]. Annual Reviews; 2014;10:393–423. Available from: <http://www.annualreviews.org/doi/10.1146/annurev-clinpsy-050212-185606>.
19. Stanton CH, Holmes AJ, Chang SWC, Joormann J. From stress to anhedonia: molecular processes through functional circuits. *Trends Neurosci* [Internet]. Elsevier Ltd; 2019;42:23–42. Available from: <https://doi.org/10.1016/j.tins.2018.09.008>.
20. Ren H, Fabbri C, Uher R, Rietschel M, Mors O, Henigsberg N, et al. Genes associated with anhedonia: a new analysis in a large clinical trial (GENDEP). *Transl Psychiatry*. 2018;8. <https://doi.org/10.1038/s41398-018-0198-3>. **A genome-wide association study (GWAS) followed by investigation of biological pathway enrichment using an anhedonia dimension for 759 patients with MDD in the GENDEP study. They found some markers significantly associated with anhedonia, and some suggestive findings of related pathways and biological functions, which could be further investigated in other studies.**
21. Green IW, Pizzagalli DA, Admon R, Kumar P. Anhedonia modulates the effects of positive mood induction on reward-related brain activation. *Neuroimage* [Internet] Elsevier; 2019;193:115–25. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1053811919301582>.
22. Pornpattananakul N, Leibenluft E, Pine DS, Stringaris A. Association of brain functions in children with anhedonia mapped onto brain imaging measures. *JAMA Psychiatry*. 2019;76:624–33.
23. Gorwood P. Neurobiological mechanisms of anhedonia. *Dialogues Clin Neurosci* [internet]. Les Laboratoires Servier; 2008;10:291–9 Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18979942>.
24. Rizvi SJ, Lambert C, Kennedy S. Presentation and neurobiology of anhedonia in mood disorders: commonalities and distinctions. *Curr Psychiatry Rep* [Internet]. Springer; 2018;20:13 Available from: <https://doi.org/10.1007/s11920-018-0877-z>.
25. Michel-Chávez A, Estañol-Vidal B, Senties-Madrid H, Chiquete E, Delgado-García G, Castillo-Maya G. Reward and aversion systems of the brain as a functional unit. Basic mechanisms and functions. *Salud Ment*. 2015;38:299–305.
26. Schultz W. Neuronal reward and decision signals: from theories to data. *Physiol Rev*. 2015;95:853–951.
27. Berridge KC, Kringelbach ML. Neuroscience of affect: brain mechanisms of pleasure and displeasure. *Curr Opin Neurobiol* [internet]. Elsevier Ltd; 2013;23:294–303 Available from: <https://doi.org/10.1016/j.conb.2013.01.017>.
28. Berridge KC, Robinson TE. Parsing reward. *Trends Neurosci* [Internet] Elsevier; 2003;26:507–13. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0166223603002339>.
29. Cardinal RN, Parkinson JA, Hall J, Everitt BJ. Emotion and motivation: the role of the amygdala, ventral striatum, and prefrontal cortex. *Neurosci Biobehav Rev* [Internet] Elsevier; 2002;26:321–52. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0149763402000076>.
30. Dickinson A, Balleine B. The role of learning in the operation of motivational systems. *Stevens' Handb Exp Psychol*. Wiley Online Library; 2002.
31. Rescorla RA. Instrumental learning: nature and persistence. *Adv Psychol Sci Biol Cogn Asp*. 1998;2:239–57.
32. Pearce JM, Bouton ME. Theories of associative learning in animals. *Annu Rev Psychol* [Internet]. Annual reviews 4139 El Camino Way, PO Box 10139, Palo Alto, CA 94303-0139, USA; 2001;52: 111–39. Available from: <https://doi.org/10.1146/annurev.psych.52.1.111>.
33. Killcross S, Blundell P. 3. Associative representations of emotionally significant outcomes. *Emot Cogn From brain to Behav* [Internet]. John Benjamins Publishing; 2002:35–73. Available from: <https://benjamins.com/catalog/aicr.44.03kil>.
34. Everitt BJ, Wolf ME. Psychomotor stimulant addiction: a neural systems perspective. *J Neurosci* [Internet]. Soc neuroscience; 2002;22:3312–20. Available from: <https://doi.org/10.1523/JNEUROSCI.22-09-03312.2002>.
35. Baxter MG, Murray EA. The amygdala and reward. *Nat Rev Neurosci* [Internet]. Nature Publishing Group; 2002;3:563–73. Available from: <http://www.nature.com/articles/nm875>.

36. Dickinson A, Balleine BW. Causal cognition and goal-directed action. *Evol Cogn* [Internet]. 2000;185. Available from: <https://psycnet.apa.org/record/2000-05517-009>.
37. Balleine BW, Killcross AS, Dickinson A. The effect of lesions of the basolateral amygdala on instrumental conditioning. *J Neurosci* [Internet]. Soc Neuroscience; 2003;23:666–75. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/12533626>.
38. Treadway MT, Zald DH. Reconsidering anhedonia in depression: lessons from translational neuroscience. *Neurosci Biobehav Rev* [Internet]. Elsevier Ltd; 2011;35:537–55. Available from: <https://doi.org/10.1016/j.neubiorev.2010.06.006>.
39. Berridge KC, Robinson TE, Aldridge JW. Dissecting components of reward: ‘liking’, ‘wanting’, and learning. *Curr Opin Pharmacol* [Internet]. Elsevier; 2009;9:65–73. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1471489208002129>.
40. Kaya, McCabe. What role does the prefrontal cortex play in the processing of negative and positive stimuli in adolescent depression? *Brain Sci*. MDPI AG; 2019;9:104 Available from: <https://doi.org/10.3390/brainsci9050104>.
41. McCabe C. Linking anhedonia symptoms with behavioural and neural reward responses in adolescent depression. *Curr Opin Behav Sci* [Internet]. Elsevier Ltd; 2018;22:143–51. Available from: <https://doi.org/10.1016/j.cobeha.2018.07.001>. **A review on current studies examining anhedonia in adolescents and what needs to be improved to increase our understanding and therefore treatment targets.**
42. Van Dijken HH, Van Der Heyden JAM, Mos J, Tilders FJH. Inescapable footshocks induce progressive and long-lasting behavioural changes in male rats. *Physiol Behav* [Internet] Elsevier; 1992;51:787–94. Available from: <https://linkinghub.elsevier.com/retrieve/pii/003193849290117K>.
43. Enkel T, Spanagel R, Vollmayr B, Schneider M. Stress triggers anhedonia in rats bred for learned helplessness. *Behav Brain Res* [Internet] Elsevier; 2010;209:183–6. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0166432810000756>.
44. Pijlman FT, Wolterink G, Van Ree JM. Physical and emotional stress have differential effects on preference for saccharine and open field behaviour in rats. *Behav Brain Res* [Internet]. Elsevier; 2003;139:131–8. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0166432802001249>.
45. Rygula R, Abumaria N, Flügge G, Fuchs E, Rütger E, Havemann-Reinecke U. Anhedonia and motivational deficits in rats: impact of chronic social stress. *Behav Brain Res* [Internet] Elsevier; 2005;162:127–34. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0166432805001038>.
46. Nikolova YS, Bogdan R, Brigidi BD, Hariri AR. Ventral striatum reactivity to reward and recent life stress interact to predict positive affect. *Biol Psychiatry* [Internet]. Elsevier; 2012;72:157–63. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0006322312002624>.
47. Corral-Frías NS, Nikolova YS, Michalski LJ, Baranger DAA, Hariri AR, Bogdan R. Stress-related anhedonia is associated with ventral striatum reactivity to reward and transdiagnostic psychiatric symptomatology. *Psychol Med*. 2015;45:2605–17.
48. Mehta MA, Gore-Langton E, Golembo N, Colvert E, Williams SCR, Sonuga-Barke E. Hyporesponsive reward anticipation in the basal ganglia following severe institutional deprivation early in life. *J Cogn Neurosci* [Internet]. MIT Press; 2010;22:2316–25. Available from: <https://doi.org/10.1162/jocn.2009.21394>.
49. Wacker J, Dillon DG, Pizzagalli DA. NIH public access. *Neuroimage*. 2010;46:327–37.
50. Hanson JL, Hariri AR, Williamson DE. Blunted ventral striatum development in adolescence reflects emotional neglect and predicts depressive symptoms. *Biol Psychiatry* [Internet]. Elsevier; 2015;78: 598–605. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S000632231500431X>.
51. Kamkar NH, Lewis DJ, van den Bos W, Morton JB. Ventral striatal activity links adversity and reward processing in children. *Dev Cogn Neurosci* [Internet] Elsevier; 2017;26:20–7. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1878929316302249>.
52. Hanson JL, Albert D, Iselin A-MR, Carré JM, Dodge KA, Hariri AR. Cumulative stress in childhood is associated with blunted reward-related brain activity in adulthood. *Soc Cogn Affect Neurosci* [Internet]. Oxford University Press; 2016;11:405–12 Available from: <https://doi.org/10.1093/scan/nsv124>.
53. Admon R, Lubin G, Rosenblatt JD, Stern O, Kahn I, Assaf M, et al. Imbalanced neural responsivity to risk and reward indicates stress vulnerability in humans. *Cereb Cortex* [Internet]. Oxford University Press; 2013;23:28–35 Available from: <https://doi.org/10.1093/cercor/bhr369>.
54. Porcelli AJ, Lewis AH, Delgado MR. Acute stress influences neural circuits of reward processing. *Front Neurosci* [Internet]. Frontiers; 2012;6:157. Available from: <https://doi.org/10.3389/fnins.2012.00157/abstract>.
55. Kumar P, Berghorst LH, Nickerson LD, Dutra SJ, Goer FK, Greve DN, et al. Differential effects of acute stress on anticipatory and consummatory phases of reward processing. *Neuroscience* [Internet]. Elsevier; 2014;266:1–12. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0306452214000797>.
56. Liu WH, Roiser JP, Wang LZ, Zhu YH, Huang J, Neumann DL, et al. Anhedonia is associated with blunted reward sensitivity in first-degree relatives of patients with major depression. *J Affect Disord*. Elsevier B.V. 2016;190:640–8.
57. Bogdan R, Pizzagalli DA. The heritability of hedonic capacity and perceived stress: a twin study evaluation of candidate depressive phenotypes. *Psychol Med*. 2009;39:211–8.
58. Bogdan R, Nikolova YS, Pizzagalli DA. Neurogenetics of depression: a focus on reward processing and stress sensitivity. *Neurobiol Dis* [Internet]. Elsevier; 2013;52:12–23. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0969996112001933>.
59. Drevets WC, Price JL, Furey ML. Brain structural and functional abnormalities in mood disorders: implications for neurocircuitry models of depression. *Brain Struct Funct* [Internet]. Springer; 2008;213:93–118. Available from: <https://doi.org/10.1007/s00429-008-0189-x>.
60. Dean J, Keshavan M. The neurobiology of depression: an integrated view. *Asian J Psychiatr* [Internet] Elsevier; 2017;27:101–11. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1876201816303197>.
61. Forbes EE, Dahl RE. Research review: altered reward function in adolescent depression: what, when and how? *J Child Psychol Psychiatry* [Internet]. Wiley Online Library; 2012;53:3–15. Available from: <https://doi.org/10.1111/j.1469-7610.2011.02477.x>.
62. Auerbach RP, Admon R, Pizzagalli DA. Adolescent depression. *Harv Rev Psychiatry* [Internet] NIH Public Access; 2014;22:139–48. Available from: <https://insights.ovid.com/crossref?an=00023727-201405000-00001>.
63. Kerestes R, Davey CG, Stephanou K, Whittle S, Harrison BJ. Functional brain imaging studies of youth depression: a systematic review. *NeuroImage Clin* [Internet]. The authors; 2014;4:209–31. Available from: <https://doi.org/10.1016/j.nicl.2013.11.009>.
64. Lichenstein SD, Verstynen T, Forbes EE. Adolescent brain development and depression: a case for the importance of connectivity of the anterior cingulate cortex. *Neurosci Biobehav Rev* [Internet]. Elsevier; 2016;70:271–87. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0149763416301348>.
65. Forbes EE, Christopher May J, Siegle GJ, Ladouceur CD, Ryan ND, Carter CS, et al. Reward-related decision-making in pediatric major depressive disorder: an fMRI study. *J Child Psychol Psychiatry* [Internet]. Wiley Online Library; 2006;47:1031–40. Available from: <https://doi.org/10.1111/j.1469-7610.2006.01673.x>.

66. Forbes EE, Hariri AR, Martin SL, Silk JS, Moyses DL, Fisher PM, et al. Altered striatal activation predicting real-world positive affect in adolescent major depressive disorder. *Am J Psychiatry* [Internet]. Am Psychiatric Assoc; 2009;166:64–73. Available from: <https://doi.org/10.1176/appi.ajp.2008.07081336>.
67. Rzepa E, Fisk J, McCabe C. Blunted neural response to anticipation, effort and consummation of reward and aversion in adolescents with depression symptomatology. *J Psychopharmacol* [Internet]. Sage Publications Sage UK: London, England; 2017;31:303–11. Available from: <https://doi.org/10.1177/0269881116681416>.
68. Rzepa E, McCabe C. Dimensional anhedonia and the adolescent brain: reward and aversion anticipation, effort and consummation. *bioRxiv*. Cold Spring Harbor Laboratory; 2018;473835.
69. Chen C, Takahashi T, Nakagawa S, Inoue T, Kusumi I. Reinforcement learning in depression: a review of computational research. *Neurosci Biobehav Rev* [Internet]. Elsevier; 2015;55: 247–67. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0149763415001311>.
70. Gradin VB, Kumar P, Waiter G, Ahearn T, Stickle C, Milders M, et al. Expected value and prediction error abnormalities in depression and schizophrenia. *Brain*. 2011;134:1751–64.
71. Bakker JM, Goossens L, Kumar P, Lange IMJ, Michielse S, Schruers K, et al. From laboratory to life : associating brain reward processing with real-life motivated behaviour and symptoms of depression in non-help-seeking young adults. *Psychol Med*. 2018: 1–11.
72. Rothkirch M, Tonn J, Köhler S, Sterzer P. Neural mechanisms of reinforcement learning in unmedicated patients with major depressive disorder. *Brain* [Internet]. 2017;140:1147–57. Available from: <https://academic.oup.com/brain/article-lookup/doi/10.1093/brain/awx025>.
73. Frey A-L, Frank M, McCabe C. Social reinforcement learning as a predictor of real-life experiences in individuals with high and low depressive symptomatology. *PsyArXiv*. 2019. <https://doi.org/10.31234/osf.io/dq64x>. **This is the first study to examine how learning about social rewards in the lab predicts real-life experiences in those with depression symptoms using computational modelling.**
74. Hasler G, Northoff G. Discovering imaging endophenotypes for major depression. *Mol Psychiatry* [internet]. Nature Publishing Group; 2011;16:604–19. Available from: <http://www.nature.com/articles/mp201123>.
75. Vinckier F, Gourion D, Mouchabac S. Anhedonia predicts poor psychosocial functioning: results from a large cohort of patients treated for major depressive disorder by general practitioners. *Eur Psychiatry* [Internet]. Elsevier; 2017;44:1–8. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0924933817327657>.
76. Cao B, Zhu J, Zuckerman H, Rosenblat JD, Brietzke E, Pan Z, et al. Pharmacological interventions targeting anhedonia in patients with major depressive disorder: a systematic review. *Prog Neuro-Psychopharmacology Biol Psychiatry* [Internet]. Elsevier; 2019;92:109–17. Available from: <https://doi.org/10.1016/j.pnpbp.2019.01.002>.
77. Carl H, Walsh E, Eisenlohr-Moul T, Minkel J, Crowther A, Moore T, et al. Sustained anterior cingulate cortex activation during reward processing predicts response to psychotherapy in major depressive disorder. *J Affect Disord* [Internet]. Elsevier; 2016;203:204–12. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S0165032716304402>.
78. Walsh EC, Eisenlohr-Moul TA, Minkel J, Bizzell J, Petty C, Crowther A, et al. Pretreatment brain connectivity during positive emotion upregulation predicts decreased anhedonia following behavioral activation therapy for depression. *J Affect Disord* [Internet]. Elsevier; 2019;243:188–92. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0165032718309819>.
79. Goodyer IM, Reynolds S, Barrett B, Byford S, Dubicka B, Hill J, et al. Cognitive behavioural therapy and short-term psychoanalytical psychotherapy versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre, pragmatic, observer-blind, randomised controlled superior. *The Lancet Psychiatry* [Internet]. Elsevier; 2017;4:109–19. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S2215036616303789>.

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