Altered interaction with environmental reinforcers in major depressive disorder: Relationship to anhedonia

Joanna E. Szczepanik [a, *], Maura L. Furey [b], Allison C. Nugent [a], Ioline D. Henter [a], Carlos A. Zarate Jr. [a], Carl W. Lejuez [c]

[a] Experimental Therapeutics and Pathophysiology Branch, Intramural Research Program, National Institute of Mental Health, National Institutes of Health, Bethesda, MD 20892, USA
[b] Janssen Pharmaceuticals, Neuroscience Research and Development, La Jolla, CA, USA
[c] Department of Psychology, University of Kansas, Lawrence, KS, USA

ABSTRACT

Anhedonia—defined as loss of interest or pleasure—is one of two core symptoms of major depressive disorder (MDD). Anhedonia may involve decreased enjoyment of potentially rewarding activities and decreased motivation to engage in such activities. Increased engagement with reinforcers—activities with the potential to be positive experiences—is a frequent target of cognitive-behavioral therapies. Nevertheless, how environmental reinforcers are perceived, and how decisions to approach or avoid them are made by individuals with MDD, is largely unknown. We developed an experimental Behavioral Approach Motivation Paradigm to study how activities are evaluated and approached in MDD. Twenty-one MDD participants and 23 healthy controls performed an experimental task that rated activity words for their hedonic value, then engaged in an approach-avoidance joystick task with each individual's unique set of 'liked' and 'disliked' activity words. A negative correlation was observed between anhedonia and the number of 'liked' activities across participants. No significant difference between approach and avoidance behavior was found in direct comparisons between healthy controls and MDD participants; however, weaker avoidance and greater approach toward 'disliked' activities was found in MDD participants. This suggests negative bias in selecting environmental opportunities, potentially further compromising access to hedonic experiences in MDD.

© 2017 Published by Elsevier Ltd.

Anhedonia, which is a core symptom of major depressive disorder (MDD), is defined by the DSM-IV (American Psychiatric Association, 1994) and DSM-5 (American Psychiatric Association, 2013) as an impaired capacity to experience or anticipate pleasure. Behaviors associated with anhedonia include lack of engagement in previously pleasurable activities, social withdrawal, lassitude, and avoidance. Higher levels of anhedonia in depressed patients have been associated with a more severe course of illness, increased suicide risk, greater functional impairment, and greater resistance to treatment (Lally et al., 2015; McMakin et al., 2012; Uher et al., 2012; Vrieze et al., 2014). Given its importance, efforts are underway to

develop interventions that specifically target anhedonia as a clinical symptom (Craske, Meuret, Ritz, Treanor, & Dour, 2016).

Conceptually, anhedonia refers to the internal experience of an individual and their recall of the feeling of pleasure upon questioning by a clinician or when responding to a questionnaire (Franken, Rassin, & Muris, 2007; Gorwood, 2008). Clinically, no distinction is made between decreased motivation and reduction in experienced pleasure (Treadway & Zald, 2011). Because these behaviors are also associated with lack of action, with regard to the standard diagnosis of MDD, it is difficult to conclude whether an individual endorsing 'lack of interest or pleasure' is experiencing an inability to enjoy an activity in general versus a reluctance to approach and take part in pleasurable activities. Thus, as a symptom, experiential anhedonia—historically associated with melancholic depression—may differ from lack of motivation (Treadway & Zald, 2013) and may have a distinct neurobiology (Berridge & Kringelbach, 2008; Berridge, Robinson, & Aldridge, 2009).

To understand why an individual might not engage in a

* Corresponding author. Experimental Therapeutics and Pathophysiology Branch, National Institute of Mental Health, National Institutes of Health, Building 10 (CRC), Rm 7-5565, Bethesda, MD 20892, USA.
E-mail addresses: szczepaj@mail.nih.gov (J.E. Szczepanik), mfurey1@its.jnj.com (M.L. Furey), nugenta@mail.nih.gov (A.C. Nugent), ioline.henter@nih.gov (I.D. Henter), zaratec@mail.nih.gov (C.A. Zarate), clejuez@ku.edu (C.W. Lejuez).

reinforcing activity and thereby potentially miss out on pleasure, the steps that precede actual engagement—specifically, the motivation to take action and the resulting approach of an opportunity—must be considered. Evidence suggests that hedonic deficit and approach motivation are related (Germans & Kring, 2000), and that severity of anhedonia influences task performance in different ways than severity of depression, most notably by slowing reward learning (Chase et al., 2010). Higher levels of anhedonia have also been associated with decreased willingness to exert the effort necessary to obtain rewards (Treadway, Buckholtz, Schwartzman, Lambert, & Zald, 2009). Another deficit that contributes to anhedonia in MDD is the reduced ability to *sustain* positive emotion, rather than an inability to *experience* positive emotion (Heller et al., 2009). Thus, emerging research into the nature of hedonic deficits in MDD suggests the involvement of related but distinct processes that may all underlie anhedonia. Understanding these distinct processes could lead to better therapeutic interventions by targeting motivation and hedonic expectation, or facilitating the ability to remain engaged with reinforcers in therapy, as appropriate for an individual patient. The biological distinction between hedonic experience and motivation for reward was formulated based on both animal and human studies (Berridge & Kringelbach, 2008; Berridge et al., 2009) and is often referred to as 'liking' versus 'wanting'. Neurobiological correlates of anhedonia in individuals with MDD could inform biology-based treatments (Lally et al., 2015). Both approach behavior and anhedonia have been identified as research targets based on Research Domain Criteria (RDoC) (Cuthbert & Insel, 2013; Insel et al., 2010).

This study sought to assess the 'liking' and 'wanting' components of anhedonia in MDD participants and healthy controls. Towards this end, we developed a Behavioral Approach Motivation Paradigm (BAMP) as an experimental assessment. First, we asked participants how much they 'liked' particular activities in order to establish each individual's capacity to enjoy various activities and to identify individual reinforcers. We subsequently used participant-identified 'liked' activities to study how 'wanting' of activities might differ as they were approached by healthy and MDD participants. Our hypothesis was that, in contrast to healthy controls, individuals with MDD would be less likely to recognize (that is, 'like') potentially reinforcing activities and also be less likely to approach (that is, 'want') activities that they had previously identified as 'liked'. The study also sought to evaluate the BAMP task as a potential tool—both behaviorally and in combination with neuroimaging studies—for studying MDD in general and anhedonia in particular.

1. Methods

1.1. Participants

Participants in the current study were a subset of individuals recruited for research studies (NCT00397111) at the National Institute of Mental Health (NIMH) by means of community and internet advertising (including the ClinicalTrials.gov website). All participants were between the ages of 18 and 50 and physically healthy as determined by medical history, laboratory testing, drug screening, and physical examination. The psychiatric diagnosis of MDD participants currently experiencing a major depressive episode was established using the Structured Clinical Interview for DSM-IV (SCID-IV) (First, Spitzer, Gibbon, & Williams, 2002) as well as a semi-structured clinical interview with a psychiatrist. MDD participants were excluded if they had serious suicidal ideation or behavior, major medical or neurological disorders, a history of drug or alcohol abuse within the past year, or a lifetime history of drug or alcohol dependence. Lack of psychiatric diagnosis for healthy

controls was assessed via the Structured Clinical Interview for DSM-IV-Non-Patient Edition (SCID-NP) (SCID-I/NP) (First et al., 2002). In addition, healthy controls were excluded if there was any history of psychiatric disorder including alcohol or drug addiction or the presence of a first-degree relative with an Axis I diagnosis. All of the participants were fluent in English (either native speakers or educated in English beyond high school). After signing an informed consent form, participants completed a 2-h testing session that included self-ratings (described below), questionnaires, two computerized tasks, and a debriefing.

A final sample of 44 participants (21 with MDD (13M/8F) and 23 healthy controls (14M/9F)) was included in the study. All MDD participants were medication-free for at least 14 days at the time of testing but were not taken off medications to participate in this study. Demographic information is provided in Table 1.

1.2. Assessment measures

Measures of mood, anhedonia, and approach/avoidance tendencies were administered as part of the study (see Table 1). Mood was assessed using the self-reported Beck Depression Inventory-II (BDI-II) (Beck, Steer, Ball, & Ranieri, 1996), which estimates the level of current depressive symptoms in both clinical and non-clinical populations. Anhedonia was assessed via the widely used Chapman scales, specifically the Physical Anhedonia Scale/Social Anhedonia Scale (CPAS/CSAS) (Chapman, Chapman, & Raulin, 1976); both measure trait-level hedonic capacity. To assess current (state-level) hedonic capacity, the Snaith Hamilton Pleasure Scale (SHAPS) with modified scoring was included (Snaith et al., 1995). The psychological processes underlying the tendency to approach or avoid activities and social situations were assessed using the Behavior Inhibition/Behavior Activation Scales (BIS/BAS) (Carver & White, 1994; Smillie & Jackson, 2005). The Jackson Appetitive Motivation Scale (JAMS) was included to measure established trait levels of reward motivation (Jackson & Smillie, 2004; Smillie & Jackson, 2005).

1.3. The Behavioral Approach Motivation Paradigm (BAMP): word rating and lexical decision tasks

The BAMP paradigm comprised two tasks: rating of activity words (the Word Rating Task (WRT)) and a reaction time joystick task (the Lexical Decision Reaction Time Task (LDT)) (Fig. 1). The WRT required each participant to rate 150 two-to four-syllable verbs representing activities such as 'bowling', 'hiking', or 'cooking' on a five-point Likert scale (0–4) ranging from 'can't stand' to 'like a lot' (see Appendix 1 for the complete list of words). We chose the most negative anchor to promote a possible active rejection of a 'disliked' activity, thereby strengthening the disparity between an activity that participants would potentially approach or avoid. Each word thus acquired a number representing an individually assessed appetitive value; scores of 0 and 1 represented 'disliked' items, scores of 2 represented neutral items, and scores of 3 or 4 represented 'liked' items. The participants used a mouse to click a button on the screen representing the choices and had an option to skip up to 10 words if they could not relate to an activity or if they did not wish to rate it for any other reason. The task was self-paced, and time to decision was not measured. The selection of words was loosely based on the Pleasant Events Schedule (Lewinsohn & Graf, 1973), but was expanded and supplemented to include potentially neutral and aversive actions in order to enable a wide variety of ratings. From this task, data were generated for how the words were rated by each participant. Furthermore, the words from each rating category ('can't stand'/'disliked', neutral, 'liked'/'liked a lot') served as a pool from which stimuli for the LDT were randomly selected.