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What, Me Worry and Ruminate About *DSM-5* and RDoC? The Importance of Targeting Negative Self-Referential Processing

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Abstract

Rumination, worry, and other forms of negative self-referential processing (NSRP) are familiar to everyone, as reflecting on the self is perhaps our most human characteristic. However, for a substantial subgroup of patients, NSRP arises in response to intense emotionality, worsening the clinical presentation, and diminishing the treatment response. The combination of emotionality and NSRP likely reflects an endophenotype of complicated and treatment refractory patients who fail to achieve a satisfactory treatment response in our trials and our clinics. An important next step is to personalize treatments by deliberately targeting NSRPs within established treatment protocols or in as yet novel treatments. Enriching treatments with mindfulness meditation is one possible avenue for personalized care of patients with this hypothesized endophenotype.

Keywords

decentering; emotionality; mindfulness; rumination; self-referential processing; worry

Rumination and worry are core cognitive processes central to many forms of psychopathology and to human functioning, writ large. As Olatunji, Naragon-Gainey, & Wolitzky-Taylor (2013) point out, although distinguished in content (i.e., loss versus threat, past versus future, and relationships to depression and anxiety), rumination and worry share features and are structurally related (e.g., Segerstrom, Tsao, Alden, & Craske, 2000). Indeed, rumination, worry, as well as other cognitive responses to emotions, such as self-criticism, may be considered manifestations of a core process of negative self-referencing in contexts of emotional/motivational salience (i.e., negative self-referential processing [NSRP]; Northoff, 2007). NSRP is common among humans because the contexts of discrepancy between a current emotional/motivational state and a representation of the future (i.e., planning), the past (i.e., failures/losses), or an idealized self (i.e., self-criticism) are easy to engage given a human capacity for higher-level self-consciousness and the reinforcing properties of this type of cognitive activity for achieving goal states (e.g., Borkovec, Alcaine, & Behar, 2004; Carver, 2004). This self-conscious ability can clearly be helpful for managing a world in which there is ambiguity and uncertainty. Reflecting on the past, the

future, and one's sense of self can help one mentally prepare for action toward desired goals and avoid undesired ones. This same ability, however, may be associated with clear dysfunction (e.g., Olatunji et al., 2013).

Even in its dysfunctional forms, NSRP is seen in people with relatively high functioning (i.e., “the worried well”) as well as in many disorders (i.e., “transdiagnostically”). However, despite this ubiquity, some individuals utilize these cognitive processes more often and to a more dysfunctional extent. Understanding the functional (i.e., purposeful) nature of NSRP is key to understanding how it becomes reinforced to a pathological degree. Theorists (e.g., Borkovec et al., 2004; Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008; Watkins, 2008) have argued that NSRP including worry and rumination becomes negatively reinforced by the reduction in aversive emotions. Individuals with high emotional/motivational intensity (i.e., “neuroticism”), given their greater likelihood to experience affective states, may be particularly likely to rely on these processes to avoid aspects of emotional experience. High levels of NSRP are associated with considerable deficits in cognitive and behavioral responding (e.g., Lissek, 2012; Whitmer, Frank, & Gotlib, 2012) as well as an inferior treatment response and greater relapse (e.g., Jones, Siegle, & Thase, 2008). However, despite a clear need to better elucidate their role in the nature and treatment of psychopathology, current nosological systems all but ignore NSRPs. Improving classification of NSRPs and developing treatments that specifically target the subgroup of patients who rely on NSRPs to avoid aversive emotional experiences may help narrow the current treatment efficacy gap.

In the remainder of this commentary, we propose that (a) worry, rumination, and self-criticism reflect aberrations of normative self-referential processes with reliable biobehavioral mechanisms; (b) these NSRPs, in the context of psychopathology, are best understood by their functional nature in response to emotional/motivational contexts; (c) nosological systems should better categorize individuals who are more apt to utilize NSRP given greater emotional/motivational intensity (i.e., neuroticism); and (d) treatment approaches would best serve refractory patients by specifically targeting NSRP.

NORMATIVE SELF-REFERENTIAL PROCESSING

The ability to reflect on one's self is a defining characteristic of being human and may represent the default state of the brain (e.g., Raichle et al., 2001). Most forms of self-referential processing are associated with activation of brain regions commonly referred to as the *default mode network* (DMN) or *task-negative network* (TNN; Greicius, Krasnow, Reiss, & Menon, 2003; Raichle et al., 2001) and are believed to represent the normative, default state of the resting but wakeful brain when individuals are left undisturbed to think to themselves (e.g., Buckner, Andrews-Hanna, & Schacter, 2008). Notable nodes of the DMN include the medial prefrontal cortex (mPFC; associated with the narrative and autobiographical self) and the posterior cingulate cortex (PCC; associated with experiential and nonjudgmental self-reflection). The DMN can be contrasted with other identified *task-positive networks* (TPN), including the *salience network* and the *executive control network*. The salience network comprises neural regions including the anterior insular cortex (e.g., seat of interoception, sensing the physical condition of the body; Craig, 2009) and the dorsal

anterior cingulate cortex (dACC; associated with monitoring and evaluation of error detection); it is important for monitoring and drawing our attention to the salience of interoceptive and external events occurring in our daily lives (e.g., Craig, 2009). The executive control network, which includes regions of the dorsolateral, ventrolateral, and dorsomedial prefrontal cortex (PFC), is crucial for complex cognitive tasks such as working memory, cognitive control, and decision making in the context of goal-directed behavior (Menon & Uddin, 2010) and coordinates with the salience network to respond to already identified salient stimuli. In most instances, the DMN is anticorrelated with one or more of the TPNs—meaning when one is more active, the other is less active. However, optimal human mentation is reflected in a delicate balance of activations and coactivations of the TPN and the DMN, and, in some instances, cooperation between nodes from each network to meet the internally and externally generated demands placed upon us (e.g., Buckner et al., 2008; Spreng, 2012).

Several forms of healthy self-referential processing have received considerable theoretical and empirical attention. For instance, according to Morin (2011), individuals adept at self-reflection tend to possess superior self-knowledge (e.g., greater accuracy in one's self-concept) and superior self-regulation (e.g., the ability to alter one's behavior, resist temptation, change one's mood, effectively select an adaptive behavioral response from various options, and better filter irrelevant information; Baumeister & Vohs, 2007). Self-awareness is also integral to adaptive social cognition and the ability to infer and respond to the mental states of others (e.g., their goals, intentions, beliefs, desires, thoughts, feelings). Similarly, Suddendorf and Corballis (2007, p. 299) proposed *mental time travel* as the ability of humans to “mentally project themselves backwards in time to re-live or forwards to prelive events.” The ability to draw upon past events and relate them to possible outcomes in the future is likely an evolutionary advantage enjoyed by humans, and it results from the careful coordination of frontal and medial temporal memory systems (Addis, Wong, & Schacter, 2007; Okuda et al., 2003; Szpunar, Watson, & McDermott, 2007). Finally, another potentially advantageous form of self-directed mental activity is mind wandering, which is sometimes referred to as stimulus-independent thought or task-unrelated thought. Mind wandering is associated with a future-oriented mentation and may represent the anticipation and planning of personally relevant future goals (Mooneyham & Schooler, 2013). Further, mind wandering promotes creative thinking and may be a source of relief from boredom and drudgery (Mooneyham & Schooler, 2013).

Despite these obvious benefits, considerable evidence reveals that reflecting on the self is associated with notable deficits and disruptions (e.g., reading comprehension, sustained attention, working memory capacities), which in turn can undermine performance on measures of general intelligence (Mooneyham & Schooler, 2013). Mind wandering has also been implicated in the fluctuations of our mood and often precedes negative mood states (Killingsworth & Gilbert, 2010); especially during times of distress or high emotionality, the prospect of confronting danger to the self or facing a painful disappointment or loss often results in temporary NSRP that prevents optimal switching to the TPN and possibly worsening and prolonging the emotional upset (e.g., Coelho & Purkis, 2009).

DISORDERED SELF-REFERENTIAL PROCESSING

The extant literature on normative self-reflection may offer insights into understanding the nature of destructive self-referencing that marks so many commonly occurring emotional disorders. In particular, three forms of NSRP have received considerable theoretical and empirical attention: rumination (e.g., repetitive thinking about past mistakes aimed at reducing distress related to perceived losses; Nolen-Hoeksema et al., 2008), worry (e.g., repetitive thinking about future events aimed at reducing distress that arises from conflicting emotional and motivational states; Borkovec et al., 2004; Mennin & Fresco, in press; Newman & Llera, 2011), and self-criticism (e.g., evaluation of the emotional self characterized by unworthiness, inferiority, failure, guilt, and chronic fear of disapproval and rejection; Blatt, 1995). The clinical consequences of these NSRPs are well documented elsewhere (e.g., Olatunji et al., 2013; Watkins, 2008). However, considerable evidence now reveals that many forms of psychiatric illness are marked by NSRP often resulting in inordinate activation of the DMN and correspondingly, an inability to switch to the TPN, which in turn undermines cognitive load and emotion regulation capacities (e.g., Brewer et al., 2011; Whitfield-Gabrieli & Ford, 2012). For instance, as compared to healthy control participants, depressed individuals show stronger resting state connectivity between the PCC and the subgenual ACC, a region when hyperactivated is associated with increased sadness, less cortical control over emotional reactivity, and an inferior treatment response with medication and psychotherapy (e.g., Hamani et al., 2011). Similarly, Hamilton et al. (2011) found that among depressed participants, concurrent levels of self-reported rumination were associated with DMN dominance over activations of the TPN. With respect to worry, Etkin, Prater, Schatzberg, Menon, and Greicius (2009) found that generalized anxiety disorder (GAD) patients, as compared to healthy control participants, evidenced stronger resting state connectivity between the amygdala, the ventromedial PFC, and the dorsolateral PFC, and this connectivity was stronger as a function of anxiety severity. Consistent with Borkovec and colleagues' (2004) view that worry serves to help reduce distress caused by emotional arousal, Etkin et al. (2009) interpreted the role of the dorsolateral prefrontal cortex (DLPFC) here as a form of compensatory, but not necessarily optimal, neural adaptation.

Given these prominent cognitive and emotion regulation deficits promoted by NSRP, individuals with emotional disorders often exhibit deficiencies in reward (e.g., Bogdan & Pizzagalli, 2006) and threat learning (e.g., Lissek, 2012; Whitmer et al., 2012) that result in impoverished and inflexible repertoires of behavior in response to the situations that typically function to promote escape, avoidance, or inactivity as a means of attempting to manage emotional/motivational signals (e.g., Ferster, 1973). With respect to reward learning, depressed individuals, as compared to healthy controls, are less responsive to future opportunities (e.g., Bogdan & Pizzagalli, 2006) and fail to distinguish between options yielding large versus small rewards (Forbes, Shaw, & Dahl, 2006). Whitmer et al. (2012) found that instructing depressed individuals to ruminate interfered with learning the probability that a particular stimulus would be associated with punishment. With respect to threat and safety learning, individuals prone to anxiety disorders are less successful in discriminating the properties of stimuli that share characteristics with an aversive stimulus that was trained as a conditional stimulus (Lissek, 2012). Moreover, resorting to worry to

regulate perceived threat experiences has been shown to impede emotional processing (Borkovec et al., 2004; Newman & Llera, 2011).

Behavioral mechanisms of these deficits likely involve the negative reinforcement of NSRP in response to emotional/motivational contexts. Indeed, based on a corpus of studies, Borkovec et al. (2004) have argued that the use of worry becomes strengthened via the reduction in emotional arousal. Newman and Llera (2011) have further demonstrated that worry is utilized to maintain a predictable emotional state to avoid any unexpected emotional shifts or contrasts. Consistently, Mennin and Fresco (in press) posit that conflicting approach/avoidance motivations may underlie such contexts. Similarly, Nolen-Hoeksema et al. (2008) suggested that rumination may be reinforced by suppressing aversive negative emotions such as sadness and may also subsequently promote behavioral withdrawal from rewarding contexts. Moulds, Kandris, Starr, and Wong (2007) found correlational evidence for a relationship between avoidance, rumination, and behavioral withdrawal. A more recent study by Dickson, Ciesla, and Reilly (2012) found that both rumination and worry prospectively mediated the relationship of cognitive avoidance with anxiety over a 7-day period, but only rumination mediated the relationship of cognitive avoidance with sadness. Paulus and Stein (2010) highlight the neural underpinnings of this relationship between emotional/motivational contexts and NSRP. They argue that detection of motivationally salient internal or external stimuli is mediated through the insula (i.e., interoception), but with greater connectivity within the mPFC (e.g., NSRP) in depressed and anxious individuals—thereby further impacting the processing of subsequent emotional and motivational stimuli in the insula, forming a pathological feedback loop.

The avoidance functions of NSRP may be particularly problematic and responsible for their ubiquitous presence in many forms of psychopathology. Indeed, these processes have been shown to be “transdiagnostic” and present in multiple disorders (e.g., Kertz, Bigda-Peyton, Rosmarin, & Björgvinsson, 2012; Watkins, 2009). However, not all individuals utilize NSRP in service of emotional avoidance to the same degree. For instance, individuals with GAD have been distinguished from other individuals in their greater likelihood to utilize worry to distract themselves from emotional topics (Borkovec & Roemer, 1995). It may be that individuals who are more sensitive to emotional/motivational contexts (i.e., higher in neuroticism) are most likely to be vulnerable to the deleterious usage of NSRP in service of emotional avoidance. Indeed, Olatunji et al. (2013) note that NSRP is not synonymous with neuroticism and that the former has been found to mediate the relationship between the latter and depression over a 15-year period (Mezulis, Priess, & Hyde, 2011). Similarly, Roelofs, Huibers, Peeters, Arntz, and van Os (2008) found that rumination (but not worry) mediated the relationship between neuroticism and depression. Overall, despite the widespread presence of NSRP in psychopathology, some individuals may be at particular risk for the use of NSRPs to avoid emotional states, which may, in turn, reinforce their usage and maintain negative emotional states.

Despite the clear importance of NSRP and its role in emotional dysfunction, individuals with high levels of neuroticism, who are more apt to utilize NSRP in service of avoidance, are not well categorized in current psychiatric nosology. With the exception of GAD, a disorder routinely questioned for its significance despite considerable evidence of its negative impact

as well as that of its chief symptom, worry (e.g., Wittchen, 2002), NSRP is absent from the diagnostic criteria of all disorders in the most recent Diagnostic and Statistical Manual of Mental Disorders (*DSM-5*; American Psychiatric Association [APA], 2013)—even though self-referential processing is such a core aspect of normative and disordered human mentation. Additionally, alternative nosological systems that are showing promise, such as the Research Domain Criteria (RDoC; Insel et al., 2010) initiative at the National Institute of Mental Health (NIMH), also do not directly address NSRP phenomena given their focus on more molecular components (e.g., attention, working memory, learning processes), which are likely constituent mechanisms of NSRP but not specific to it. Brown and Barlow (2009) suggested an alternative model that remains symptom-based, but provides a structural alternative to the *DSM*. In their proposed system, an individual could meet temperamental criteria for neuroticism/negative affect at a higher-order level as well as NSRP at a lower-order level (termed “cognitive avoidance” in their model). As our understanding of biobehavioral mechanisms of disorder advances, nosological debates will continue, but it will be particularly imperative that any diagnostic system be effective in categorizing pathological NSRP given its impairing and refractory characteristics.

TREATING REFRACTORY SELF-REFERENTIAL PROCESSING

Of the many important conclusions drawn from Olatunji et al. (2013), two findings in particular stand out. Specifically, diagnostic comorbidity composed of mood and anxiety disorders was associated with greater levels of rumination, and concurrent levels of worry partially accounted for the association between rumination to depression and anxiety symptoms. Interestingly, these findings may also shed light on one of the most vexing issues in the treatment of adult psychiatric disorders. Despite significant treatment advances (e.g., Butler, Chapman, Forman, & Beck, 2006), a sizeable subgroup of individuals with co-occurring disorders such as GAD and major depressive disorder (MDD) fail to make sufficient treatment gains, thereby prolonging their deficits in life functioning and satisfaction. For instance, Borkovec and Ruscio (2001) found that only 50–60% of GAD patients treated with cognitive behavior therapy (CBT) demonstrated clinically meaningful change. Relatedly, despite achieving acute treatment gains, GAD patients with comorbid MDD experience deterioration of depression symptom improvements (Newman, Przeworski, Fisher, & Borkovec, 2010). Finally, patients with mixed anxiety–depressive disorder (e.g., MDD + apprehensive anxious symptoms) treated in the NIMH-funded Sequenced Treatment Alternatives to Relieve Depression Study were especially treatment refractory (Farabaugh et al., 2010). One possible inference from these treatment findings coupled with the work of Olatunji et al. (2013) is that these treatment refractory patients reflect the patient subgroup that exhibits a propensity to engage in NSRP. For instance, GAD and MDD are two conditions especially marked by destructive forms of negative self-referencing (e.g., Watkins, 2008). A review of the treatment literature reveals numerous examples of how NSRPs (e.g., rumination, worry, self-criticism) contribute to an inferior treatment response and/or a more fragile recovery. Specifically, pretreatment levels of rumination predict an inferior acute treatment response in MDD and dysthymic disorder (e.g., Ciesla & Roberts, 2002; Jones et al., 2008; Schmalzing, Dimidjian, Katon, & Sullivan, 2002) as well as panic disorder (Papageorgiou & Wells, 2003; Wells, 1990). Similarly, higher levels of residual

depression symptoms and rumination are associated with a greater likelihood of relapse following acute treatment for MDD with CBT (Watkins et al., 2011) and mindfulness based cognitive therapy (MBCT; Michalak, Hölz, & Teismann, 2011). Like rumination, self-criticism has also shown deleterious effects on treatment efficacy both in the terms of acute treatment gains and in treatment durability (Blatt, 1995; Blatt, Quinlan, Pilkonis, & Shea, 1995; Blatt, Zuroff, Bondi, Sanislow, & Pilkonis, 1998; Blatt, Zuroff, Hawley, & Auerbach, 2010). Finally, deliberate efforts to target forms of negative self-referencing (worry and rumination) improve treatment durability (e.g., van Aalderen et al., 2011; Watkins et al., 2011; Wells et al., 2012).

Taken together, the meta-analytic results from Olatunji et al. (2013) and the various treatment findings showing the corrosive effects of rumination, worry, and self-criticism indicate that NSRPs represent an individual difference factor that cuts across many forms of emotional disorders, complicates the clinical presentation and treatment of these disorders, and appears to be a crucial factor to address if treatment gains are to be made durable. The need to specifically target NSRP corresponds with a recent initiative from NIMH's National Advisory Mental Health Council, which emphasized "treatment personalization" as a means to identify factors that predict who will benefit from a given intervention process and then to systematically determine ways of matching patients to a particular treatment as well as optimizing and augmenting care. In line with this initiative, one positive development comes from treatments that deliberately target NSRPs, which appear to have begun to close the treatment efficacy gap among patients with and without NSRPs. For example, treatments enriched with mindfulness meditation may be well suited to addressing the problems of NSRP that arise in response to avoidant-oriented emotional/motivational intensity. One of the putative by-products of developing a meditation practice is reducing the reliance on self-referential processing in favor of an orientation that is largely nonjudgmental, nonreactive, and present-centered in terms of one's attention and awareness (e.g., Vago & Silbersweig, 2012). Among largely normative individuals, training in mindfulness meditation has been shown to reduce recruitment of neural regions associated with the DMN (e.g., Brewer et al., 2011; Farb et al., 2007) and reduce mind wandering while improving working memory capacity (e.g., Mrazek, Franklin, Phillips, Baird, & Schooler, 2013). Considerable evidence demonstrates the benefits of mindfulness meditation for a wide array of physical (Ospina et al., 2007) and psychiatric conditions (Hofmann, Sawyer, Witt, & Oh, 2010).

Increasingly, benefits from mindfulness-based meditation and therapies are associated with reductions in NSRPs and/or gains in *decentering*, defined as a meta-cognitive capacity to observe items that arise in the mind (e.g., thoughts, feelings, memories) with healthy psychological distance, greater self-awareness, and perspective taking (Fresco, Moore, et al., 2007; Fresco, Segal, Buis, & Kennedy, 2007). A series of studies have validated decentering as a construct important in the acute and enduring treatment of MDD and anxious depression (Fresco, Moore, et al., 2007; Fresco, Segal, et al., 2007; Mennin & Fresco, 2011) and in the prevention of MDD relapse following prophylactic treatment with MBCT (Bieling et al., 2012). fMRI assessment and neural correlates of treatment following MBCT revealed that normalization of mPFC activity coupled with an ability to approach emotion provocation with a nonjudgmental, nonreactive, awareness-predicted treatment durability (Farb, Segal, & Anderson, 2011).

One positive development in recent years has been the emergence of CBT packages that are enriched with mindfulness meditation and/or more deliberately target NSRPs: dialectical behavior therapy (Linehan, 1993), acceptance and commitment therapy (Hayes, Strosahl, & Wilson, 1999), MBCT (Segal, Williams, & Teasdale, 2002), behavioral activation (Jacobson, Martell, & Dimidjian, 2001), acceptance-based behavioral therapy (Roemer, Orsillo, & Salters-Pedneault, 2008), the unified protocol (Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010), rumination-focused cognitive-behavioral therapy (Watkins et al., 2011), and emotion regulation therapy (ERT; Mennin & Fresco, in press). These latter two, rumination-focused CBT and ERT, explicitly target NSRPs especially in relation to emotional/motivational intensity. For instance, these treatments incorporate training in early cue detection to help clients attend to the arising of NSRP, the context in which it is arising, and the function it may be serving in the given moment, whether helpful or unhelpful (Mennin & Fresco, in press; Watkins et al., 2011). In doing so, early cue detection facilitates clients adopting a more distanced or decentered perspective and taking actions that are potentially more goal directed and less marked by a self-referential perspective. Coupled with training in mindfulness meditation, cue detection can reduce the reliance of resorting to NSRPs and the cognitive and learning consequences that result.

CONCLUSION

Olatunji et al. (2013) are to be commended for bringing into sharp relief the perils and broad reach of rumination and worry as they relate to the severity of mood and anxiety disorders. The clinical relevance of this work is quite possibly amplified when NSRPs are considered in the context of emotional/motivational intensity. Individuals who experience greater emotionality (i.e., neuroticism) may be more prone to resort to NSRPs as a desperate approach to managing the emotions that mark their lives. In all likelihood, this combination of emotionality and NSRPs reflects one of the endophenotypes of complicated and treatment refractory patients who fail to achieve a satisfactory treatment response in our trials and in our clinics. Yet, this characteristic is largely overlooked in our systems of nosology (e.g., *DSM-5*, RDoC) and rarely becomes a major focus even in our efficacious treatments. An important next step to improve the plight of these patients is to personalize our treatments (e.g., through the incorporation of mindfulness) by deliberately targeting NSRPs in the context of established treatment protocols or perhaps in as yet novel treatments. Such efforts hold promise in narrowing the gap of treatment efficacy that separates patients with considerable NSRP from other patients.

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