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# Physiological and behavioral indices of emotion dysregulation as predictors of outcome from cognitive behavioral therapy and acceptance and commitment therapy for anxiety

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ABSTRACT

*Background and objectives:* Identifying for whom and under what conditions a treatment is most effective is an essential step toward personalized medicine. The current study examined pre-treatment physiological and behavioral variables as predictors and moderators of outcome in a randomized clinical trial comparing cognitive behavioral therapy (CBT) and acceptance and commitment therapy (ACT) for anxiety disorders.
*Methods:* Sixty individuals with a DSM-IV defined principal anxiety disorder completed 12 sessions of either CBT or ACT. Baseline physiological and behavioral variables were measured prior to entering treatment. Self-reported anxiety symptoms were assessed at pre-treatment, post-treatment, and 6- and 12-month follow-up from baseline.
*Results:* Higher pre-treatment heart rate variability was associated with worse outcome across ACT and CBT. ACT outperformed CBT for individuals with high behavioral avoidance. Subjective anxiety levels during laboratory tasks did not predict or moderate treatment outcome.
*Limitations:* Due to small sample sizes of each disorder, disorder-specific predictors were not tested. Future research should examine these predictors in larger samples and across other outcome variables.
*Conclusions:* Lower heart rate variability was identified as a prognostic indicator of overall outcome, whereas high behavioral avoidance was identified as a prescriptive indicator of superior outcome from ACT versus CBT. Investigation of pre-treatment physiological and behavioral variables as predictors and moderators of outcome may help guide future treatment-matching efforts.
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## 1. Introduction

The effectiveness of cognitive behavioral therapy (CBT) for the treatment of anxiety disorders is well established (Hofmann & Smits, 2008; Tolin, 2010), and other behavioral treatments, such as acceptance and commitment therapy (ACT; Hayes, Strosahl, & Wilson, 2011), are garnering support (Arch et al., 2012; Craske et al., in press). However, responses vary widely, with some patients achieving long-lasting remission and others remaining symptomatic or experiencing a return of symptoms at follow-up (Arch & Craske, 2009). In an effort to improve outcomes, the National Institutes of Health has called for an increased emphasis on personalized medicine. Identifying both prognostic factors (predictors of overall treatment success), as well as prescriptive factors (moderators of response to different treatments), incrementally improves our capacity to match anxious individuals to the most appropriate treatments (Wolitzky-Taylor, Arch, Rosenfield, & Craske, 2012).

Anxiety disorders are largely characterized by poor regulation of negative emotion (Campbell-Sills & Barlow, 2007; Hofmann, Sawyer, Fang, & Asnaani, 2012), and behavioral treatments for anxiety often target emotion regulation difficulties (Papa, Boland, & Sewell, 2012). In CBT, emotion regulation is addressed through

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cognitive reappraisal, an antecedent-focused emotion regulation strategy used to limit the emotional impact of an event by reframing its meaning or anticipated outcome (Gross, 1998), and exposure, which serves to change expectations and emotional responses associated with feared stimuli (Papa et al., 2012). ACT, a newer behavioral therapy that centers itself within contextual behavioral theory (Hayes et al., 2011), uses mindfulness, acceptance, and cognitive defusion strategies to promote nonjudgmental awareness and increase value-oriented living. These strategies in ACT are thought to reduce the use of maladaptive response-focused emotion regulation strategies (e.g., suppression) by encouraging patients to distance themselves from rigid thoughts, increase contact with the present moment, and reduce experiential avoidance (Hofmann & Asmundson, 2008).

As ACT and CBT both address emotion regulation, pre-treatment levels of emotion dysregulation may provide prognostic or prescriptive information. Emotion dysregulation has been indexed by heightened self-reported negative affect (Lang & McTeague, 2009), heightened amygdala activity in response to threat (Rauch et al., 2000), reduced high-frequency heart rate variability (Friedman & Thayer, 1998; Pittig, Arch, Lam, & Craske, 2013), and avoidance behavior (Chambless & Gracely, 1989). Despite the relevance of each of these indices of emotion dysregulation to the phenomenology of anxiety, only a handful of studies have examined them as predictors of treatment outcome (McClure et al., 2007; Wolitzky-Taylor et al., 2012). Even fewer studies have examined these indices as moderators of outcome from two distinct treatments for anxiety disorders (Meuret, Hofmann, & Rosenfield, 2010; Wolitzky-Taylor et al., 2012).

Increasingly, researchers are examining pre-treatment neural activity as a potential predictor of treatment outcome. Pre-treatment amygdala hyperactivity during complex emotion-processing tasks[1] has been found to predict better outcome from behavioral treatment for generalized anxiety disorder (McClure et al., 2007) and depression (Canli et al., 2005). Assuming that amygdala hyperactivity represents poor emotion regulation (e.g., Schaefer et al., 2002), then one explanation is that individuals with poorly-regulated emotional responses prior to treatment are more likely to benefit from treatment that targets this dysfunction. Thus, physiological and behavioral correlates of amygdala hyperactivity may similarly predict outcome.

High-frequency heart rate variability (Thayer, Åhs, Fredrikson, Sollers, & Wager, 2012) and avoidance behavior (Schlund & Cataldo, 2010) have been linked to amygdala activity and therefore may be considered peripheral markers of such activity. Low resting heart rate variability and low heart rate variability in response to stressors are associated with autonomic inflexibility and poor emotion regulation (Appelhans & Luecken, 2006; Hughes & Stoney, 2000; Sahar, Shalev, & Porges, 2001; Thayer & Lane, 2000), as well as increased amygdala activity (Mujica-Parodi et al., 2009) and decreased activity in prefrontal cortex regions responsible for amygdala down-regulation (Lane et al., 2009). Avoidance behavior, an emotion regulation strategy that maintains anxiety and interferes with inhibitory learning (Craske et al., 2008), is also associated with increased amygdala activation during tasks in which individuals avoid or escape an aversive event (e.g., monetary loss; Schlund & Cataldo, 2010; Schlund et al., 2010). Conceivably, these peripheral markers of emotion dysregulation may predict treatment outcome in the same way as amygdala activity. However, the current evidence for their prediction effects is limited.

A number of studies have examined physiological responses *during* treatment as predictors of outcome from behavioral treatments for anxiety. For example, increased heart rate during exposure sessions has been associated with superior treatment outcome for specific phobia (Lang, Melamed, & Hart, 1970), PTSD (Pitman et al., 1996), and claustrophobia (Alpers & Sell, 2008). Some researchers have interpreted these results to signify that elevated autonomic activity indicates activation of the fear structure (bio-informational theory; Lang, Cuthbert, & Bradley, 1998), which allows the fear structure to be modified during treatment (Foa & Kozak, 1998). However, this theory has received inconsistent support (see Craske et al., 2008); several studies indicate no relationship (e.g., Baker et al., 2010; van Minnen & Hagenaars, 2002; Sloan & Telch, 2002) or an inverse relationship (e.g., Telch, Valentiner, Ilai, Petruzzi, & Hehmsoth, 2000) between heart rate reactivity during exposure and subsequent treatment outcome. Moreover, studies examining *pre-treatment* heart rate reactivity as a predictor of outcome are mixed (e.g., Craske, Sanderson, & Barlow, 1987; Kozak, Foa, & Steketee, 1988). One explanation for this inconsistency is that elevated heart rate reflects multiple constructs, including incentive-related activation and active avoidance (Fowles, 1980), and is affected by both sympathetic and parasympathetic activation (Katona, McLean, Dighton, & Guz, 1982). Thus, it is possible that heart rate is too broad of a measure to provide prognostic or prescriptive utility. Instead, heart rate variability, which reflects cardiac parasympathetic activity and is a more reliable measure of emotion regulation (Appelhans & Luecken, 2006; Thayer & Lane, 2000), may provide more consistent and useful results.

Though existing research is sparse, studies investigating the effects of behavioral treatment on heart rate variability suggest that exposure and mindfulness-based treatments increase heart rate variability. Increases in resting heart rate variability were found following successful CBT for panic disorder (Craske, Lang, Aikins, & Mystkowski, 2005) and PTSD (Garakani et al., 2009), and after mindfulness-based treatment for substance use (Brewer et al., 2009). These findings suggest that low heart rate variability may be targeted by strategies in CBT and ACT. One small study found that individuals who were unresponsive to exposure therapy for flight phobia had higher baseline heart rate variability (Bornas, del Amo, Tortella-Feliu, & Llabrés, 2012), supporting the notion that targeting emotion regulation may be more effective for individuals with low, rather than high, heart rate variability. However, no studies to our knowledge have examined heart rate variability as a predictor or moderator of outcome from CBT or ACT.

Avoidance plays a central role in anxiety disorders and thus may also predict treatment outcomes. Individuals with anxiety disorders discontinue anxiogenic challenges such as voluntary hyperventilation sooner than healthy controls, reflecting greater avoidance of interoceptive sensations (Arch & Craske, 2010). Though particularly evident in panic disorder, avoidance of sensations is observed across multiple anxiety disorders (Arch & Craske, 2010; Chawla & Ostafin, 2007; Roemer, Salters, Raffa, & Orsillo, 2005). CBT targets avoidance of sensations through interoceptive exposure (Craske, 2005), whereas ACT targets avoidance by encouraging clients to "lean into" anxious sensations (Eifert & Forsyth, 2005). Indeed, acceptance training has been found to increase participants' willingness to endure physical sensations brought on by $CO_2$ inhalation (Eifert & Heffner, 2003; Levitt, Brown, Orsillo, & Barlow, 2004), suggesting that acceptance specifically targets behavioral avoidance of physical sensations. However, no studies to date have investigated whether baseline behavioral avoidance predicts outcome from ACT and CBT.

[1] Conversely, amygdala activity during tasks requiring minimal emotional processing (e.g., viewing rapidly-presented emotional stimuli) was unrelated to treatment outcome in two studies (Bryant et al., 2008; Doehrmann, 2013). As amygdala activation during more complex emotional processing tasks is likely a better index of emotion regulation (e.g., Schaefer et al., 2002), it is therefore emphasized.

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