ABSTRACT

Cynical Hostility Relates to a Lack of Habituation of the Cardiovascular Response to Repeated Acute Stress

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Hostility is associated with cardiovascular disease risk. Heightened cardiovascular reactivity (CVR) to psychological stress has been proposed as a mechanism. Recent work has emphasized a need to measure CVR across multiple stress exposures to assess potential adaptation over time. In the current study, 196 participants completed 2 separate laboratory sessions, consisting of a 20-minute baseline and 15-minute stressor. Heart rate (HR) and systolic/diastolic blood pressure (SBP/DBP) were recorded throughout. Reactivity was calculated separately for HR, SBP, and DBP (stress – baseline). Participants also completed the Cook-Medley Hostility Scale. Results indicated that greater cognitive hostility (i.e., cynicism) was associated with blunted CVR at Visit 1 and less CVR habituation between visits, even when controlling for confounding variables. No significant relationships were found for emotional or behavioral hostility. These results identify a potential pathway through which hostility contributes to disease risk. This study utilized previously collected data from the Pittsburgh Cold Study 3.

Cynical Hostility Relates to a Lack of Habituation of the Cardiovascular Response to Repeated Acute Stress

by

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ATTRIBUTIONS

Four authors contributed to this research: Alexandra T. Tyra, B.S., B.S., Ryan C. Brindle, Ph.D., Brian M. Hughes, Ph.D., and Annie T. Ginty, Ph.D. With regards to the specific contributions made, Alexandra T. Tyra devised the idea for the study, undertook all statistical analyses, and drafted the entire manuscript. Annie T. Ginty helped secure the dataset to address the research question and also provided input during the drafting of the manuscript. Ryan C. Brindle and Brian M. Hughes contributed edits and revisions for the final version of the manuscript. All chapters represent the same study and were submitted for publication as one manuscript, with the exception of Chapter Two, which was written solely for this thesis by Alexandra T. Tyra.

CHAPTER ONE

Introduction

This chapter is currently under review as part of the following manuscript: Tyra, A.T., Brindle, R.C., Hughes, B.M., & Ginty, A.T. (under review). Cynical hostility relates to a lack of habituation of the cardiovascular response to repeated acute stress. *Psychophysiology*

Hostility and Cardiovascular Health

Hostility has been associated with poor health outcomes, such as coronary heart disease (for reviews see Chida & Steptoe, 2009; Miller, Smith, Turner, Guijarro, & Hallet, 1996), carotid atherosclerosis (Everson-Rose et al., 2006; Pollitt et al., 2005), metabolic syndrome (Goldbacher & Matthews, 2007), and all-cause mortality (Klabbers, Bosma, van den Akker, Kempen, & van Eijk, 2013). A multidimensional construct, hostility is often defined as consisting of three components: emotional, cognitive, and behavioral (Buss, 1961; Spielberger et al., 1985). Research has emphasized a need to individually assess the components of hostility to determine which one may be the most predictive of poor health outcomes (Barefoot, Dodge, Peterson, Dahlstrom, & Williams, 1989; Siegman, Dembroski, & Ringel, 1987). Indeed, prior research has demonstrated that each of these components are related to cardiovascular and immune-related disease outcomes (e.g., Finney, Stoney, & Engebretson, 2002; Janicki-Deverts, Cohen, & Doyle, 2010; Lahad, Heckbert, Koepsell, Psaty, & Patrick, 1997; Why & Johnston, 2008). Particular emphasis has been placed on the cognitive component (i.e., cynicism) and cardiovascular disease (e.g., Arthur, 1998; Assari, 2016; Chaput et al., 2002; Jennings, Pardini, & Matthews, 2017; Julkunen, Salonen, Kaplan, Chesney, & Salonen, 1994;

Šmigelskas, Joffė, Jonynienė, Julkunen, & Kauhanen, 2017; Wong, Sin, & Whooley, 2014). Additionally, while the literature is more or less in agreement that greater hostility is associated with adverse health outcomes, specifically cardiovascular disease risk, the mechanisms behind this relationship remain unclear.

Hostility and Cardiovascular Reactivity

It has been proposed that exaggerated CVR during stress may be one mechanism that could explain the association between hostility and cardiovascular disease risk (Williams, 1987). According to this hypothesis, individuals with high-hostility profiles are more likely to experience heightened CVR to psychological stress and as a result are more vulnerable to cardiovascular disease. Indeed, exaggerated CVR to stress has been implicated in cardiovascular disease risk, including hypertension (Carroll, Phillips, Der, Hunt, & Benzeval, 2011; Chida & Steptoe, 2010), atherosclerosis (Barnett, Spence, Manuck, & Jennings, 1997), and cardiovascular disease mortality (Carroll et al., 2012). However, research examining the associations between hostility and CVR has produced mixed results. Most studies support the association between high hostility and exaggerated CVR (Fredrickson et al., 2000; Gump, Matthews, & Räikkönen, 1999; Jamner, Shapiro, Goldstein, & Hug, 1991; Lepore, 1995; Powch & Houston, 1996; Shapiro, Goldstein, & Jamner, 1995; Suls, 2013; Vögele, 1998) but, some report no association (Sallis, Johnson, Trevorrow, Kaplan, & Hovell, 1987), and one study demonstrated higher levels of hostility and lower CVR (Carroll, Smith, Sheffield, Shipley, & Marmot, 1997). A meta-analysis including 281 studies, all of which examined either hostility, aggression, or Type-A behavior, found significant associations between higher levels of these traits and exaggerated CVR to stress (Chida & Hamer, 2008).

Potential explanations for inconsistencies in the literature may be the type of stressors utilized (social versus nonsocial; Suls & Wan, 1993) as well as potential moderating variables, such as race (Assari, 2016; Finney et al., 2002), and gender (Girdler, Jamner, & Shapiro, 1997; Lawler, Harralson, Armstead, Schmied, 1993; Smith & Gallo, 1999; Suarez, Kuhn, Schanberg, Williams, & Zimmermann, 1998; Suarez & Williams, 1990; Suarez & Williams, 1989). Another potential explanation for inconsistencies could be the measurement of hostility, with some studies focusing on total score (e.g., Jamner et al., 1991; Hughes, 2007) and others focusing on various subcomponents (e.g., Gump et al., 1999; Lepore, 1995; Why & Johnston, 2008).

Adaptations of Cardiovascular Reactivity

A recent review proposed that CVR research should examine the adaptation pattern of cardiovascular responses to repeated exposure to the same stress task, and how such adaptation patterns relate to health outcomes (Hughes, Lü, & Howard, 2018). The authors suggest that the initial upsurge in the cardiovascular response to stress is actually beneficial in that it provides the opportunity for necessary physiological changes, such as fight-or-flight preparation. If such heightened initial CVR is part of an overall short-lasting cardiovascular response, then long-term health consequences are deemed unlikely. In other words, the ability to habituate the cardiovascular response to stress, in which subsequent stress exposures elicit lessened CVR, is proposed to be adaptive by preventing continuous strain on the cardiovascular system and thus reducing risk for disease. Alternatively, the potential for long-term health consequences arises when high CVR is non-adaptively prolonged across multiple stress exposures (Hughes et al., 2018). Considerable research has documented the occurrence of CVR habituation to acute

psychological stress in the laboratory (al'Absi et al., 1997; Frankish & Linden, 1991; Kelsey et al., 1999; Schommer, Hellhammer, & Kirschbaum, 2003). Additionally, individual differences in psychosocial variables relate to different adaptation patterns. For example, neuroticism (Hughes, Howard, James, & Higgins, 2011), rumination (Johnson, Lavoie, Bacon, Carlson, & Campbell, 2012), and dominance (Lee & Hughes, 2014) are associated with diminished CVR habituation, while repressive coping (Howard, Myers, & Hughes, 2017), openness (Lü, Wang, & Hughes, 2016a), resilience (Lü, Wang, & You, 2016b), and extraversion (Lü & Wang, 2017) are related to enhanced CVR habituation. Given such findings, Hughes and colleagues (2018) argue that future research should extend traditional CVR laboratory stress protocols to include multiple stress exposures of the same stress task. They also suggest utilization of secondary analysis of pre-existing datasets that include multiple stress exposures.

Hostility and Habituation of Cardiovascular Reactivity

Interestingly, little research has examined the relationship between hostility and CVR across multiple stress exposures and hardly any research has examined the possible relationship to physiological habituation. One study with a mixed-gender sample found that high-hostile university students displayed significant CVR habituation (only for DBP, not SBP or HR) to a cognitive stress task, while low-hostile university students did not (Hughes, 2007). The findings of this study are contrary to those of previously mentioned studies, in which "negative" personality traits (e.g., neuroticism, dominance) impaired habituation and "positive" traits (e.g., openness, resilience) supported habituation (e.g., Hughes et al., 2011; Lee & Hughes, 2014; Lü et al., 2016a; Lü et al., 2016b). It should be noted that the stress task utilized in the study was an asocial,

computerized, visual tracking task (Hughes, 2007). Given prior research emphasizing the important role of socially-induced stress in the relationship between hostility and heightened CVR (Suls & Wan, 1993), it is possible that a social stress task may produce different findings.

The aims of the current study were to 1) examine the individual association between each of the three main components of hostility (i.e., emotional, cognitive, and behavioral) and CVR during two separate laboratory psychological stress testing visits involving social evaluation and 2) examine the association between hostility and CVR habituation. Based on previous research (e.g., Barefoot et al., 1989; Lahad et al., 1997; Lepore, 1995) it was hypothesized that higher levels of emotional, cognitive, and behavioral hostility would each be associated with greater CVR at both testing visits. With regards to the relationship between hostility and habituation, the current study followed the theoretical approach of Hughes and colleagues (2018), as well as the majority findings of previous research examining the relationship between other "negative" personality traits and habituation (e.g., Hughes et al., 2011; Lee & Hughes, 2014). As such, the current study hypothesized that higher levels of each component of hostility would be associated with less CVR habituation.

CHAPTER TWO

Review of Literature

An Introduction to Hostility

Similar to most concepts in personality research, hostility has been defined and measured in a variety of different ways (for reviews see Chida & Steptoe, 2009; Miller et al., 1996). It is a complex concept that is easily influenced by other individual characteristics, as well as environmental and situational contexts (Barefoot, 1992; Smith & Christensen, 1992). Hostility has previously been referred to as an attitude (Berkowitz, 1993; Buss, 1961) or a sub-trait of a broader personality construct (e.g., Cattell, Eber, & Tatsuoka, 1970; Friedman & Rosenman, 1959; 1971). The most common approach in the literature has been to address hostility as a broad psychological domain which encompasses a variety of traits, such as aggression, anger, mistrust, and cynicism (Barefoot et al., 1989; Eckhardt, Norlander, Deffenbacher, 2004). However, each of these traits tend to manifest in vastly different ways and will rarely look exactly alike across persons, making hostility a difficult construct to operationalize and measure. For instance, hostility has previously been defined as reacting to negative circumstances with anger, thinking negatively about others, or acting aggressively towards others (Chida & Steptoe, 2009). In some cases, hostility may even include a desire to harm another person (Smith, 1994). Taken alone, each of these definitions describe only a portion of the hostility domain. Research in the field of health psychology has made efforts to further understand all aspects of the hostility construct to identify key predictors of later health

risks (e.g., Barefoot et al., 1989; Janicki-Deverts et al., 2010; Keith et al., 2017). As a result of these efforts, a more encompassing definition was accepted, which states that hostility is made up of emotional, cognitive, and behavioral elements, all of which underlie a person's pre-disposition to respond negatively to interpersonal interactions (Barefoot et al., 1989; Buss, 1961; Spielberger et al., 1985).

The Emotional, Cognitive, and Behavioral Aspects of Hostility

The emotional, cognitive, and behavioral components of hostility were first proposed based on the widely accepted theory that human experience is divided into these three basic elements (Hilgard, 1980). These components of hostility are not dependent on co-occurrence. Indeed, one or two components may be present without the occurrence of the others. That being said, they have been predicted to be moderately and positively correlated (Barefoot, 1992). This has been supported in previous research (e.g., Janicki-Deverts et al., 2010; Martin, Watson, & Wan, 2000).

The emotional component of hostility consists of an affective experience, such as anger, irritation, or contempt, that is triggered by or directed at another person. The experience of these emotions can range from mild to severe and, depending on the emotion, can either be a temporary state or stable disposition (Smith, 1994). The cognitive component of hostility consists of negative beliefs, thoughts, and attitudes about the motives, intentions, and trustworthiness of others (Greenglass & Julkunen, 1989). This component has also been described as cynicism or mistrust. Cynicism is further described as the general belief that others act out of selfish motives, whereas mistrust has been described as the expectancy that others are not trustworthy (Klabbers et al., 2013). The behavioral component of hostility consists of overt behaviors, such as

aggression. The behaviors can take either verbal (e.g., insults, sarcasm, or argumentativeness) or physical (e.g., assault) form, and are intentionally harmful towards others (Smith, 1994). The behavioral component of hostility is probably the most commonly referenced in everyday conversation when attempting to describe the construct of hostility. See Table 2.1 below for detailed descriptions and examples of each hostility component.

Table 2.1

Three Components of the Hostility Construct

Category	Emotional Hostility	Cognitive Hostility	Behavioral Hostility
Description	Anger, irritation, annoyance with others	Suspiciousness, lack of trust, cynical beliefs about others	Insults, sarcasm, physical assault against another
Real-world example	John is angry that Sue forgot to clean the dishes	Anne thinks her friends are talking negatively about her when she is not around	Kelly calls her coworker an idiot after he makes a mistake on a simple task
Item example from the Cook-Medley Hostility Scale	"People often disappoint me"	"I think most people would lie to get ahead"	"I would certainly enjoy beating a crook at his or her own game"

An important note is the difference between the experience and expression of hostility. The experience of hostility is comprised of internal and subjective processes, such as emotions (i.e., anger) and cognitions (i.e., cynicism), while the expression of hostility is externally driven and comprised of behavioral outcomes (Smith, 1994). Another similar construct that appears often in the literature is the distinction between anger-in and anger-out (Spielberger et al., 1985). Each of these constructs attempt to

differentiate between the types of hostility that are externally displayed and the types that remain unexpressed. These differentiations are important to the field of health psychology, as the experience or expression of hostility may be differently related to health outcomes (e.g., Assari, 2016; Brosschot & Thayer, 1998; Why & Johnston, 2008). For example, it has been proposed that anger inhibition may be more predictive of poor cardiovascular health outcomes than anger expression, and also more representative of how individuals typically handle anger-evoking situations in everyday life (Brosschot & Thayer, 1998).

Difficulties arise when researchers attempt to parse out these different conceptual components of hostility during operationalization and measurement. As mentioned previously, while it is not necessary for each component to occur at the same time, they often do, making it difficult to distinguish which aspect of hostility is having an effect on which outcome. Indeed, a single measure of hostility may be tapping more than one component. That being said, assessments that attempt to focus on the various components of hostility have been found to be more predictive of health outcomes than assessments of overall hostility (Barefoot et al., 1989; Siegman et al., 1987). These findings indicate the importance of individually assessing the components of hostility in order to determine which one is most predictive of health risk. As such, it is imperative that researchers use assessments of hostility that are explicit about which components are being examined (e.g., Janicki-Deverts et al., 2010; Keith et al., 2017).

Assessment of Hostility

Two meta-analytic reviews (44 and 45 studies, respectively) examining hostility and health revealed a variety of approaches taken by researchers to measure hostility,

varying from structured interviews to self-report questionnaires (Chida & Steptoe, 2009; Miller et al., 1996). While structured interviews were found to be the most predictive of the relationship between hostility and health outcomes (e.g., coronary heart disease), this method is time-consuming and requires significant training. As such, self-report measures of hostility such as the Buss-Durkee Hostility Inventory (BDHI; Buss & Durkee, 1957) or the Cook-Medley Hostility Scale (CM-Ho; Cook & Medley, 1954), have been the most commonly utilized and are also sufficiently predictive of health outcomes (Barefoot, 1992; Miller et al., 1996).

The most widely-used hostility measure in health psychology, the 50-item Cook-Medley Hostility Scale became particularly popular after it was first found to be associated with the severity of coronary artery disease in cardiac patients (Williams et al., 1980). This scale was originally derived from the Minnesota Multiphasic Personality Inventory (MMPI) to assess poor teacher rapport with students (Cook & Medley, 1954). Numerous attempts have since been made to understand the construct being measured by the Cook-Medley Hostility Scale, thus generating a variety of inconsistent operationalizations. For instance, some researchers claimed the scale was more likely a measure of cynical distrust (Greenglass & Julkunen, 1989; Smith & Frohm, 1985), whereas others argued for the division of the scale into two factors: paranoid alienation and cynicism (Costa, Zonderman, MccCrae, & Williams, 1986).

However, content analysis by Barefoot and colleagues (1989) has been most commonly cited and states that the items of the scale can be divided into 6 subscales: Hostile Attributions, Cynicism, Hostile Affect, Aggressive Responding, Social Avoidance, and Other (a subset of miscellaneous items with no clear commonality). Only

the first four of the six subscales were found to be indicative of hostility and only three (Cynicism, Hostile Affect, and Aggressive Responding) were found to be predictive of later life survival outcomes in a sample of lawyers (Barefoot et al., 1989). Interestingly, these three subscales respectively address the cognitive, emotional, and behavioral components of hostility, thus making the Cook-Medley Hostility Scale an attractive option for individually examining each aspect of hostility and the relationship to health outcomes. That being said, research revealed the cynicism subscale to be the most consistently replicable construct tapped by the Cook-Medley Hostility Scale (Greenglass & Julkunen, 1989; Han, Weed, Calhoun, & Butcher, 1995). While it is important to examine each of the subscales, a large majority of research has focused solely on the relationship between cynicism and health outcomes (e.g., Assari, 2016; Carroll et al., 1997; Jennings et al., 2017; Lepore, 1995; Šmigelskas et al., 2017; Why & Johnston, 2008).

Hostility and Health

The origins of current research examining the relationship between hostility and health outcomes can be traced back to early work conducted by Friedman and Rosenman on Type A behavior pattern (TABP). In a sample of males drawn from various vocations, (n = 212), those who displayed TABP were more likely to experience adverse health outcomes (e.g., coronary heart disease) than those who displayed opposite behavior patterns (Friedman & Rosenman, 1959). TABP is characterized by a pre-disposition towards impatience, time pressure, excessive competitiveness, need for success, and hostility (Friedman & Rosenman, 1971). A large prospective epidemiological study (the Western Collaborative Group Study) examining 3,154 males (ages 39 – 59) over the

course of 8.5 years revealed that TABP was associated with higher incidence of coronary heart disease (e.g., Rosenman et al., 1964; 1975; 1976). Further research revealed TABP to be predictive of the severity of coronary artery disease (e.g., Blumenthal, Williams, Kong, Schanberg, & Thompson, 1978; Frank, Heller, Kornfeld, Sporn, & Weiss, 1978; Friedman, Rosenman, Straus, Wurm, & Kositchek, 1968). In 1981, the National Institutes of Health published a review confirming that TABP was associated with heightened risk of coronary heart disease, more so than other well-established risk factors (Review Panel on Coronary-Prone Behavior and Coronary Heart Disease, 1981).

Interestingly, the findings of further research were surprisingly inconsistent, with numerous studies revealing no relationship between TABP and cardiovascular disease (e.g., Dembroski, MacDougall, Williams, Haney, & Blumenthal, 1985; Dimsdale et al., 1979; Krantz, Sanmarco, Selvester, & Matthews, 1979; Scherwitz et al., 1983). In particular, a second major prospective study— the Multiple Risk Factor Intervention Trial study (MRFIT)—was unable to replicate the previously established relationship between Type A and coronary heart disease in a sample of 3,110 males (Shekelle et al., 1985). The inconsistencies in the literature led some researchers to evaluate possible explanations for null findings (Siegman, 1994). The standard interview used to assess TABP was found to be methodologically inconsistent across studies, leading to varying classifications of TABP. Additionally, TABP is a multidimensional construct consisting of a variety of behaviors, some of which may be predictive of coronary heart disease, while others may be unrelated or even protective. It was therefore suggested that future research should break down the global TABP construct into individual components that can be examined separately, such as hostility (Dembroski & MacDougall, 1985;

Dembroski et al., 1985). This argument was further supported by later findings revealing that clinical assessments of hostility were related to coronary heart disease in the MRFIT sample, even though global TABP was unrelated (Dembroski, MacDougall, Costa, & Grandits, 1989; Shekelle et al., 1985). As a result, research gradually shifted to further examining hostility as a predictor of health risk rather than solely focusing on TABP.

Two meta-analyses, examining 44 and 45 studies respectively, found significant associations between anger/hostility and cardiovascular disease outcomes in both healthy and patient populations, such as a coronary heart disease, myocardial infarction, coronary artery disease, and mortality (Chida & Steptoe, 2009; Miller et al., 1996). More recent research has also established relationships between hostility and inflammatory markers of cardiovascular disease (Mwendwa et al., 2013), carotid atherosclerosis (Everson-Rose et al., 2006; Pollitt et al., 2005), metabolic syndrome (Goldbacher & Matthews, 2007; Nelson, Palmer, & Pedersen, 2004), cortisol diurnal profiles (Ranjit et al., 2009), cardiovascular disease mortality (Assari, 2016; Šmigelskas et al., 2017), and all-cause mortality (Klabbers et al., 2013). That being said, a significant portion of research reports mixed outcomes, with results differing based on sex (Chida & Steptoe, 2009), age (D'Antono, Moskowitz, & Nigam, 2013), race (Cooper & Waldstein, 2004; Finney et al., 2002), or the presence of other previously established risk factors, such as smoking or socioeconomic status (SES; Bunde & Suls, 2006; Skodova et al., 2008), suggesting the relationship between hostility and health outcomes may differ across populations.

In order to truly understand the association between hostility and health outcomes, researchers need to devote attention to the potential biological or psychological mechanisms driving this relationship. Indeed, four different models have been proposed

as an attempt to explain why differences in hostility impact the health of our bodies, particularly the cardiovascular system.

Models of Mechanisms Linking Hostility to Health

A relatively straightforward model, the health-behavior model states that hostile individuals are at a greater risk of later-life disease due to an increase in adverse health behaviors (Leiker & Hailey, 1988). Bunde and Suls (2013) conducted a meta-analysis, which reviewed 27 studies examining the relationships between scores on the Cook-Medley Hostility Scale and various disease risk factors. Significant associations with hostility scores, varying in magnitude, were discovered for the following: SES, alcohol consumption, smoking, body mass index, waist-to-hip ratio, insulin resistance, glucose, triglycerides, and lipid ratio. Further research revealed higher hostility scores to be associated with patterns of obesity, central adiposity, and insulin resistance (Niaura et al., 2000; Weider, Sexton, McLellarn, Connor, & Matarazzo, 1987). Interestingly, individuals high in cynicism or mistrust may be less likely to seek the advice of a medical professional or adhere to health recommendations, further increasing the risk of undetected or untreated disease (Smith & Christensen, 1992). In sum, this model suggests that improving health-related behaviors should be the key focus of intervention for preventing health risks in hostile individuals.

The psychophysiological reactivity model states that greater hostility is related to greater physiological responses to external stressors (Williams, Barefoot, and Shekelle, 1985), which in turn are related to greater chances of disease outcomes. Increased affective arousal (i.e., anger), aggressive behaviors, and vigilance to one's social surroundings produces exaggerated neuroendocrine and cardiovascular responses (Smith

& Christensen, 1992; Smith & Pope, 1990). Researchers have cleverly devised a way to examine this relationship by comparing hostility ratings to various physiological responses to laboratory-induced stress tasks. Curiously, this relationship has been non-significant when using cognitive, non-social stress tasks, such as mental arithmetic or computer games (Sallis et al., 1987; Smith & Houston, 1987; Suls & Wan, 1993). A meta-analysis revealed that a significant relationship is only detectable when the laboratory stress tasks are social in nature (Suls & Wan, 1993). For example, a laboratory word-identification task was only related to increased CVR when high hostile participants were being harassed by the researchers (Suarez & Williams, 1989). A separate laboratory study revealed greater blood pressure responses in high hostile participants during high-conflict interactions, but not during low-conflict interactions (Hardy & Smith, 1988). These findings are supported by the widely accepted definition of hostility as a psychological pre-disposition that is dependent upon interpersonal interaction (Smith & Christensen, 1992; Suls & Wan, 1993). This model has been the foundation of a vast literature examining the relationship between hostility and CVR (e.g., Carroll et al., 1997; Chida & Hamer, 2008; Christensen & Smith, 1993; Sallis et al., 1987; Smith & Gallo, 1999; see next section for a review of cardiovascular reactivity).

Alternatively, the psychosocial vulnerability model focuses on social context and how it contributes to stress and disease. Individuals with greater hostility also experience less social support, greater interpersonal distress, and greater isolation (e.g., Angerer et al., 2000; Hardy & Smith, 1988; Houston & Kelley, 1989; Smith et al., 1988). This is an important finding, especially when examined alongside the psychophysiological reactivity model. Not only do hostile individuals experience greater physiological

responses to stress, but they also experience a greater number of stressful interpersonal life events when compared to a low hostile person (Smith & Christensen, 1992).

Lastly, the transactional model uniquely combines both the psychophysiological reactivity and psychosocial vulnerability models to create a new perspective on possible mechanisms (Smith & Pope, 1990). This model suggests that hostile individuals are more vulnerable to health risks due to their propensity to have greater interpersonal conflict and less support, as well as heightened physiological responses to social stressors. Hostility is a trait that may exacerbate social conflict and subsequent poor social support through cynical views of others, angry episodes, and aggressive outbursts (Smith, 1994). As such, hostile persons not only respond to stressors with exaggerated physiology, but they also create additional stressors as a result of their difficult demeanors.

Out of all the models, the psychophysiological reactivity model is by far the most supported and accepted with regards to explaining the link between hostility and health (for reviews see Chida & Hamer, 2008; Smith, 1994). As such, the current study will focus primarily on examining the mechanisms posed by the psychophysiological reactivity model, particularly the relationships between hostility and CVR.

Cardiovascular Reactivity to Psychological Stress

The reactivity hypothesis, supported by nearly 40 years of research, states that risk for cardiovascular disease is increased in individuals with heightened cardiovascular responses to psychological stress (Obrist, 1981). This is contrary to what is observed in physical exercise, in which cardiovascular adjustments are deemed healthy and positive. The difference between a healthy and unhealthy cardiovascular response may be best determined by whether or not it is metabolically appropriate (Carroll, Phillips, &

Balanos, 2009b). For example, during exercise, increases in cardiovascular activity are equally matched by an increase in metabolic energy to meet the demands of muscle exertion (e.g., high blood pressure is necessary to perfuse working muscle groups). In this context, these two systems respond in a coordinated and balanced manner. However, during psychological stress, the response of the cardiovascular system is often far greater than the metabolic demand. In other words, the heart is working disproportionately harder in comparison to the rest of the body. Numerous studies have demonstrated cardiovascular responses to laboratory psychological stress tasks to be exaggerated relative to what would be expected given the minimal physical energy needed to complete these mental tasks (Balanos et al., 2010; Carroll, Turner, & Hellawell, 1986a; Carroll, Turner, & Prasad, 1986b; Carroll et al., 2009a; Lambiase et al., 2012; Sherwood, Allen, Obrist, & Langer, 1986; Turner & Carroll, 1985). Other studies demonstrate these same findings outside the laboratory, such as novice parachutists right before a jump (Stromme, Wikeby, Blix, & Ursin, 1978), aircraft pilots engaging in difficult flight maneuvers (Blix, Stromme, & Ursin, 1974), and individuals taking an exam or speaking in public (for review see Zanstra & Johnston, 2011). Further research supports that these exaggerated cardiovascular responses to psychological stress are predictive of poor cardiovascular health outcomes, such as future blood pressure status (Carroll et al., 1995; Carroll, Smith, Shipley, Steptoe, Brunner, & Marmot, 2001; Carroll, Ring, Hunt, Ford, & Macintyre, 2003), atherosclerosis (Barnett et al., 1997; Everson et al., 1997; Roemmich et al., 2011; Roemmich, Lobarinas, Joseph, Lambiase, & Archer, 2009), hypertension (Carroll et al., 2011; Chida & Steptoe, 2010; Markovitz, Raczynski, Wallace, Chettur, & Chesney, 1998), ventricular wall thickness (al'Absi et al., 2002; al' Absi et al., 2006),

increased left ventricular mass (Georgiades, Lemne, De Faire, Lindvall, & Fredriskson, 1997; Kapuku et al., 1999), and cardiovascular disease mortality (Carroll et al., 2012). These findings not only support the reactivity hypothesis (Obrist, 1981), but also allude to the assumption that, in contrast, low or blunted cardiovascular responses to psychological stress might be adaptive or even beneficial for health (Carroll et al., 2009a).

Interestingly, recent research suggests that low or blunted CVR to mental stress may be just as harmful, leading to a variety of adverse health and behavioral outcomes (Carroll et al., 2009a; Lovallo, 2011). Blunted CVR has been associated cross-sectionally and prospectively with depression, obesity, substance abuse, smoking, negative life events, low cognitive function, and disordered eating (e.g., Carroll, Phillips, Ring, Der, & Hunt, 2005; Carroll, Phillips, & Der; 2008; de Rooij, Schene, Phillips, & Roseboom, 2010; Ginty, Phillips, Der, Deary, & Carroll, 2011; Ginty, Phillips, Higgs, Heaney, & Carroll, 2012a; Ginty, Phillips, Roseboom, Carroll, & de Rooij, 2012b; Ginty et al., 2014; Phillips, 2011, Phillips, Roseboom, Carroll, & de Rooij, 2012; Phillips et al., 2013; Sorocco, Lovallo, Vincent, & Collins, 2006). This research suggests that low CVR to stress can lead to adverse health behaviors, which themselves are predictive of cardiovascular disease (e.g., Ginty et al., 2016; Carroll et al. 2017).

This evidence clearly demonstrates that mid-range cardiovascular responses to stress may be the most advantageous for health, which is similar to other genetically heritable traits (Lovallo, 2011; Hughes et al., 2018). Indeed, CVR profiles have been found to be genetically heritable (Wu, Snieder, & de Gues, 2010) and consistent over time (Dragomir, Gentile, Nolan, & D'Antono, 2014; Hassellund, Flaa, Sandvik, Kjeldsen,

& Rostrup, 2010; Sherwood et al., 1997). What is even more interesting is that CVR profiles have been found to be associated with a variety of stable personality traits. A meta-analysis of 729 studies revealed hostility, aggression, and Type A behavior to be associated with heightened CVR, whereas anxiety, neuroticism, and negative affect were associated with diminished CVR (Chida & Hamer, 2008). It has recently been proposed that CVR patterns and personality may be distinctly, yet equally influential in how individuals respond to stress in the environment, leading to both behavioral and physiological consequences (Hughes et al., 2018). In order to understand individual differences in responses to stress and subsequent health risks, researchers need to examine both physiology and personality.

Adaptation of Cardiovascular Reactivity

One of the proposed mechanisms for how exaggerated CVR to psychological stress relates to disease is the disruption of homeostasis within the body. Homeostasis is necessary for the healthy functioning of all organisms. It is best described as a state of dynamic equilibrium, which is constantly adjusted according to changes in the internal or external environment (Eisenstein, Eisenstein, & Smith, 2001). In other words, the body attempts to respond to these internal or external stimuli in ways that maintain the stability of internal functioning. Exaggerated CVR disrupts this balance as a result of the cardiovascular system responding in a way that is out of sync with the rest of the body (Carroll et al., 2009b). That being said, there are times when it is necessary for the body to briefly fall out of homeostasis in order to respond appropriately to significant stimuli. Responding to stressful life circumstances with an increase in cardiovascular functioning may actually be an evolutionarily-developed response, in which temporarily arousing the

body is necessary to confront or escape external threats (e.g., fight or flight; Hughes et al., 2018). However, stressful life circumstances rarely occur only once in a lifetime. It is important to examine how these physiological responses to stress change across multiple stress exposures. Organisms respond to repetitive stimuli with either habituation or sensitization. Habituation is defined as a decrease in the magnitude of response to a repeating stimulus, whereas sensitization is defined as an increase in the magnitude of response (Eisenstein et al., 2001). These patterns of adaptation over time may be important for further understanding the relationship between CVR and later-life disease. Unfortunately, the majority of prior research has only examined physiological responding to a single laboratory stress exposure (for review see Chida & Hamer, 2008). A recent review paper recommended that researchers begin to examine laboratory-induced stress at multiple time points in order to assess the possibility of CVR adaptation (Hughes et al., 2018).

Hughes and colleagues (2018) recommend that future research should consider examining the possibility of four patterns of CVR over time: persistent reactors, persistent blunters, habituators, and sensitizers. Similar to prior research, it is still proposed that some individuals will initially respond to a psychological stressor with either an exaggerated or blunted cardiovascular outcome. This is easily examined utilizing traditional protocols with one stress exposure. However, the importance of the CVR adaptation hypothesis rests on what happens to the cardiovascular response at a subsequent exposure. Persistent reactors are individuals who reveal an exaggerated response during first exposure and maintain this response at second exposure. Similarly, persistent blunters reveal a blunted response during first exposure as well as second

exposure. Unique to this theory are habituators and sensitizers. Habituators will reveal an initial exaggerated response, which will markedly decrease upon subsequent exposures. Alternatively, the sensitizer will reveal a markedly higher response at the second exposure compared to the first exposure. Sensitization is predicted to be the least adaptive response and most likely to lead to cardiovascular disease risk due to increased strain on the cardiovascular system. See Table 2.2 for a detailed review of each of the four adaptation typologies.

Table 2.2

Four Patterns of Cardiovascular Reactivity Adaptation

Time	Persistent Reactor	Persistent Blunter	Habituator	Sensitizer
First stress exposure	Substantial increase in cardiovascular response	Low or minimal cardiovascular response	Substantial increase in cardiovascular response	Low or minimal cardiovascular response
Second stress exposure	High response persists	Low response persists	Decreased response compared to first response	Increased response compared to first response

Note. These patterns of adaptation are drawn from the cardiovascular reactivity adaptation hypothesis posed by Hughes et al., 2018.

As mentioned previously, the habituation profile is theorized to be the most adaptive and beneficial for long-term health (Hughes et al., 2018). An initial increase in cardiovascular response to stress is considered healthy only if it is short-lasting, thus reducing long-term strain on the cardiovascular system. Habituation is the process of reducing the initial exaggerated response to a new stressor to more sustainable, mid-range responses at subsequent exposures. Previous research has not only confirmed the occurrence of CVR habituation in the laboratory (e.g., al'Absi et al., 1997; Frankish &

Linden, 1991; Kelsey et al., 1999; Schommer et al., 2003), but has also found it to be differentially related to a variety of psychosocial variables (e.g., Hughes et al., 2011; Johnson et al., 2012; Lü & Wang, 2017). Refer back to chapter one for a more thorough review of the habituation literature.

Study Hypotheses

Based on previous research (e.g., Barefoot et al., 1989; Hughes et al., 2011; Lahad et al., 1997; Lepore,1995; Lee & Hughes, 2014), it was hypothesized that higher levels of emotional, cognitive, and behavioral hostility would each be individually associated with an increase in CVR at two, separate testing visits. It was also hypothesized that higher levels of each hostility component would be associated with a decrease in cardiovascular response habituation measured across visits.

CHAPTER THREE

Materials and Methods

This chapter is currently under review as part of the following manuscript: Tyra, A.T., Brindle, R.C., Hughes, B.M., & Ginty, A.T. (under review). Cynical hostility relates to a lack of habituation of the cardiovascular response to repeated acute stress. *Psychophysiology*

Participants

Secondary data for the current study was previously obtained for the Pittsburgh Cold Study 3 (PCS3), a prospective viral challenge study conducted by researchers at the Laboratory for the Study of Stress, Immunity, and Disease at Carnegie Mellon University under the directorship of Sheldon Cohen, Ph.D. The purpose of the PCS3 was to experimentally expose healthy adults to a common cold virus and monitor their subsequent health symptoms and development of infection during a brief quarantine period, while also collecting a variety of psychological and health measurements. The PCS3 was uniquely valuable to the current study in that it also included measurements of CVR at two separate visits. Data collection took place from 2007 to 2011 and included 213 healthy volunteers drawn from the Pittsburgh, Pennsylvania area, ranging in ages from 18 to 55 (Mean = 30.1; SD = 10.9; 42.3% female, 66.7% Caucasian). Out of the 213 individuals who participated in PCS3, 15 were excluded from the current study due to missing physiological readings at either baseline or stress for either visit (Missing from Visit 1 (n = 7); missing from Visit 2 (n = 8)), which were needed to calculate main variables of interest (i.e., cardiovascular reactivity). In addition, preliminary analyses led to the removal of two statistical outliers (> 4 standard deviations above the mean for heart

rate reactivity and diastolic blood pressure reactivity at Visit 1). As such, a final total of 196 participants (Mean age = 29.9, SD = 10.8 years; 42.9% female, 67.3% Caucasian) were included in the current analyses. The PCS3 had the following exclusion criteria: previous nasal surgery, psychiatric hospitalization within the last 5 years, history of chronic illness or psychiatric disorder treated within one year of study enrollment, human immunodeficiency virus seropositivity, abnormal clinical profile (discovered through urinalysis, complete blood count, or blood chemistry analysis), regular medication regimen, pregnant or lactating, previous participation or planned enrollment in another study within the last 30 days, cold or flu-like illness within 30 days of quarantine, living with someone who has chronic obstructive pulmonary disease or an immunodeficiency, previous hospitalization due to flu-like illness, use of steroids or immunosuppressants within 3 months, or allergies to eggs/egg products. Eligible participants were given a physical examination to screen for good health. Volunteers who completed the entire study protocol received $1000 for their participation. The study was approved by both the Carnegie Mellon University and University of Pittsburgh Internal Review Boards. All data was electronically accessed from the Common Cold Project Website (www.commoncoldproject.com; grant number NCCIH AT006694).

Psychological Stress Protocol

Participants engaged in two laboratory visits, averaging about 48 (SD = 6.6) days apart (Visit 1: 2-4 weeks prior to virus inoculation and Visit 2: 4-6 weeks after the quarantine period). The individual stress sessions were conducted at the University of Pittsburgh and lasted approximately 2 ¼ hours. Participants attended the laboratory session between the hours of 3 p.m. and 9 p.m. Prior to arrival, participants were

requested to refrain from drinking alcohol for 48 hours, engaging in exercise and non-prescription medications for 24 hours, eating and drinking (except water) for 2 hours, and smoking for 1 hour prior to the session. A pre-session interview was conducted to ensure participants followed these instructions. The two laboratory visits included identical stress testing protocols.

Participants entered the experimental chamber and were equipped with an automated blood pressure cuff (Critikon Dynamap® Vital Signs Monitor 1846SX, GE Healthcare, U.S) to measure systolic and diastolic blood pressure (SBP and DBP) and heart rate (HR). Once situated in an upright chair, participants were asked to relax and sit quietly for 20 minutes. This was considered the baseline period. BP and HR were measured 4 times (every 120 seconds) during the last 6 minutes of this period. Immediately following the baseline period, participants engaged in the 15-minute stress protocol, which consisted of a modified version of the Trier Social Stress Test (TSST). Participants were first given 5 minutes to formulate a speech to defend themselves against a suspected transgression (either traffic violation or shoplifting, which were counterbalanced between the two laboratory visits). They were told their speech would be videotaped and evaluated. At the completion of the speech task (5 minutes of anticipatory preparation, 5 minutes to perform the speech), participants were then asked to engage in a 5-minute mental arithmetic task (i.e., subtracting the number 13 from either 1,022 or 1,039, depending on the visit) while also under evaluation. HR and BP were recorded every two minutes during the entire stress protocol. Nine measurements were taken; three during each of the stress phases (speech prep, speech delivery, mental arithmetic).

Cardiovascular Stress Reactivity

Baseline cardiovascular activity was defined as the average of the four readings during resting baseline. Stress cardiovascular activity was the average of the nine readings taken across the three stress tasks (speech preparation, speech, mental arithmetic). Previous research suggests that averaging cardiovascular responses across multiple stress tasks is a more reliable method of examining differences in stress reactivity at the individual level (e.g., Kamarck, Jennings, & Manuck, 1992). Baseline, stress, and CVR values were calculated separately for each laboratory visit (Visit 1 stress – Visit 1 baseline and Visit 2 stress – Visit 2 baseline). In total there were six CVR values calculated: HR reactivity Visit 1, HR reactivity Visit 2, SBP reactivity Visit 1, SBP reactivity Visit 2, DBP reactivity Visit 1, and DBP reactivity Visit 2.

Components of Hostility

A modified version of the Cook-Medley Hostility Scale (Cook & Medley, 1954; Barefoot et al., 1989) was utilized to examine the three main components of hostility. The emotional component of hostility (i.e., hostile affect) was a measurement of vulnerability to anger or annoyance of others. An example item for this component is “people often disappoint me”. The behavioral component (i.e., aggressive responding) was measured as aggression towards others. An example item for this component is “I would certainly enjoy beating a crook at his or her own game”. The cognitive component (i.e., cynicism) was a measurement of cynical or suspicious thoughts about others. An example item for this component includes “I think most people would lie to get ahead”. In total, there were 20-items on the scale consisting of dichotomous “true/false” response options, which can be separated into three subscale totals: nine items for Aggressive Responding, five items

for Hostile Affect, and six items for Cynicism. These subscales have been previously found to be more predictive of adverse health outcomes than the original 50-item Cook-Medley Hostility Scale taken as a whole (Barefoot et al., 1989). This questionnaire was administered immediately prior to the quarantine period and for the current sample revealed good overall internal consistency ($\alpha = 0.71$). Additionally, prior research has confirmed the overall scale to have good test-retest reliability (e.g., Barefoot, Dahlstrom, & Williams, 1983).

Covariates

Demographic information such as age, race/ethnicity (coded as 1 = white/Caucasian, 0 = non-white/Caucasian), and sex were collected via a self-report questionnaire completed prior to the quarantine period. Virus exposure was also assessed utilizing seroconversion, based on pre-challenge viral-specific Ab titer to post-challenge viral-specific Ab titer (0 = did not seroconvert, 1 = 4-fold increase detected).

Statistical Analyses

Repeated-measures ANOVAs, examining baseline and stress values, were carried out to examine if the stress tasks perturbed the cardiovascular system. Pearson's product-moment correlations were used to examine the individual relationships between CVR scores for each variable at Visit 1 and Visit 2. Subsequent repeated-measures ANOVAs examined if CVR for HR, SBP, and DBP differed significantly from Visit 1 to Visit 2.

Pearson's product-moment correlations were utilized to assess whether or not CVR scores at Visit 1 or Visit 2 related to each of the three subscale scores (Hostile Affect, Aggressive Responding, Cynicism). Reactivity change scores were calculated for

HR, SBP, and DBP by obtaining the difference between reactivity at Visit 1 and Visit 2 for each cardiovascular variable (i.e., habituation values). Additional Pearson's product-moment correlations were used to examine the relationships between change in reactivity across visits and each of the subscale scores.

Repeated-measures ANCOVAs were performed to further examine the hypothesized association between hostility and habituation of CVR. Following the analytical approach of Johnson and colleagues (2012), CVR (either HR, SBP, or DBP) at each visit was utilized to create a two-level within-subjects factor, denoted as Visit (reactivity at Visit 1 versus reactivity at Visit 2). The predictive role of hostility (subscale score) was examined as a covariate in each of the analyses. Separate analyses were performed for reactivity of HR, SBP, and DBP, resulting in three independent repeated-measures ANCOVAs for each of the three subscale scores (nine ANCOVAs in total). Nine subsequent repeated-measures ANCOVAs examined the relationship between hostility and habituation of CVR while also controlling for age, sex, race/ethnicity, virus exposure, and respective cardiovascular baseline levels. Greenhouse-Geisser correction values were reported for repeated-measures ANOVAs and ANCOVAs when appropriate (Greenhouse & Geisser, 1959; Jennings, 1987). Results were considered to be statistically significant if p values were $\leq .05$. SPSS version 25 (IBM Corp, USA) was utilized for statistical analyses.

CHAPTER FOUR

Results

This chapter is currently under review as part of the following manuscript: Tyra, A.T., Brindle, R.C., Hughes, B.M., & Ginty, A.T. (under review). Cynical hostility relates to a lack of habituation of the cardiovascular response to repeated acute stress. *Psychophysiology*

Cardiovascular Stress Reactivity

Repeated-measures ANOVAs examining the differences between mean cardiovascular variables at baseline and stress revealed that the TSST protocol significantly increased HR, $F(1, 195) = 382.80$, $p < .001$, $\eta^2 = .66$; SBP, $F(1, 195) = 449.10$, $p < .001$, $\eta^2 = .70$; and DBP, $F(1, 195) = 578.96$, $p < .001$, $\eta^2 = .75$ at Visit 1, as well as HR, $F(1, 195) = 314.88$, $p < .001$, $\eta^2 = .62$; SBP, $F(1, 195) = 411.68$, $p < .001$, $\eta^2 = .68$; and DBP, $F(1, 195) = 529.42$, $p < .001$, $\eta^2 = .73$ at Visit 2. Means and standard deviations are presented in Table 4.1.

Table 4.1

Mean (SD) Cardiovascular Activity During Baseline and Stress at Visit 1 and Visit 2

Protocol Phase	HR bpm	SBP mmHg	DBP mmHg
Baseline – Visit 1	69.27 (10.72)	114.60 (12.27)	67.45 (8.21)
Stress – Visit 1*	80.00 (12.50)	130.52 (14.47)	77.96 (8.17)
Baseline – Visit 2	71.35 (11.36)	116.94 (12.28)	68.62 (8.16)
Stress – Visit 2*	81.46 (12.82)	130.90 (15.33)	77.57 (7.83)

Note. * = stress significantly differed from respective baseline at the $p < .001$ for all cardiovascular variables.

Cardiovascular Stress Reactivity between Visit 1 and Visit 2

Significant correlations between CVR for all variables at Visit 1 and Visit 2 are depicted in Table 4.2. Repeated-measures ANOVAs revealed statistically significant differences in mean CVR across Visit 1 and Visit 2 for SBP ($p = .003$) and DBP ($p < .001$), but not for HR ($p = .145$). As depicted in Table 4.3, mean CVR decreased at Visit 2 compared to Visit 1, revealing physiological habituation.

Table 4.2

Correlations Between Cardiovascular Reactivity Measures at Visit 1 and Visit 2

Measure	1	2	3	4	5	6
1. Δ HR – Visit 1	___					
2. Δ SBP – Visit 1	.56**	___				
3. Δ DBP – Visit 1	.48**	.72**	___			
4. Δ HR – Visit 2	.71**	.38**	.37**	___		
5. Δ SBP – Visit 2	.49**	.58**	.51**	.58**	___	
6. Δ DBP – Visit 2	.43**	.46**	.53**	.43**	.68**	___

Note. ** $p < 0.01$ level (2-tailed); Δ = difference between stress and baseline (i.e., reactivity).

Relationships between Hostility Subscales

Correlations between the emotional, behavioral, and cognitive subscales (Hostile Affect, Aggressive Responding, and Cynicism) are presented in Table 4.4. The relationships between each of the subscales are moderate, revealing some independence between the measured constructs. These findings are supported by prior research (Barefoot, 1992; Janicki-Deverts et al., 2010).

Table 4.3

Mean Cardiovascular Reactivity at Visit 1 and Visit 2

	Visit 1				Visit 2						
Measure	Mean	SD	Min	Max	Mean	SD	Min	Max	*F*	*p*	Partial η^2
Δ HR	10.73	7.68	-4.64	38.81	10.11	7.98	-9.50	39.92	2.14	.145	.011
Δ SBP	15.92	10.52	-13.47	41.81	13.97	9.64	-10.75	46.67	8.78	.003*	.043
Δ DBP	10.52	6.12	-6.94	25.36	8.95	5.44	-8.19	30.39	15.11	.000*	.072

Note. * = significance at the $p \leq 0.05$ level; Δ = difference between stress and baseline (i.e., reactivity).

Table 4.4

Relationships Between Cook-Medley Hostility Subscale Scores

Measure	1	2	3
1. Cynicism	___		
2. Hostile Affect	.40**	___	
3. Aggressive Responding	.35**	.31**	___

Note. ** $p < 0.01$ level (2-tailed).

Cardiovascular Stress Reactivity Habituation and Hostility

Correlation analyses demonstrated a statistically significant, negative relationship between cynicism and all CVR variables at Visit 1 but not Visit 2, as well as change in SBP and HR reactivity across visits. Hostile affect and aggressive responding were not statistically significantly related to CVR at either visit and were also not related to change in CVR across visits. The correlations between each of the hostility subscales with CVR, as well as change in CVR are depicted in Table 4.5.

Repeated measures ANCOVAs demonstrated significant visit–by–cynicism subscale interactions for SBP, $F(1, 194) = 13.04$, $p < .001$, $\eta^2 = .063$ and HR, $F(1, 194) = 7.14$, $p = .008$, $\eta^2 = .036$, but not for DBP ($p = .054$). When controlling for respective cardiovascular baseline levels at Visit 1, as well as age, sex, race/ethnicity, and virus exposure, results remained significant for SBP, $F(1, 188) = 6.80$, $p = .010$, $\eta^2 = .035$ as well as HR, $F(1, 188) = 5.24$, $p = .023$, $\eta^2 = .027$. No significant visit-by-hostility interactions were found for the hostile affect or aggressive responding subscales in initial or fully adjusted repeated measures ANCOVAs.

Graphic illustrations of the interactions between the cynicism subscale and SBP/HR reactivity at both visits are presented in Figures 4.1a and 4.1b respectively. For the figures, participants are divided into lowest and highest tertiles of the cynicism scores (these figures are for illustrative purposes only). As revealed by the figures, participants with lower cynicism display enhanced habituation of cardiovascular reactivity across Visit 1 and Visit 2 compared to those with greater cynicism.

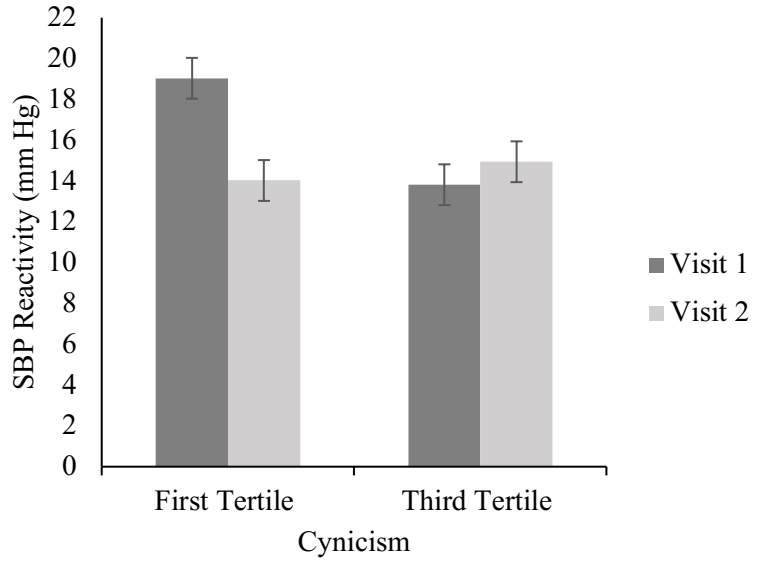
Table 4.5

Correlations Between Hostility Scores and Cardiovascular Reactivity at Visit 1 and Visit 2 and Change in Reactivity

	Visit 1			Visit 2			Δ Reactivity		
Measure	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP
Cynicism	-.16*	-.22**	-.16*	-.01	.00	-.04	-.19**	-.25**	-.14
Hostile Affect	-.11	-.14	-.07	-.06	-.04	-.08	-.06	-.11	.01
Aggressive Responding	-.06	-.11	-.03	-.13	-.13	-.08	.09	.02	.04

Note. * = Significance at the $p \leq 0.05$ (2-tailed); ** = Significant at the $p < 0.01$(2-tailed); Δ = difference between reactivity at Visit 1 and Visit 2 (i.e., cardiovascular reactivity habituation).

a)



b)

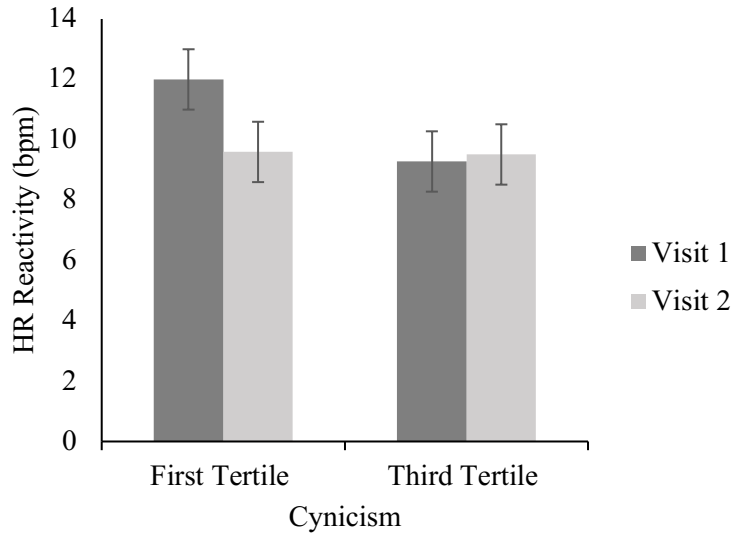


Figure 4.1. Interactions Between Cynicism and Cardiovascular Reactivity at Visit 1 and Visit 2.
(a) Systolic blood pressure (SBP) reactivity in mm Hg and (b) heart rate (HR) reactivity in bpm at Visit 1 and Visit 2 for participants in the first and third tertiles of cynicism subscale scores. Error bars represent standard error of the mean.

CHAPTER FIVE

Discussion

This chapter is currently under review as part of the following manuscript: Tyra, A.T., Brindle, R.C., Hughes, B.M., & Ginty, A.T. (under review). Cynical hostility relates to a lack of habituation of the cardiovascular response to repeated acute stress. *Psychophysiology*

The present study examined the association between hostility and CVR to acute psychological stress at multiple time points. Higher levels of cynicism, the cognitive component of hostility, were related to less reactivity across all variables at Visit 1 and less habituation of SBP and HR reactivity across both Visit 1 and Visit 2. In contrast, lower scores on the cynicism subscale were associated with greater CVR across all variables at Visit 1, as well as reductions in SBP and HR reactivity at Visit 2 (i.e., greater CVR habituation). These findings remained significant after controlling for confounding variables (age, race/ethnicity, sex, virus exposure, and baseline levels). No significant relationships were found between the emotional (hostile affect subscale) or behavioral (aggressive responding subscale) components of hostility and CVR or habituation.

The outcomes of the current study reveal the importance of separately examining the emotional, cognitive, and behavioral components of the hostility construct. It has been suggested that possible behavioral risk factors for disease may differ depending on the type of disease examined (Siegman, 1994). As such, each component of hostility may be predictive of different disease outcomes and should be examined individually. While some research has found cynicism to be related to a variety of adverse health outcomes such as inflammation (Janicki-Deverts et al., 2010) or all-cause mortality (Kriegbaum,

Lund, Schmidt, Rod, & Christensen, 2019), the majority of previous research has specifically demonstrated a relationship between higher levels of cynicism and increased risk of cardiovascular disease (e.g., Arthur, 1998; Assari, 2016; Chaput et al., 2002; Julkunen et al., 1994; Šmigelskas et al., 2017; Wong et al., 2014).

Interestingly, the emotional and behavioral components of hostility were not found to be related to CVR or habituation. It is possible the lack of findings could be a result of the type of hostility assessment utilized. Prior research using other hostility self-report questionnaires found affective arousal to be associated with CVR (Suarez & Williams, 1989), whereas standard interview assessments of hostile behaviors have been found to be correlated with severity of cardiovascular disease (Barefoot, 1992). Prior research has questioned the choice of using the Cook-Medley Hostility Scale to examine constructs other than cynicism (Barefoot & Lipkus, 1994). This is due to the cynicism subscale being the most consistently replicable construct tapped by the Cook-Medley Hostility Scale (Greenglass & Julkunen, 1989; Han et al., 1995). Other possible explanations may be potential physiological differences behind the experience (internal emotions and cognitive processes) and expression (external behaviors) of hostility (Smith, 1994). Lastly, it is quite possible that the lack of findings was due to a true lack of relationship between the emotional and behavioral components of hostility and cardiovascular outcomes. As mentioned previously, it has been predicted that the different components may be predictive of different types of diseases (Siegman, 1994). Future research should aim to examine the relationship between the hostility components and CVR utilizing behavioral measures of hostility rather than questionnaires.

The negative relationship found between the cognitive component of hostility and CVR during Visit 1 does not support our first hypothesis, in which it was predicted that greater self-reported hostility would be related to greater CVR. Additionally, these results contradict the majority of previous research (for review see: Chida & Hamer, 2008). However, the current findings are in accordance with a study examining approximately 1,000 male public servants showing an association between higher levels of cynical hostility (i.e., cynicism) and lower SBP reactivity (Carroll et al., 1997). This negative relationship may indicate that hostility is also related to cardiovascular disease through indirect pathways. While it has been proposed that heightened CVR is directly related to long-term cardiovascular health outcomes, evidence shows that low or blunted CVR is also related to poor cardiovascular health outcomes through indirect routes, such as obesity and smoking (Carroll et al., 2009a; Ginty et al., 2016; Phillips, Ginty, & Hughes, 2013). Interestingly, higher levels of hostility have been associated with similar adverse health behaviors, such as increased smoking, increased alcohol use, greater caloric intake, and lack of activity (Bunde & Suls, 2006). It is possible that higher hostility may thus also be indirectly linked to cardiovascular disease through poor health behaviors that often accompany lower CVR. Additionally, it has been proposed that an initial heightened response to stress may be beneficial in that it allows for necessary physiological changes, such as the fight or flight response (Hughes et al., 2018). Individuals with higher hostility reveal less of this initial response and as a result, may be unable to engage such beneficial physiological changes. Future research should aim to examine the longitudinal relationships between hostility, CVR, and cardiovascular disease.

The current findings (i.e., cynicism related to lack of habituation) partially support our second hypothesis, in which it was hypothesized that higher levels of hostility would be associated with less CVR habituation. This is consistent with other studies examining personality traits and habituation, in which higher levels of "negative" traits were found to be related to diminished habituation (e.g., Hughes et al., 2011; Johnson et al., 2012). According to the CVR habituation hypothesis posed by Hughes and colleagues (2018), habituation may be the most beneficial adaptation profile with regards to long-term health, consisting of a necessarily heightened immediate response to stress, followed by a reduced response upon subsequent exposures. The results of the current study add support to this theory, such that the cardiovascular habituation pattern revealed with lower levels of hostility may be considered a possible physiological mediator in the established relationship between less hostility and better cardiovascular health outcomes (Arthur, 1998; Assari, 2016; Chaput et al., 2002; Julkunen et al., 1994; Šmigelskas et al., 2017; Wong et al., 2014). No apparent adaptation pattern was revealed with higher levels of hostility. It is plausible that this lack of an ability to adapt to subsequent stressors leads to increased strain on the cardiovascular system over time and may be a key factor in why hostile individuals are predicted to have later life cardiovascular health risks (e.g., Kriegbaum et al., 2019).

The results of the present study are at odds with a previous study examining hostility and CVR habituation. The previous study demonstrated high-hostile university students to have higher initial CVR and also significantly greater DBP habituation to acute psychological stress (Hughes, 2007). Unlike the social stress tasks utilized in the current study, the stress task utilized in the previous study was a 10-minute, asocial

computer task (Hughes, 2007). When examining the relationship between hostility and physiological stress responses, researchers have emphasized the need to utilize laboratory stress tasks that are social in nature (Suls & Wan, 1993). Future research should examine the relationship between hostility and CVR using both social and asocial tasks. Additionally, in the previous study, habituation was measured during a single laboratory session in which the task was given twice, whereas the current study measured habituation across two separate laboratory sessions, in which the task was given once during each session. It has yet to be established whether or not differences in the evaluation of habituation will lead to different outcomes. Future research should examine differences between habituation patterns in a single session consisting of multiple stress exposures versus multiple, separate sessions consisting of a single stress exposure in each session (Hughes et al., 2018). Lastly, the previous study conducted separate median-splits for males and females, resulting in a high-hostility and low-hostility group for each gender. Given the current study examined hostility as a continuous measure, it is possible different outcomes were obtained due to different operationalizations of hostility. Future research should examine whether different methods of assessing the hostility construct reveal different relationships to CVR and habituation.

The outcomes of this study support Hughes and colleagues (2018) suggestion for extending CVR laboratory stress protocols to include multiple exposures of the same stress task. Traditional protocols including only a single stressor may be unable to accurately identify the reactivity profile of a participant. For example, if the current study only examined reactivity at Visit 1, the relationship between lower hostility and exaggerated CVR would have been misidentified as a persistent, heightened reaction to

psychological stress and further classified as a risk factor for later disease. However, examining CVR from Visit 1 to Visit 2 reveals an entirely different type of profile, demonstrating lower hostility to be related to greater CVR habituation, which has been identified as the most optimal for protecting against long-term health risks (Hughes et al., 2018). As such, examining CVR across multiple exposures to psychological stress allows researchers to evaluate the consistency and changes of reactivity responses over time, thus providing a more comprehensive perspective.

This research is not without limitations. First, the study was cross-sectional and prevents the determination of causality. While it is possible that greater hostility may induce less CVR as well as less habituation across multiple stress exposures, such determination of causality is not definitive in observational research due to possible unmeasured or poorly measured variables confounding the results (Christenfeld, Sloan, Carroll, & Greenland, 2004). That being said, the present study demonstrated significant results after adjusting for a variety of potential important confounders (age, race/ethnicity, sex, virus exposure, baseline cardiovascular activity). Second, the measure of hostility was self-report and only administered once, prior to the first laboratory stress testing visit. As a result, potential changes in reported hostility over time were not obtained or controlled. However, research on hostility has found it to be a relatively stable trait (Han et al., 1995; Woodall & Matthews, 1993). Third, the observed associations between hostility and CVR were relatively small, as were the observed effect sizes after controlling for potential confounders. Due to secondary data analysis, we were unable to conduct appropriate *a priori* power analyses. However, an examination of sample sizes in previous similar literature reveals that the current study was likely

sufficiently powered (Hughes, 2007; Hughes et al., 2011; Johnson et al., 2012; Lee & Hughes, 2014). Lastly, it may have been helpful to have acquired a more comprehensive profile of reactivity rather than simply focusing on BP and HR. Prior research has also established a relationship between hostility and inflammation (Hackett, Lazzarino, Carvalho, Hamer, & Steptoe, 2015), salivary cortisol (Brydon et al., 2010) total peripheral resistance (Girdler et al., 1997; Why & Johnston, 2008) as well as stroke volume and cardiac output (Bongard, Al'Absi, & Lovallo, 1998).

Future research should continue to examine the proposed relationships and underlying mechanisms between hostility and cardiovascular disease outlined in this study. Hostility is proposed to be related to cardiovascular disease through individual differences in cardiovascular responses to psychological stress, which may further be influenced by a variety of external factors (e.g., other dispositional traits, environmental and situational contexts; see Figure 5.1). The results of the current study suggest a need for the continued separate examination of each of the three hostility components and how they differentially relate to health outcomes. Additionally, it may be beneficial to examine these hostility components utilizing a variety of assessment methods, such as other versions of self-report questionnaires, standard interviews, or behavioral assessments.

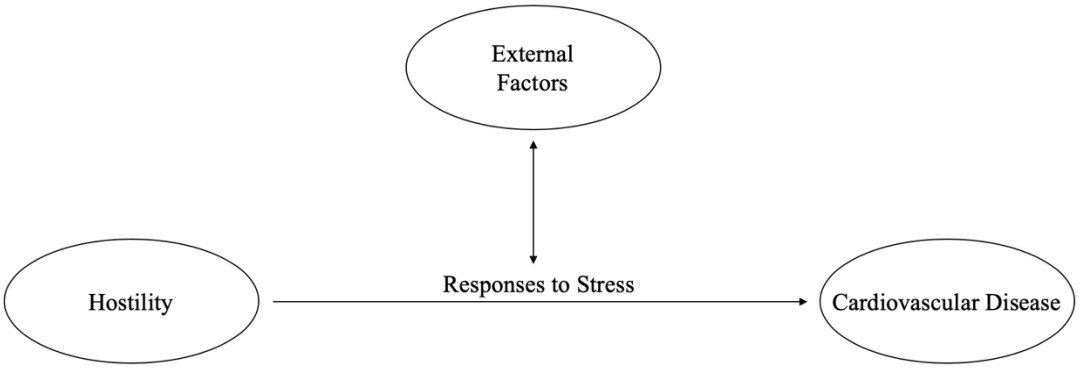


Figure 5.1. Proposed Model of the Relationship between Hostility and Cardiovascular Disease.

The present study also highlights the importance of future studies using extended laboratory stress protocols to assess changes in CVR across multiple stress exposures. For example, traditional protocols consisting of only one stress exposure will be unable to differentiate between persistent reactors and habituators (Hughes et al., 2018), resulting in vastly different interpretations. The understanding of CVR adaptation may provide further insight into how individual differences in responses to stress contribute to disease risk. It is also suggested that future research should examine the relationships between hostility and other reactivity variables (e.g., inflammation, cortisol, cardiac output) in order to build a more comprehensive narrative. In addition, it may be useful to examine how other possible external factors may be influencing the relationship between hostility and CVR, such as state anger or social support (e.g., Lepore, 1995; Why & Johnson, 2008). Lastly, this area of research is in need of a longitudinal design, in which the relationships between hostility, CVR, and cardiovascular disease are observed over time. For example, future longitudinal studies might examine the relationship between hostility and progression of carotid artery thickness or risk of myocardial infarction.

In summary, this study demonstrated that the relationship between higher levels of the cognitive component of hostility (i.e., cynicism) and poor cardiovascular health outcomes may potentially be explained by an inability to habituate cardiovascular responses to subsequent acute psychological stress exposures. Additionally, it is proposed that the relationship between hostility and CVR may be dependent upon other environmental and dispositional characteristics, revealing exaggerated CVR under some conditions and blunted CVR under others. However, both exaggerated and blunted CVR, when combined with a lack of ability to adapt these responses, are deleterious for health.

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