A PROSPECTIVE EXAMINATION OF URINARY STRESS HORMONES AND POSTTRAUMATIC STRESS DISORDER SYMPTOMS FROM MOTOR VEHICLE ACCIDENT TO POST-TRAUMA RECOVERY

A dissertation submitted to Kent State University in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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December, 2007
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ACKNOWLEDGMENTS

I would like to extend my sincere and genuine thanks to Dr. Douglas Delahanty and Dr. Kristin Mickelson for their wisdom, guidance, and patience. I would also like to thank the rest of my committee members for their added support.

Without question I extend a gigantic thanks to my husband, daughter, family, and friends all of whom slaved through this project with me. I thank you for your love and support.
CHAPTER I

INTRODUCTION

Approximately 69% of Americans have experienced a traumatic event in their lifetime (Kessler et al., 2005); however, incidence rates of PTSD in the general population range from 7-10% (Kessler et al., 2005), suggesting that meeting diagnostic criteria for PTSD is likely contingent upon the presence of a combination of variables rather than trauma exposure alone. Physiological responses to trauma may contribute considerably to the onset and progression of post-traumatic symptoms. A significant proportion of trauma survivors with PTSD have exhibited biological alterations contrary to that of similarly traumatized individuals that do not meet PTSD criteria (for a review see Rasmusson, Vythilingam, & Morgan III, 2003), suggesting that biological correlates and/or predictors may influence individual risk for PTSD. However, very little is known about the interaction between biological alterations and psychological symptoms associated with PTSD, their onset, and their progression over time. Thus, the purpose of the present study was to examine the relationships between and among physiological and psychological responses to trauma over the course of trauma recovery beginning shortly after a motor vehicle accident (MVA) and continuing through 1 year of post-trauma recovery.
PTSD Symptoms and Diagnostic Criteria

According to the DSM-IV (American Psychiatric Association, 1994), to meet diagnostic criteria for PTSD, an individual must first have experienced or been exposed to a traumatic or life-threatening event that elicited responses of intense fear, helplessness, or horror (Criterion A). Furthermore, a diagnosis requires the presence of 3 different types of symptoms including (1) re-experiencing of the trauma (e.g. nightmares, intrusive thoughts; Criterion B), (2) avoidance and emotional numbing (e.g. avoiding reminders of an accident, feeling withdrawn; Criterion C), and (3) increased arousal (e.g. difficulty sleeping, hypervigilance, exaggerated startle response; Criterion D). One intrusive symptom, three avoidant symptoms, and two hyperarousal symptoms must be present, persist for at least one month (Criterion E), and must cause clinically significant distress or disturb daily functioning (Criterion F) to meet diagnosis (DSM-IV; American Psychiatric Association, 1994). Symptoms that persist for at least one month but less than 3 months are diagnosed as acute PTSD, and symptoms lasting 3 months or more are considered chronic PTSD (DSM-IV; American Psychiatric Association, 1994).

Peri-traumatic and Acute Psychological Responses to Trauma

PTSD has been described as a multistage disorder, in which the onset and temporal progression of symptoms varies with each traumatized individual (McFarlane, 2000). Most commonly, symptoms of posttraumatic stress peak immediately post-trauma in both frequency and intensity, and decline with time (Blanchard & Hickling, 1997; Cardena & Spiegel, 1993; Feinstein, 1989, Freinkel, Koopman, & Spiegal, 1994; Hillman, 1981; North et al., 1989; Shalev et al., 1998; Sloan, 1988). However, symptoms
can also increase with the passage of time (Bremner et al., 1996; McFarlane, 2000; Shalev et al., 1996) or consistently fluctuate throughout recovery (McFarlane, 2000). Additionally, pre-trauma risk factors and resiliency characteristics (sex, race, trauma history), peri-traumatic experiences (perceived life threat and dissociation, injury severity), and post-trauma responses (coping, seeking social support) all contribute to the course of post-traumatic symptomatology and subsequent diagnosis of PTSD (Blanchard et al., 1995; Delahanty, Raimonde, Spoonster, & Cullado, 2003; Hetz et al., 1996; Ozer, Best, Lipsey, & Weiss, 2003; Resnick, Yehuda, Pitman, & Foy, 1995). Thus, understanding the course and critical periods at which PTSS emerge and progress involves the examination of both immediate and chronic responses to trauma.

Research has demonstrated that peri-traumatic and acute psychological responses to a traumatic event may be predictive of subsequent PTSD diagnosis (Koopman, Classen, & Spiegel, 1994; McFarlane, 1989; Rothbaum et al., 1992). Birmes and colleagues (2003) examined 35 male and female assault victims and found that self-reported peri-traumatic dissociation and acute stress symptoms assessed within 24 hours of an assault were correlated with subsequent PTSS and PTSD diagnoses at the 3-month follow-up. Initial self-reported (1-8 days post-accident) peritraumatic dissociation symptoms, perceived threat, anger, and worry were significantly correlated with PTSD diagnosis and severity of symptoms 3- and 12-months post-MVA in 967 MVA victims (Ehlers et al., 1988). Similarly, Koren and colleagues (1999) found that MVA survivors who self-reported more severe PTSS 1 week post-MVA were more likely to meet PTSD criteria 1 year post-accident, compared to those with less severe symptomatology. In
addition, intrusive thoughts and avoidant behaviors one week after a severe burn (Difede & Barocas, 1999), physical injury (Shalev et al., 1996), and orthopedic trauma (Feinstein & Dolan, 1991) predicted subsequent PTSD diagnoses at 6 months post-trauma. Furthermore, early symptoms of hyperarousal, obtained on average 11.5 ± 9.5 days following admission, predicted PTSD severity at follow-up among severely injured trauma survivors (Mellman et al., 2001). These studies suggest that initial psychological responses, during or within the immediate aftermath of their trauma, are crucial to the onset, course, and development of PTSS.

In contrast, a study of 200 MVA survivors found that psychological distress experienced the day after an MVA did not predict PTSD diagnosis six months post-accident (McFarlane et al., 1997). Furthermore, participants meeting PTSD diagnostic criteria (n=36) at the six-month follow up did not differ from controls on self-reports of intrusive thoughts, avoidance, anxiety, dissociation, hyperarousal or flashbacks the day after the accident. In addition, Shalev and colleagues (1997) found that reports of intrusion, avoidance, and hyperarousal one-week post-trauma were poor predictors of subsequent PTSD among terrorist attack survivors. These findings question the extent to which acute psychological responses to trauma are predictive of subsequent PTSD diagnosis. Given that different symptom clusters may afford differing degrees of risk for the development and/or maintenance of more persistent PTSD, research has begun to focus on the development of individual symptom clusters over time.
Several theories have posited mechanisms through which the various symptom clusters emerge, interact, and remit following trauma exposure. Initially, Horowitz (1979; 1986) proposed that symptoms of intrusion and re-experiencing are immediate responses to trauma exposure, and avoidance symptoms develop later as a defensive coping mechanism used to pacify unwanted recollections of a trauma. Furthermore, consistently re-experiencing a particular trauma perpetuates avoidance, thereby sustaining subsequent trauma symptoms (Horowitz, 1986; Foa et al., 1995). In support of this theory, McFarlane (1992) found that firefighters’ self-reports of intrusion symptoms were directly related to self-reported symptoms of avoidance, but that avoidance was not related to brushfire trauma exposure, suggesting that avoidance was a defensive coping mechanism used to manage trauma-related intrusive thoughts. Furthermore, Solomon (1998) demonstrated that symptoms of intrusion emerged first within 2 years following combat-related stress and avoidance symptoms subsequently developed.

Riggs (1993) suggested that intrusion and avoidance symptoms might perpetuate PTSS over time, such that avoidance symptoms may not allow trauma survivors to emotionally process their trauma experience, thereby sustaining PTSD symptomatology. Furthermore, the persistent and unwanted nature of intrusive symptoms may intensify already existing feelings of helplessness and hopelessness, thus promoting the chronicity of PTSS (Foa & Riggs, 1993).

An alternative theory suggests that hyperarousal symptoms precede avoidance and intrusion symptoms (Bremner et al., 1996). In a longitudinal study of 61 Vietnam
veterans, hyperarousal symptoms (i.e. increased startle response and being on guard) were most commonly reported as the first PTSD symptom experienced following combat exposure, followed by symptoms of avoidance and then intrusion (Bremner et al., 1996). The long intervals between assessments (2 years) as well as the extended duration of this study (20 years) may have accounted for results that contrast Horowitz’s theory. Additionally, symptoms of increased startle response and being on guard are not uncommon in combat veterans and may have been an artifact of military training and survival (Bremner et al., 1996). Similarly, Southwick and colleagues (1993) examined Desert Storm veterans and found that hyperarousal symptoms were the first and most severe symptoms experienced post-combat, followed by intrusions and avoidance. This may further suggest that the type of trauma or specific characteristics of combat-exposed populations may demonstrate different relationships between post-trauma symptoms. Contributing greatly to these inconsistent findings is the lack of prospective studies examining psychological responses to trauma over time; cross-sectional designs are limited in their ability to make inferences about causal relationships between symptom clusters and make it difficult to compare and identify complex and changing symptom patterns.

To date, only a few studies have examined the reciprocal relationship between symptom clusters over time among adult trauma survivors. Schell, Marshall, and Jaycox (2004) were the first to examine the progression of PTSD symptoms within a sample of predominately Hispanic, adult survivors of community violence ranging in age from 18-35. Participants were assessed for PTSS shortly after hospital admission, and again at 3
and 12 months post-trauma. Assessments of PTSS included self-reported accounts of PTSS symptom severity and the 17-item PTSD Checklist (PCL; Civilian Version; Weathers, Litz, Herman, Huska, & Keane, 1993) on which participants were instructed to indicate the degree to which they had been bothered by each symptom. Using a cross-lagged panel design (Kessler & Greenberg, 1981; Mayer & Carol, 1987) they examined the extent to which each symptom predicted subsequent changes in other symptoms over time. Results revealed that all four PTSD symptom clusters (i.e. intrusion, avoidance, hyperarousal, and emotional numbing) weakened with time, with intrusive symptoms declining at the fastest rate. Hyperarousal had the most direct impact on subsequent symptom severity across both time intervals compared to the other symptom clusters. In other words, individuals with the most severe hyperarousal symptoms at the first time point were least likely to demonstrate a decline in PTSD symptomatology over time.

Marshall and colleagues (2006) conducted a replication of the Schell et al., (2004) study in which change in self-reported symptom clusters, using the Posttraumatic Stress Diagnostic Scale (PDS; Foa, 1995), was examined over time in 264, predominately African-American, individuals that had undergone orofacial injury. This study replicated Schell et al.’s (2004) findings, reported above, even after restricting their sample to individuals that had endorsed experiencing feelings of intense fear, helplessness, or horror (Criterion A) in relation to their injury and changing their study design to include frequency of symptoms rather than intensity.

O’Donnell and colleagues (2007) also examined change in PTSS over a year among 363 individuals that had experienced either an MVA (74.9%), workplace injury
(12.4%), or assault (2.9%). Assessment of PTSS occurred prior to hospital discharge, and 3 and 12 months post-trauma using the CAPS. Symptom trajectories were analyzed using curvilinear growth modeling and yielded results indicating that individuals diagnosed with PTSD at the one-year follow-up had significantly higher intrusion, avoidance, and hyperarousal symptoms at the in-hospital assessment that increased with time compared to individuals not subsequently diagnosed with PTSD.

In summary, research examining both acute and chronic psychological responses to trauma has produced mixed results; with some studies finding that early responses to trauma are predictive of PTSS and diagnosis and others finding that initial responses to trauma are poor indicators of symptom development or PTSD diagnosis. Similarly, research examining the development of PTSS over time has also produced mixed results. Several studies have suggested that intrusive symptoms may promote subsequent avoidance symptoms that, over time, continue to coexist through a cyclical, reciprocal pattern. Other studies have suggested that symptoms of hyperarousal may not only precede but may promote symptoms of intrusion and avoidance. Inconsistent findings concerning the interrelationship between PTSD symptom clusters, symptom expression and progression may be attributed to a number of variables. In addition to a lack of prospective studies designed to investigate the change and interrelationship between psychological responses over time, there is also a lack studies designed to examine physiological responses over time. As research has continuously suggested, how an individual physiologically responds to their trauma both in the immediate aftermath and over time may not only be a product of experiencing a life-threatening trauma but may
also contribute to and/or predict subsequent PTSD or psychopathology in general. Thus, research that fails to provide a more prospective examination of the interactive relationship between psychological and physiological responses to trauma, among other concomitant variables, is likely to yield results that only partially explain PTSD symptom cluster onset and course.

**Physiology of PTSD**

The majority of studies examining physiological responses to trauma have focused on the role of two primary stress pathways (Yehuda & Harvery, 1997), the sympathetic nervous system (SNS) and the hypothalamic pituitary adrenal (HPA) axis (Stratakis & Chrousos, 1995). Research has suggested that the SNS and the HPA axis may contribute to the onset, progression, and maintenance of post-traumatic stress symptoms and subsequent PTSD diagnosis. Specifically, research into the biology of PTSD has focused on alterations in stress hormone levels (i.e. catecholamines and cortisol) and their association with PTSD symptoms and diagnoses (Delahanty, Raimonde, & Spoonster, 2000; McFarlane, Atchison, & Yehuda, 1997).

**Sympathetic Nervous System (SNS) Response to Stress**

Under conditions of stress, activation of the SNS results in the release of catecholamines (epinephrine from the adrenal glands and norepinephrine from sympathetic neurons: Chrousos & Gold, 1992). Individually and collectively, these catecholamines prepare the body for action (“fight” or “flight”) by mobilizing a number of essential physiological responses and suppressing superfluous functions. Specifically,
epinephrine stimulates the metabolic system to increase glycolysis and blood glucagon concentrations and decrease insulin secretion. This allows stored nutrients in the muscles to be readily available to provide energy for strenuous activity, such as fighting or running away (Chrousos & Gold, 1992). Epinephrine also elevates heart rate and increases cardiac output (Chrousos & Gold, 1992). In conjunction with epinephrine, norepinephrine works to regulate blood pressure through the vasoconstriction of arteries and dilation of skeletal and blood vessels (Chrousos & Gold, 1992). Norepinephrine also increases arousal, vigilance, and anxiety, which prepare the body for action (Chrousos & Gold, 1992). Catecholamines also influence memory such that norepinephrine is instrumental in memory formation, and moderate levels of epinephrine are memory enhancing while extreme (low or high) amounts impair memory (Parsons & Gold, 1992).

*Urinary catecholamine alterations associated with PTSD.* Research examining catecholamine levels in PTSD has produced mixed results. Although some studies have indicated that individuals with PTSD generally do not differ from trauma survivors without PTSD in levels of plasma catecholamines (Blanchard et al., 1991; McFall, Murburg & Ko, 1990; Murburg, McFall, Lewis & Veith, 1995), research has consistently found that individuals with PTSD have higher 24-hr urinary catecholamines than similarly traumatized individuals who did not develop PTSD (Friedman, 1991; Lemieux & Coe, 1995; Kosten et al., 1987; Southwick et al., 1995; Yehuda et al., 1992). This discrepancy is likely due to the differing time span represented by urine versus plasma measurements. Plasma measurements typically are assessed via a single needle stick
(blood sample), that represents an isolated point in time. Furthermore, the distress associated with drawing blood may result in short-term elevations in catecholamine levels. In contrast, urinary measurements obtained over a 24-hour period encompass a longer time span and include the entire diurnal cycle (Baum & Grunberg, 1995). Significant differences in urinary catecholamine excretion suggest a persistent elevation of sympathetic hormones in PTSD rather than the acute differences suggested by plasma levels.

The majority of research examining catecholamine levels in individuals with PTSD has focused on long-term or chronic PTSD following combat-related traumas. These studies have consistently demonstrated SNS hyperarousal under basal and experimental conditions of stress (for a review see Southwick et al., 1995). Elevated urinary epinephrine and norepinephrine have been characteristic of hospitalized Vietnam veterans compared to other psychiatric groups (Kosten, Mason, Giller, Harkness, & Ostroff, 1987; Yehuda, Southwick, Ma, Giller, & Mason, 1992b). Moreover, trauma survivors with PTSD have demonstrated greater SNS arousal when exposed to both trauma reminders (Blanchard, Kolb, & Gerardi, 1986; Blanchard et al., 1996; Pitman, Orr, Forgue, de Jong, & Claiborn, 1987) and non-reminiscent stimuli (Butler et al., 1990; Orniz & Pynoos, 1989).

Similarly, non-combat related studies have also found SNS arousal to trauma-related stimuli (Blanchard, Kolb, & Gerardi, 1986; Blanchard et al., 1996; Pitman, Orr, Forgue, de Jong, & Claiborn, 1987). Individuals living near Three Mile Island (Davidson & Baum, 1986) and mothers of child cancer survivors (Glover & Poland, 2002) also had
elevations in urinary norepinephrine, suggesting that both combat and non-combat related studies consistently demonstrate that elevations in catecholamines are characteristic of individuals diagnosed with PTSD.

_Hypothalamic Pituitary Adrenal (HPA) Axis Response to Stress_

The HPA axis initially aids the SNS in facilitating the stress response (Chrousos & Gold, 1992; Munck et al., 1984) and then serves to modulate SNS activity. The HPA axis includes parts of the hypothalamus, the anterior pituitary gland, the adrenal cortices, hormones, and a number of pathways and feedback mechanisms responsible for the transport of stress hormones from the adrenal glands back to the hypothalamus and to other parts of the brain. The amygdala innervates the locus coeruleus, which activates the hypothalamus. Activation of the hypothalamus results in the release of corticotrophin releasing hormone (CRH), thereby signaling the secretion of adrenocorticotropic hormone (ACTH) from the anterior pituitary gland (Chrousos & Gold, 1992). The release of ACTH into general circulation stimulates the release of stress hormones called glucocorticoids (e.g. cortisol in humans; corticosterone in animals) from the adrenal cortex (Chrousos and Gold, 1992; Horrocks et al, 1990). This cascade of events is repeated until the amount of cortisol in circulation is sufficient. Specifically, when cortisol binds to glucocorticoid receptors (Svec, 1985) on specialized areas in the brain (i.e., pituitary and hippocampus) the system is signaled to discontinue the secretion of ACTH, inhibiting further release of cortisol (negative feedback inhibition: for an overview, see Dallman et al., 2000; Munck et al., 1984; Tsigos and Chrousos, 2002).
Stress-induced cortisol elevations are coupled with fluctuations in norepinephrine levels in the locus coeruleus, hippocampus, amygdala, and cerebral cortex (Anisman et al., 1991; Charney, Woods, Goodman, & Heninger, 1987; Irwin, Ahluwalia, & Anisman, 1986; Laakmann et al., 1984; Yehuda et al., 1990). Like epinephrine and norepinephrine, cortisol helps the body metabolize food, releases stores of nutrients for energy, increases blood flow, and suppresses other functions not needed for fight or flight (Chrousos & Gold, 1992). Additionally, cortisol impacts the immune system and the cardiovascular system, and plays a role in affective and cognitive processes (Mason 1968; Mason, 1975; Whybrow & Ferrell 1974).

In addition to facilitating the initial SNS response to stress, the HPA axis and cortisol serve to eventually shut down sympathetic activation following stress, to protect the body from long-term elevations of sympathetic hormones (deKloet, 1991; Munck et al., 1984). However, when cortisol is unable to regulate elevations in epinephrine and norepinephrine levels, alterations may occur in the amygdala and hippocampus. Thus, a combination of high catecholamine levels with low cortisol levels has been hypothesized to be involved in the development of PTSD (Kosten et al., 1987; Yehuda & Harvey, 1997).

**Urinary cortisol alterations associated with PTSD.** Research examining the biopsychology of PTSD has also produced mixed results concerning urinary cortisol alterations among individuals diagnosed with PTSD. Relatively equal numbers of studies have found that individuals with PTSD excrete higher urinary cortisol (Friedman et al., 2001; Lemieux & Coe, 1995; Maes et al., 1998; Pitman & Orr, 1990; Rasmusson et al.,
lower urinary cortisol (Mason et al., 1986; McFarlane, Atchison, Yehuda, 1997; Yehuda et al., 1990; Yehuda et al., 1993; Yehuda et al., 1995), or do not differ in cortisol excretion from similarly traumatized individuals without PTSD (Baker et al., 1999; Kosten et al., 1990; Mason et al., 2002). These mixed results may be due to a variety of methodological and participant variables. For example, urinary cortisol levels are often assessed using 24-hour urine specimens, which, because they are collected continuously throughout the day are often confounded by participant-specific variables such as physical activity, diet, or alcohol or drug abuse. Studies rarely match individuals on daily routine or variables that may influence HPA axis activity or urinary cortisol output (Rasmusson et al., 2003). Failure to control for a variety of variables such as sex, genetic factors, reproductive status, isolation, pharmacological agents (i.e., caffeine, cocaine, nicotine, alcohol, and prescribed medications), hospitalization, and injury severity has been hypothesized to contribute to the large discrepancy between studies examining urinary cortisol levels among trauma survivors (Rasmusson, et al., 2003).

A large number of studies suggest that trauma survivors with PTSD have lower levels of cortisol in response to their trauma and in response to subsequent reminders of that trauma (Mason et al., 1986; Yehuda et al., 1990; Yehuda et al., 1993; Yehuda et al., 1995). Research has attributed low urinary cortisol excretion among individuals diagnosed with PTSD to an enhanced negative feedback inhibition of the HPA axis. This theory has been supported by additional studies demonstrating that individuals with PTSD have greater numbers of lymphocyte glucocorticoid receptors compared to similarly traumatized individuals without PTSD (Yehuda, Lowy, Southwick, Shaffer, &
Giller, 1991; Yehuda et al., 1993; Yehuda, Boisoneau, Lowy, & Giller 1995), suggesting that increases in glucocorticoid receptors represent an effort by the HPA axis to counterbalance the effect of low cortisol levels.

Concordant with low cortisol and greater numbers of lymphocyte glucocorticoid receptors, people with PTSD have been found to be hyperresponsive to dexamethasone suppression tests (DST). DSTs involve the administration of dexamethasone, a synthetic steroid comparable to cortisol, and the measurement of cortisol response. Dexamethasone promotes the suppression of ACTH, thereby decreasing cortisol levels in normal individuals. However, trauma survivors with PTSD are hypersuppressors in response to the DST. In other words, ACTH and cortisol levels are hypersuppressed in PTSD versus non-PTSD groups (Yehuda et al., 1995), suggesting an attempt by the HPA axis to suppress any further release of cortisol, also referred to as enhanced negative feedback inhibition (Goenjin et al., 1996; Yehuda, Southwick, Krystal, Charney, & Mason 1993, Yehuda et al., 1995; Yehuda, Halligan, Golier, Grossman, & Bierer, 2004; Yehuda, Yang, Buchsbaum, & Goiler, 2005).

Enhanced feedback sensitivity of the HPA axis has also been demonstrated through the administration of metyrapone, a glucocorticoid receptor antagonist that prevents the release of cortisol into the bloodstream without disrupting the synthesis and release of epinephrine (Roozendaal, Bohus, & McGaugh, 1996; Strashimirov & Bohus, 1966). Thus, metyrapone frees the pituitary gland from negative feedback inhibition influences, allowing the release of ACTH by the pituitary to be examined free of any influence exerted by cortisol (Lisansky et al., 1989). Yehuda and colleagues (1996)
demonstrated that metyrapone stimulation tests resulted in a significantly greater increase in ACTH among combat veterans with PTSD (n=11) compared to healthy controls (n=8), supporting an enhanced negative feedback inhibition in individuals with PTSD.

Elevated levels of urinary cortisol among trauma survivors have been more commonly found in studies that have adequately controlled for confounds associated with HPA axis responsivity (for a review see Rasmusson et al., 2003). For example, Lemieux and Coe (1995) examined three groups of females (n=28); 11 individuals had a history of childhood sexual abuse and PTSD, 8 individuals had a history of childhood sexual abuse without PTSD, and 9 were unabused controls. After controlling for medications known to affect HPA-axis functioning, polyuria (excess urine production), obesity, mood, physical pain, smoking status, alcohol consumption, and matching participants on age, results showed that individuals with PTSD excreted higher urinary catecholamines than trauma survivors without PTSD and nonabused controls.

Rasmusson and colleagues (2001) found similar results among premenopausal women with PTSD. Eleven non-traumatized control and 12 PTSD women were tested using a corticotropin-releasing factor stimulation test, and an ACTH stimulation test, and a 24-hour urine collection for free cortisol to examine pituitary and adrenal axis reactivity. Analyses controlled for the use of oral contraceptives, antidepressants, psychiatric disorders, smoking status, substance abuse, and menstrual cycle phase. Results indicated that traumatized women with chronic PTSD had increased ACTH and cortisol responses to ovine CRF administration and had exaggerated cortisol responses to ACTH administration. Furthermore, cortisol responses to the CRF stimulation test,
cortisol responses to the ACTH stimulation test, and urinary-free cortisol levels were positively correlated, suggesting that high levels of urinary cortisol were consistent with PTSD pathophysiology.

In sum, research examining urinary stress hormone markers associated with chronic PTSD has reported mixed results. Some research supports the notion that individuals with chronic PTSD have a specific neuroendocrine profile characterized by low urinary cortisol excretion coupled with a high catecholaminergic response to trauma and stress. However, research has also demonstrated that individuals living with chronic PTSD excrete higher levels of urinary cortisol compared to individuals without chronic PTSD, especially among studies specifically designed to control for HPA axis dysfunction as well as a variety of potential confounds. Mixed findings concerning catecholaminergic responses and altered HPA axis functioning in PTSD patients has prompted researchers to examine the relationship between these two stress pathways as well as the possible mechanism through which acute physiological responses to trauma may contribute to chronic distress and psychopathology.

Mechanisms through which Immediate and Acute Phase Physiological Responses may Lead to PTSD. Pitman (1989) was the first to propose that heightened catecholaminergic levels such as those seen in chronic PTSD, could lead to aberrant memory formation and the development of “overconsolidated” memories if present during and soon after trauma. Overconsolidation may further promote intrusive thoughts post-trauma, coupled with hyperarousal associated with the act of the reliving the trauma event, both of which are classic symptoms of PTSD (Pitman et al., 1993). Yehuda and
colleagues (Yehuda & Harvey, 1997; Yehuda, McFarlane, & Shalev, 1998) extended Pitman’s theory to suggest that exaggerated catecholamine increases, during and immediately following the trauma, without the regulatory influence of accompanying cortisol increases may enable elevated levels of catecholamines in the brain to persist (Pacak, Palkovits, Kopin, & Goldstein, 1995); potentially leading to over salient or fragmented memories. This hypothesis is supported by animal research that has demonstrated that exogenously administering catecholamines has memory-enhancing effects (Cahill et al., 1994; De Wied & Croiset, 1991). Both animal and human research have demonstrated that stress and its accompanying neuroendocrine alterations play significant roles in learning and memory processing (De Wied, 1984; McGaugh, 1985, 1989; McGaugh, Liang, Bennett, & Sternberg, 1984). Animal studies using conditioned avoidance paradigms have shown that catecholamines promote memory formation and facilitate learning (McGaugh, 1985). Administration of exogenous epinephrine and norepinephrine immediately following avoidance training has been shown to enhance the retention of various inhibitory avoidance-training tasks (Borrell, de Kloet, Versteeg, & Bohus, 1983; Cahill and McGaugh, 1991; Gold & van Buskirk, 1975; Izquierdo & Diaz, 1985; Liang, Juler, & McGaugh, 1986; McGaugh, Ferry, Vazdarjanova, & Roozendaal, 2000; Sternberg, Isaacs, Gold, & McGaugh, 1985).

Human studies have also demonstrated that administration of small to moderate doses of epinephrine could cause memory enhancement (Eysenck, 1982; Taylor and Cahill, 2002). Cahill and colleagues (1994) found an increase in memory-retention errors on recall details pertaining to a provocative slide show presentation among college
students pretreated with propranolol, a β-adrenergic blocker (catecholamine blocker) used to decrease sympathetic activation. Propranolol’s memory-suppressing effect supports the hypothesis that arousal plays a significant role in the process of memory consolidation of arousing memories. In addition, these findings suggest that physiological arousal during or immediately following an emotionally taxing event, such as a trauma, may contribute to the development of PTSS. Thus an examination of pre- and peri-traumatic physiological arousal may be a significant step toward determining whether the degree of physiological arousal influences PTSD symptom onset and development.

*Initial Hormonal Response to Trauma*

Currently, only three adult studies have looked at the relationship between urinary hormone responses immediately following trauma exposure and risk for subsequent PTSD. Resnick et al (1995) examined female rape victims within 51 hours of their rape and found that those most likely to develop PTSD had lower plasma cortisol levels. McFarlane and colleagues (1997) found that motor vehicle accident (MVA) victims meeting PTSD criteria 6 months post-trauma had significantly lower plasma cortisol levels than those with major depressive disorder, but did not differ from individuals without a PTSD diagnosis. Delahanty et al. (2000) found that MVA victims subsequently diagnosed with acute PTSD excreted lower urinary cortisol levels in the first 15 hours following their accident. Furthermore, individuals that reported experiencing intrusive thoughts within the first few days of their accident had lower cortisol and epinephrine levels than those that did not report intrusive thoughts. In
addition, urinary epinephrine and cortisol levels were significantly correlated with scores on a self-report measure of PTSD symptomatology (i.e. Impact of Event Scale); however, they did not find any differences in catecholamine levels obtained immediately post-MVA between individuals subsequently diagnosed with versus without PTSD.

Further support for early hormone levels predicting subsequent PTSD comes from secondary intervention studies that have attempted to alter or block acute hormone levels to prevent or reduce subsequent PTSD development and diagnosis. Schelling and colleagues (1999; 2001) found that the incidence of PTSD was significantly lower among sepsis patients that received a regimen of 100mg of hydrocortisone during their sepsis episode, followed by a .18mg/kg/hr dose of hydrocortisone until shock reversal, compared to sepsis patients not receiving this hydrocortisone regime. Of the nine patients administered hydrocortisone, only one patient was subsequently diagnosed with PTSD 31-months post-hospital discharge. However, 7 out of 11 patients given the placebo met PTSD criteria at the 31-month follow-up assessment. Results obtained from these studies suggest that administering hydrocortisone during a time of extreme psychological and physical stress (i.e. sepsis) may impact the cognitive appraisal of the traumatic incident by diminishing the intensity or emotionality of the traumatic event. Furthermore, this type of early intervention may disrupt traumatic memory retrieval, thereby buffering against subsequent PTSD diagnosis. However, these results must be interpreted with caution, as there was a tendency for faster shock reversal among patients receiving the hydrocortisone regimen. In other words, hydrocortisone administration may have lessened the intensity or emotionality of the traumatic experience, resulting in a less
traumatized sample. Additionally, patients assigned to the placebo regimen also received a higher dose of norepinephrine in-hospital, which, given the above-mentioned facilitating role of catecholamines in emotional memory, could have contributed to higher rates of PTSD in this group.

Schelling and colleagues (2004) followed a similar protocol in a test of the efficacy of hydrocortisone at buffering symptoms of PTSD in patients recovering from cardiac surgery. The study consisted of 48 cardiac surgery patients, 26 of whom received preoperative hydrocortisone treatments and 22 controls that did not receive hydrocortisone treatments. Results revealed that patients assigned to the hydrocortisone condition reported significantly fewer chronic PTSD symptoms than patients receiving standard treatments without hydrocortisone (p < .05), suggesting that preoperative hydrocortisone helped to buffer against the stress effects associated with peri-operative stress exposure, thereby, decreasing subsequent chronic stress responses to surgery.

In addition to intervening by manipulating levels of HPA axis hormones, Pitman and colleagues (2002) have examined the extent to which moderating sympathetic arousal soon after trauma results in a buffering of PTSD symptom development. More specifically, they have administered propranolol to patients within 6 hours of a traumatic event. Propranolol is a β-adrenergic receptor blocker that effectively hinders the activation of both central and peripheral β-receptors which are activated in times of stress ultimately contributing to heightened physiological responding (Taylor and Cahill, 2002; Introini-Collison, Saghati, Novack, & McGaugh, 1992) and intensification trauma-related memories (Ferry, Roozendaal, & McGaugh, 1999). This double-blind study randomly
assigned 18 trauma survivors to receive a propranolol regimen and 23 similarly traumatized individuals to receive a placebo regimen. The first dose (40 mg) of treatment medication was administered within 6 hours of the patient’s traumatic event and was continued four times a day for 10 days with a 6-day taper. Results indicated that propranolol and placebo groups did not differ in incidence of PTSD at follow-up. However, among those that completed the one-month follow-up, 6 placebo and zero propranolol recipients were considered physiological responders during a script-driven imagery of their traumatic event. These results suggested that while early administration of propranolol may have efficaciously reduced the retention of a conditioned fear response, thereby, reducing acute PTSD symptoms, propranolol did not influence ability to meet full diagnostic criteria for chronic PTSD.

The efficacy of early propranolol treatment has also been examined in a nonrandomized sample of 19 MVA and physical assault survivors (Vaiva et al., 2003). Eleven of 19 trauma patients agreed to receive 40 mg of propranolol post-trauma and continued three times daily for seven days followed by a 8-12 day taper, while 8 of 19 trauma patients refused this medication regimen. PTSD rates and symptom levels were higher among those that refused the propranolol regimen, further supporting the efficacy of early propranolol treatment to prevent or reduce subsequent development of PTSD symptomatology and subsequent diagnosis.
Present Study

Research examining the onset and progression of PTSS and the physiological predictors and correlates of PTSD has produced mixed results. The current lack of prospective research examining PTSD and the neuroendocrine alterations associated with trauma exposure has made it difficult to conclude whether there is a specific psychological and/or physiological profile that may put an individual at greater risk of subsequent PTSD diagnosis. Identify individuals that are at greater risk for PTSD, based on a specific symptom profile, will allow clinicians to administer early intervention strategies that may buffer against the chronic maintenance of PTSS and ultimately decrease the chance of being diagnosed with PTSD. Thus, the present study examined both acute and chronic physiological responses to a MVA longitudinally, using urinary stress hormone levels obtained at numerous time points to represent physiological responsivity. This examination of urinary cortisol and catecholamine levels and their relationship to symptom cluster change over time extends the Schell et al. (2004) findings because it provides a more complete picture of the interactive relationship between psychological and physiological responses to trauma and their collective influence on symptom cluster onset and course. Contrary to that of Schell et al., 2004, the present study benefited from the inclusion of more frequent assessments and the use of both self-report and clinician-assessed PTSD symptomatology.

Specifically, the proposed study implemented hierarchical linear modeling (HLM) to systematically track changes in urinary stress hormone levels and PTSS over time. Urinary catecholamine and cortisol measurements collected from MVA victims
immediately upon hospital admission, and approximately 3-, 6-, and 12-months post-trauma and acute and chronic PTSD symptoms measured in-hospital, 6 weeks, 6 months, and 1 year post-trauma were examined.

Hypotheses

The present study hypothesized that (1) PTSD symptom scores would be highest shortly following a MVA and would gradually lessen over time. We hypothesized that (2) the hyperarousal symptom cluster would demonstrate the slowest rate of improvement over time. Furthermore, we posited that (3) hyperarousal symptoms would most likely predict or promote changes in subsequent PTSS over time. Additionally, it was hypothesized that (4) acute PTSS, reported in-hospital, would predict chronic PTSS at the 3-, 6-, and 12-month follow-up assessments. As an extension of the current literature, it was hypothesized that (5) cortisol and catecholamines would predict the formation and change in PTSS over time. Additionally, in accordance with prior research, it was hypothesized that (6) change in cortisol and catecholamines over time would differ between individuals that scored high or low on chronic PTSS symptoms, such that individuals with greater chronic PTSS would have lower urinary cortisol and higher catecholamine levels immediately post-MVA and would continue to have lower cortisol and higher catecholamine levels throughout recovery compared to MVA survivors with little to no PTSS.
CHAPTER II

METHOD

Participants

Participants consisted of 386 (231 males, 155 females) English-speaking MVA victims recruited from one of two local Level 1 trauma centers, Akron City Hospital or Akron General Hospital. This sample was 87% Caucasian, 11% African American, 1% Hispanic, and 1% other. Participants ranged in age from 18 to 87, with an average age of 38.3 (SD = 16.0). 81% of participants were drivers in their MVA (as opposed to a passenger), and participants ranged in severity of injuries suffered during the MVA, with Injury Severity Scale (ISS) scores ranging from 1 to 45 (M = 7.5, SD = 6.1). On average, participants completed some college with individuals having at least an education level equivalent to that of trade school degree or vocational training. Most participants were actively working and reported an income of $20,000 to $30,000 per year. The majority (87.3%) of participants were car accident victims, with 12.7% being motorcycle accident victims.

Procedure

The human participants review boards of Kent State University, Akron General Medical Center, and Summa Health System approved the following procedures. Data
were collected as part of a 4-year NIMH-funded grant study (R01 MH 62042-01 Psychophysiological predictors of PTSD) designed to examine initial hormonal predictors of acute and chronic PTSD. Upon hospital admission, urine samples were collected for the first 10 hours (in two 5-hour increments; 0-5 hour sample and 5-10 hour sample) from all potential participants. According to standard hospital protocol, nearly all trauma patients are catheterized for urine collection upon arrival to the trauma center. Urine samples from catheterized patients were collected in foley bags, and individuals not in need of catheterization (approximately 7%) were instructed to urinate in a polypropylene container. All urine samples were stored on ice for the collection period. At the end of the collection period aliquots of the urine (60 mL) were frozen for catecholamine and cortisol assays. Patients discharged prior to the completion of the urine collection period and those with Glasgow Coma Scale (GCS; Teasdale & Jennett, 1974) scores below 14 (at the time of eligibility screening) were not eligible.

The head trauma nurse (Akron City Hospital) or trained researcher (Akron General Hospital) screened all potential participants with the Mini Mental Status Exam (MMSE; Folstein, & McHugh, 1975: See Appendix A) to determine ability to give informed consent. Upon passing the MMSE, a member of the research team described the study to the patient in detail and obtained informed consent (See Appendix B). As part of the consent procedure, participants gave permission to have their medical charts reviewed for the collection of physiological data, medications received in hospital, injuries suffered, and results of toxicology screening.
Enrolled participants were assessed, in-hospital, by a member of the research team. Initial assessments took place on average 53 hours following trauma admission (range 1.55hrs-545.6 hrs; SD = 72.5 hrs). During this initial assessment, participants completed a number of interviewer-administered measures including a demographics questionnaire (See Appendix C) and the Impact of Event Scale-Revised (IES-R; Weiss & Marmar, 1997: See Appendix D), which is a measure of intrusive thoughts, avoidant behavior, and hyper-arousal symptoms. In addition, researchers recorded behaviors prior to the accident (e.g., foods, and drinks ingested, smoking, and drug or medication use: See Appendix E) that could have compromised the validity of the hormone levels obtained through the urine collection. Upon completion of the in-hospital assessment, participants received $25.00.

A Masters-level clinical graduate student conducted follow-up assessments in participants’ homes at approximately 6 weeks, 6 months, and 1-year post-MVA. The Clinician Administered PTSD Scale (CAPS; Blake et al., 1995: See Appendix F) was administered at the 6-week, 6-month, and year follow-ups. PTSS were also assessed through the self-report IES-R (IES-R: Weiss & Marmar, 1997: See Appendix D) at 3 months post-MVA.

Participants were also asked to provide urine samples for testing of cortisol and catecholamine levels at the 3-month, 6-month, and one-year follow-ups. Polypropylene containers were provided for each in-home urine collection. Participants were instructed to collect all urine voided from 6 PM in the evening until 9 AM the following morning. Collected urine specimens were kept on ice between and upon completion of the each
urine collection until a member of the research team retrieved them. Upon completion of each of the follow-up time points, participants received $25.00.

Measures

Demographics. A member of the research team collected demographic data from each participant. Age, gender, race, education level, employment status, annual income, relationship status, and medical care status were among the demographic characteristics collected (See Appendix C).

Measures of Consciousness. The Glasgow Coma Scale (GCS; Teasdale & Jennett, 1974) is a 15-item measure of level of consciousness. The GCS is scored on a scale of 3 (the very worst) to 15 (the very best). The total score is based on the composite score of three parameters: best eye response, best verbal response, and best motor response. A GCS score of 13 and above is representative of a mild brain injury; 9-12 is a moderate injury, and 8 or less a severe brain injury.

The Mini-Mental Status Exam (MMSE; Folstein et al., 1975) is a widely used method for assessing cognitive impairment. This instrument is a 30-point measure of orientation, short-term recall, attention, calculation, language and ability to follow verbal and written instructions. Patients were deemed competent to give informed consent if they scored 25 or greater on the MMSE (See Appendix A).
**Psychological Measures**

**Impact of Event Scale-Revised (IES-R).** The IES-R is a 22-item self-report measure that measures the 3 symptom clusters associated with a PTSD diagnosis (See Appendix D). Participants were asked to answer the questionnaire in relationship to their motor vehicle accident. Each item is rated for frequency and severity and weighted on a 5-point Likert scale (i.e., 0 = not at all; 4 = extremely). Total subscale scores were calculated. Prior to running HLM analyses, the in-hospital and 3-month IES-R subscale scores were centered on the group mean. Cronbach’s alphas were as follows: hyperarousal subscale $\alpha = .77$, intrusion subscale $\alpha = .83$, and avoidance subscale $\alpha = .79$

**Clinician Administered PTSD Scale (CAPS).** A trained clinician assessed PTSS at 6 weeks, 6 months, and 1 year post-MVA using the Clinician Administered PTSD Scale (CAPS; Blake et al., 1995; See Appendix F). The CAPS is a structured interview used to assess the frequency and intensity of each PTSD symptom cluster using a set of standard prompt questions and behaviorally-anchored rating scales. The CAPS is based on a 5-point scale (i.e., 0 = no symptom frequency and severity, 4 = frequency and intensity are severely impacting functioning) provides both continuous and dichotomous scores for current and lifetime PTSD symptoms. Given the low prevalence of diagnostic levels of PTSD, the proposed analyses focused on current continuous PTSD symptom scores for each individual subscale. The CAPS has good convergent and discriminant validity and is sensitive to clinical change (Weathers, Keane, & Davidson, 2001). Cronbach’s alphas
were as follows: hyperarousal subscale $\alpha = .80$, intrusion subscale $\alpha = .82$, and avoidance subscale $\alpha = .86$. Interrater reliability for the CAPS for the present study was $r = .96$.

**Medical Chart Information.** Height, weight, length of stay, time of admit and discharge, GCS score, medicines administered, blood alcohol concentration, and presence of chronic diseases were collected. Objective injury data were collected from the participants’ charts and used to compute the Injury Severity Scores (ISS; Baker, O’Neil, Haddon, & Long, 1974). ISS range from 0-75, with a score of less than 10 suggesting a minor injury, 10-15 indicating serious injury, and a score of greater than 25 suggesting severe injuries.

**Urinary Catecholamines and Cortisol.** Quest Diagnostics (San Juan Capistrano, CA) conducted all free urinary catecholamine assays and the Cleveland Clinic conducted cortisol assays. Free urinary catecholamines were assayed following standard high-pressure liquid chromatography procedures using reverse phase chromatography with electrochemical detection (Shoupe & Keife, 1980). In-hospital epinephrine and norepinephrine levels were computed as amount per 5-hour sample ($\mu$g/5 hours) and follow-up time points were computed as amount per 15-hour sample. Similarly, urinary cortisol levels were measured by fluorescent polarization immunoassay (Abbott TDx Diagnostics, Abbott Laboratories, Abbott Park, IL) and were calculated as amount per 5-hour sample (microgram (ug)/5 hours) for the in-hospital specimens and amount per 15-hour sample for the samples obtained at the follow-up time points. All 15-hour samples were collected from participants between 6pm and 9am the following morning. Because
urinary cortisol levels were also correlated with urine volume, analyses were also conducted on cortisol levels per volume of urine excreted (µg/dL). According to laboratory procedures, all samples were run in duplicate, and those differing by more than 20% were reassayed. No duplicates in the present study differed by more than 20%. For the present study HLM analyses were conducted 3 different ways using only the 0-5 hr sample, only the 5-10 hr sample, and using an average of the two samples to represent the time one (T1) assessment of cortisol and catecholamines.
CHAPTER III

DATA ANALYSIS PLAN

Overview of Hierarchical Linear Modeling (HLM)

The present study’s longitudinal design, repeated assessments of psychological and physiological responses, and obstacle of missing data made hierarchical linear modeling (HLM) an ideal statistical technique for the examination of individual change over the course of MVA trauma recovery. Traditionally, ordinary-least-squares regression (OLS) techniques or analyses of variance (ANOVAs) have been the statistical analyses of choice used to examine data collected within groups and/or repeatedly over time (Raudenbush & Bryk, 2002). OLS and ANOVA designs rely on the knowledge of group membership to predict subject’s responses on the outcome; in other words, the pattern of change observed within a group generalizes across all individuals, disregarding any individual differences in change (Raudenbush & Bryk, 2002). Furthermore, ANOVAs and OLS designs assume that repeated observations within individuals are independent of antecedent or subsequent assessments, such that there is no interrelationship or interdependence among observations within individuals. Thus, these traditional statistical techniques are estimations of an overall average across individuals at a given time point or estimates of group trajectories. In contrast, HLM (a maximum likelihood design) is sensitive to the associations present between observations, within
individuals, by providing an estimate of random effects or within-individual error that varies randomly across individuals (Raudenbush & Bryk, 2002). HLM is able to examine both within-individual change and between-individual variation and provide an estimated growth trajectory for each individual (Raudenbush & Bryk, 2002).

Specifically, HLM allows for the regression of a lower level variable (e.g., individual level) on another lower level variable or that of a higher-level variable (e.g., group level). HLM analyses require the inclusion of at least 3 measurement time points (the current study had 5 time points for subscale analyses and 4 time points for physiological levels analyses), to test linear growth or change over time. However, the amount and timing of assessments can vary from participant to participant (e.g. some participants may have 3 data points, some four, etc.). The availability of data obtained at numerous time points allows HLM to estimate the mean growth trajectory for the entire group, track fluctuations in individual change around the mean growth, and identify differences in change attributed to individual-level characteristics (Raudenbush, 2001).

HLM tests linear growth by interpreting repeated measurements of each individual over time in terms of slopes of the latent trajectory which best describes the data. Thus, a slope (i.e. $\beta_{1ij}$) can be obtained for this trajectory that illustrates the rate of change in hypothesized relationships over time. HLM analyzes nested data with a multi-step, model building approach. At the most basic level, HLM is similar to that of a one-way ANOVA with random effects (Raudenbush & Bryk, 2002) such that $\beta_{1ij}$ (the slope) in the
Level I model is set to zero for all groups \((j)\), yielding for example:

\[ y_{ij} = \beta_{0ij} + r_{ij} \]

As compared to

\[ y_{ij} = \beta_{0ij} + \beta_{1ij} X_{ij} + r_{ij} \] (typical regression equation or Level I model)

The first level (Level I model) yields individual (within-subjects) growth curves plus random error, relative to a particular variable. Thus, HLM analyses at this level enabled us to examine individual differences in personal characteristics over time that contributed to the onset and progression of PTSS. For example, cortisol levels at each time point could be used to predict hyperarousal symptoms at each time point.

**Level I:** Hyperarousal Symptoms

\[ y_{ij} = \beta_{0ij} + \beta_{1ij} (\text{time}) + \beta_{2ij} (\text{cortisol levels}) + r_{ij} \]

Where…

Hyperarousal symptoms \((y_{ij})\) = the outcome variable

\(\beta_{0ij}\) intercept = mean hyperarousal symptoms \((y_{ij})\) for each individual’s observation when all other variables are held constant

\(\beta_{1ij}\) slope = the slope of the relationship between time and hyperarousal symptoms for each individual’s observation at each time point

\(\beta_{2ij}\) slope = the slope of the relationship between time and hyperarousal symptoms for each individual’s observation at each time point

\(r_{ij}\) = within-individual random error from the assessment of individual \(j\) at observation \(i\)

Then, additional predictors are used to establish a second level (Level II model), in which individual trajectories vary based on individual differences between subjects, within a designated group (Bryk and Raudenbush, 1987). The slope of the relationship from Level I becomes the outcome variable in Level II. In Level II, time invariant
measures (e.g., sex) can be used as predictors. Thus, an HLM analysis at this level allowed us to infer causality based on trends in individual PTSD trajectories.

For Example:

\[
\begin{align*}
\beta_0_{ij} &= \gamma_{00ij} + \gamma_{01ij} (\text{race}) + \gamma_{02ij} (\text{sex}) + \mu_{0ij} \\
\beta_1_{ij} &= \gamma_{01ij} + \gamma_{11ij} (\text{race}) + \gamma_{02ij} (\text{sex}) + \mu_{0ij}
\end{align*}
\]

Where…

\[
\begin{align*}
\beta_0_{ij} &= \text{the mean of cortisol levels for each individual’s observation} \\
\beta_1_{ij} &= \text{the relationship between cortisol levels and hyperarousal symptoms for each individual’s observation} \\
\gamma_{00ij} &= \text{the mean of the individual’s observation means (}\beta_{0j}\text{ from Level I) on hyperarousal symptoms across all individuals} \\
\gamma_{01ij} &= \text{the main effect of race} \\
\gamma_{02ij} &= \text{the main effect of sex} \\
\mu_{0ij} &= \text{the unique increment to the intercept associated with a given participant.} \\
\gamma_{10ij} &= \text{the average cortisol level slope (}\beta_{1j}\text{ from the Level I) across all individuals} \\
\gamma_{11ij} &= \text{the cross-level interaction between cortisol levels and sex} \\
\mu_{1ij} &= \text{the unique increment to the intercept associated with a given participant.}
\end{align*}
\]

Data Preparation

Prior to running HLM analyses, repeated measures data were restructured to reflect a nested format. Each participant was designated a separate line of data for each observation. All other variables were entered in the traditional manner. Individual-level (Level I) and group-level (Level II) variables were divided into two separate data sets to accommodate the varying sample sizes at each level.
Unbalanced or Missing data

HLM is based on maximum likelihood estimation and utilizes all the available level-1 data at each time point to create an overall model by estimating the missing time points (Little & Rubin, 1987; Little & Schenker, 1994). Thus, HLM yields results as if there are no missing data, given that the data are missing at random (MAR). However, it was not feasible to test whether missing data points were MAR, rather it was more appropriate to test whether the data was missing completely at random (MCAR: Allison, 2003). Thus, chi-square analyses were conducted to determine whether the proportion of the cases with missing data significantly differed by between group variables. Chi-square analyses indicated that there were significant gender differences between individuals with and without missing data at the 3 month ($\chi^2 [1, N=386] = 4.83, p < .05$), 6 month $\chi^2 [1, N=386] = 4.76 p < .05$), and year ($\chi^2 [1, N=386] = 4.41, p < .05$) follow-up assessments, suggesting that males were more likely to have missing data than females. Hence, gender was entered as a control variable in all analyses and the final estimation of fixed effects with robust standard errors was used to report a more conservative set of results for each HLM model.

Additionally, some individuals were missing items on the IES-R resulting in missing subscale total scores. Thus, for individuals missing 3 or fewer items per subscale, missing items were imputed using the mean for that individual’s subscale score. Only 26 individuals were missing items from IES-R at the in-hospital assessment and 18 individuals were missing items from the 3-month follow-up assessment. All other missing data at Level I was accounted for through HLM estimation. However, HLM
does not allow for missing data to be present at Level II. Five individuals were missing ISS scores due to insufficient hospital records; hence, for these individuals, ISS scores were mean-imputed. Additionally, one individual failed to endorse their race, thus, this individual was included in the “Other” category.

*Power*

Currently, there is no agreement concerning the number of participants in a sample needed to detect statistical significance (i.e. power) when conducting analyses using HLM (Raudenbush & Liu Xiao-Feng, 2001). According to Kreft (1996), the present study has an adequate sample size. Kreft found adequate statistical power for 150 individuals with 5 observations each. The present study has well over 150 individuals with 5 observations each.

*HLM Model Building and Analysis*

HLM 6.04 (Raudenbush, Bryk, & Congdon, 2007) was used to conduct all HLM analyses. All HLM analyses used maximum likelihood estimations (MLE) to compare the full model to the nested model (i.e. model fit). Model fit was determined using the deviance statistic, based on a chi-square distribution, with lower deviance scores suggesting a better fit. Chi-square difference tests were performed to decipher whether the full model (using regression coefficients and variance components) was significantly different from the nested model. If a chi-squared difference test indicated that there was not a significant difference between models, model parameters were adjusted to improve goodness of fit.
Hypothesized Models

The models provided for each hypothesis below reflect only one PTSD symptom cluster. All PTSS were tested using the same equations given below; however, if earlier analyses yielded nonsignificant results concerning a given PTSD symptom cluster, that symptom cluster was dropped from subsequent analyses. All level-1 variables were centered around the group mean and continuous level-2 variables were centered around the grand mean for ease of interpretation. To appropriately examine change over assessment time points, a variable called “occasion” was created. “Occasion” represents the assessment time points: in-hospital (occasion 0), 6 weeks (occasion 1), 3 months (occasion 2), 6 months (occasion 3), and 1-year (occasion 4) post-MVA. Within-individual random error for occasion was fixed for all models.

Hypotheses 1, 2, & 3: It was hypothesized that PTSD symptom scores would be highest in frequency and intensity shortly following a MVA and would gradually lessen over time. In addition, the hyperarousal symptom cluster was hypothesized to show the slowest rate of improvement. It was also hypothesized that hyperarousal would most likely to predict or promote changes in subsequent PTSS over time.

Level I: \( \Delta \text{Hyperarousal}_{ij} = \beta_{0ij} + \beta_{1ij} (\text{Occasion}) + \beta_{2ij} (\text{Intrusion}) + \beta_{3ij} (\text{Avoidance}) + r_{ij} \)

Level II: 
\[
\begin{align*}
\beta_{0ij} &= \gamma_{00ij} + \gamma_{01ij} (\text{gender}) + \gamma_{02ij} (\text{age}) + \gamma_{03ij} (\text{amnesic status}) + \mu_{0ij} \\
\beta_{1ij} &= \gamma_{01ij} + \gamma_{11ij} (\text{gender}) + \gamma_{02ij} (\text{age}) + \gamma_{03ij} (\text{amnesic status}) + \mu_{0ij} \\
\beta_{2ij} &= \gamma_{01ij} + \gamma_{11ij} (\text{gender}) + \gamma_{02ij} (\text{age}) + \gamma_{03ij} (\text{amnesic status}) + \mu_{0ij} \\
\beta_{3ij} &= \gamma_{01ij} + \gamma_{11ij} (\text{gender}) + \gamma_{02ij} (\text{age}) + \gamma_{03ij} (\text{amnesic status}) + \mu_{0ij}
\end{align*}
\]
HLM analyses were conducted for all remaining PTSD symptom clusters using the same Level I equation as above. However, group variables entered into Level II were determined through preliminary analyses and differed for each symptom cluster. Note that the above model includes all variables for each original model. See results for a description of the final model.

**Hypothesis 4:** Early PTSS would predict later, more chronic PTSS at subsequent follow-up assessments.

Level I: \( \Delta \) Chronic Hyperarousal\(_{ij} = \beta_{0ij} + \beta_{1ij} \text{(Occasion)} + \beta_{2ij} \text{(Acute Intrusion)} + \beta_{3ij} \text{(Acute Avoidance)} + \beta_{4ij} \text{(Acute Hyperarousal)} + r_{ij} \)

Level II: \( \beta_{0ij} = \gamma_{00ij} + \gamma_{01ij} \text{(gender)} + \gamma_{02ij} \text{(age)} + \mu_{0ij} \)

\( \beta_{1ij} = \gamma_{10ij} + \gamma_{11ij} \text{(gender)} + \gamma_{02ij} \text{(age)} + \mu_{0ij} \)

\( \beta_{2ij} = \gamma_{10ij} + \gamma_{11ij} \text{(gender)} + \gamma_{02ij} \text{(age)} + \mu_{0ij} \)

\( \beta_{3ij} = \gamma_{10ij} + \gamma_{11ij} \text{(gender)} + \gamma_{02ij} \text{(age)} + \mu_{0ij} \)

\( \beta_{4ij} = \gamma_{10ij} + \gamma_{11ij} \text{(gender)} + \gamma_{02ij} \text{(age)} + \mu_{0ij} \)

* HLM analyses were conducted for all remaining PTSD symptom clusters using the same Level I equation as above. However, group variables entered into Level II were determined through preliminary analyses and differed for each symptom cluster. Note that the above model includes all variables for each original model. See results for a description of the final model.
Hypothesis 5: Both cortisol and catecholamines would predict the formation of PTSD symptom clusters over time.

Level I: $\Delta$ Hyperarousal$_{ij} = \beta_{0ij} + \beta_{1ij} (\text{Occasion}) + \beta_{2ij} (\text{Intrusion}) + \beta_{3ij} (\text{Avoidance}) + \beta_{4ij}$ (Cortisol) 

$+ r_{ij}$

Level II: $\beta_{0ij} = \gamma_{00ij} + \gamma_{01ij} (\text{gender}) + \gamma_{02ij} (\text{age}) + \mu_{0ij}$

$\beta_{1ij} = \gamma_{01ij} + \gamma_{11ij} (\text{gender}) + \gamma_{02ij} (\text{age}) + \mu_{0ij}$

$\beta_{2ij} = \gamma_{01ij} + \gamma_{11ij} (\text{gender}) + \gamma_{02ij} (\text{age}) + \mu_{0ij}$

$\beta_{3ij} = \gamma_{01ij} + \gamma_{11ij} (\text{gender}) + \gamma_{02ij} (\text{age}) + \mu_{0ij}$

$\beta_{4ij} = \gamma_{01ij} + \gamma_{11ij} (\text{gender}) + \gamma_{02ij} (\text{age}) + \mu_{0ij}$

* HLM analyses were conducted for all remaining PTSD symptom clusters using the same Level I equation as above for cortisol analyses. For analyses examining catecholamines to predict change in PTSS an identical equation, as shown above, was used; however epinephrine and norepinephrine replaced cortisol. However, group variables entered into Level II were determined through preliminary analyses and differed for each symptom cluster. Note that the above model includes all variables for each original model. See results for a description of the final model.

Hypothesis 6: Individuals with chronically high PTSS have a different catecholamine and cortisol trajectory compared to individuals with low chronic PTSS.
Level I: \( \Delta \text{Cortisol}_{ij} = \beta_{0ij} + \beta_{1ij} (\text{Occasion}) + r_{ij} \)

Level II: 
\[
\begin{align*}
\beta_{0ij} &= \gamma_{00ij} + \gamma_{01ij} (\text{hi/low chronic hyperarousal}) + \mu_{0ij} \\
\beta_{1ij} &= \gamma_{01ij} + \gamma_{11ij} (\text{hi/low chronic hyperarousal}) + \mu_{0ij}
\end{align*}
\]

* HLM analyses were conducted for all remaining high/low chronic symptom groups using the same Level-I equation as above for cortisol analyses. For analyses examining chronic high/low group differences in catecholamine trajectories an identical equation, as shown above, was used; however epinephrine and norepinephrine replaced cortisol.
CHAPTER IV

RESULTS

Preliminary Analysis

The Statistical Package for the Social Sciences Version 12.0 (SPSS; SPSS 2003) was used to run bivariate Pearson Product Moment correlations (for continuous variables) to identify potential covariates and control variables. Preliminary one-way ANOVAs were conducted to determine whether PTSD symptom clusters differed by categorical variables (e.g. race, sex). Several demographic and MVA-related variables were examined as potential control variables; however, variables were kept to a minimum so as to not jeopardize the power of the present study. Descriptive statistical analyses for all symptom clusters for each assessment time point are presented in Table 1.

Table 1. Means and Standard Deviations for Symptom Cluster Scores for the Whole Sample (N = 386)

<table>
<thead>
<tr>
<th></th>
<th>In-hospital (N = 365)</th>
<th>6 weeks (N = 264)</th>
<th>3 months (N = 223)</th>
<th>6 months (N = 208)</th>
<th>1 year (N = 189)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoidance</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Intrusion</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Hyperarousal</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
</tbody>
</table>

Note. The IES-R was given in-hospital and at the 3-month follow-up. The CAPS was given at the 6 week, 6 month, and 1 year follow-ups. The N’s for each time point represent the number of individuals that completed all subscales for each time point.

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Initial bivariate Pearson Product Moment correlation (see Table 2) coefficients indicated that there were significant negative correlations between age and in-hospital subscale scores of hyperarousal, intrusions, and avoidance, and with intrusions at the 6-week follow-up assessment, suggesting that the younger individuals on average scored higher. Injury severity scores were also negatively correlated with hyperarousal and intrusive symptoms at the 3-month follow-up assessment, such that individuals with higher ISS scores were on average more likely to score lower on subscale assessments of hyperarousal and intrusion. Additionally, one way ANOVAs indicated that there were significant gender differences in all of the subscales at each time point (all p’s ≤ .03) except for avoidance and hyperarousal subscale scores at the in-hospital assessment and hyperarousal and avoidance scores at the 1 year assessment, such that females consistently scored higher on all subscale scores compared to their male counterparts (see Table 3). Subscale scores also differed by race at the in-hospital assessment of intrusion (F[3, 362]=3.43, p < .05) and on the avoidance (F[3, 185]= 3.18, p < .03) subscale at the 1 year follow-up, with Caucasian individuals on average scoring lower than African
Table 3
Mean (SD) Subscale Scores by Gender

<table>
<thead>
<tr>
<th></th>
<th>In-hospital (N = 365)</th>
<th>6 weeks (N = 264)</th>
<th>3 months (N = 223)</th>
<th>6 months (N = 208)</th>
<th>1 year (N = 189)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Avoidance</strong></td>
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<tr>
<td>Males</td>
<td>8.57</td>
<td>6.73</td>
<td>8.92*</td>
<td>8.47</td>
<td>5.29**</td>
</tr>
<tr>
<td>Females</td>
<td>9.88</td>
<td>7.05</td>
<td>11.88</td>
<td>11.07</td>
<td>9.06</td>
</tr>
<tr>
<td><strong>Intrusion</strong></td>
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<tr>
<td>Males</td>
<td>10.06*</td>
<td>7.44</td>
<td>5.35*</td>
<td>6.58</td>
<td>5.61**</td>
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<td>Females</td>
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<td></td>
</tr>
<tr>
<td>Males</td>
<td>6.65</td>
<td>5.71</td>
<td>8.35</td>
<td>7.07</td>
<td>3.56**</td>
</tr>
<tr>
<td>Females</td>
<td>7.54</td>
<td>6.46</td>
<td>10.98</td>
<td>8.56</td>
<td>7.51</td>
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* p<.05, ** p<.01
Note. The N’s for each time point represent the number of individuals that completed all subscales for each time point. N = 386 for the entire sample.

Americans and other minorities. However, it should be noted that due to the large difference in the number of individuals in each ethnic category this relationship should be examined with caution. Additionally, subscale scores significantly differed by amnesic status. There was a significant difference in the avoidance subscale at all but the 3-month assessment (in-hospital: F[2, 362] = 9.68, p ≤ .000; 6 week follow-up: F[2, 261] = 13.33, p ≤ .000; 6 month follow-up: F[2, 205] = 9.52, p ≤ .000; 1 year follow-up: F[2, 188] = 9.32, p ≤ .000), such that individuals with a full memory for the event surrounding their accident scored significantly lower on avoidance scales at each time point compared to those that had no or little memory of their accident. Therefore, analyses examining the longitudinal relationship between individual PTSD symptom clusters over time controlled for race, gender, ISS scores, age, and amnesic status in each relevant analysis.
HLM Linear Growth Models Examining Change in PTSS Over Time

HLM growth models were conducted to test the hypotheses that PTSD symptom scores would be highest shortly following a MVA and would gradually lessen over time with the hyperarousal symptom cluster showing the slowest rate of improvement and most likely to predict or promote changes in subsequent PTSS over time.

Avoidance. HLM analyses were conducted to examine the average within person change in avoidance given an increase in occasion, hyperarousal symptoms, and intrusion symptoms. First, the original model included occasion, intrusion, and hyperarousal as level-1 independent variables. Next, gender, age, and, amnesic status were added as level-2 moderator variables to explore and control for their effects on the relationship between avoidance symptoms and the level-1 predictors. While mean avoidance at the in-hospital assessment significantly differed by all level-2 variables, amnesic status was the only level-2 variable that significantly moderated the relationship between avoidance and hyperarousal. Thus, amnesic status was dropped from the slope equation for intrusion and age and gender were dropped from all subsequent level-2 equations, leaving a final conditional model. The final estimation of fixed effects with robust standard errors (see Table 4) indicated that the mean avoidance score at the in-hospital assessment differed by gender, age, and amnesic status such that females (M = 8.81), individuals with little or no memory (M = 8.38), and younger individuals (M = 5.61 + .05 for every year that an individual is younger) scored significantly higher than their older male counterparts that had full memory of their MVA (M = 5.61). As hypothesized within individual change in avoidance decreased by .34 units for every increase in occasion;
Table 4

Effect of Time, Hyperarousal, and Intrusion on Avoidance Symptoms

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>p-value</th>
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<tr>
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<td>Avoidance(Intercept)</td>
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<td>Hyperarousal slope</td>
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<td>Intrusion slope</td>
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<td><strong>Inter-Individual</strong></td>
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<tr>
<td>Avoidance(Intercept)</td>
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<tr>
<td>Intercept</td>
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<td>Amnesia</td>
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<td>Age</td>
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<tr>
<td>Occasion slope</td>
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<td>Amnesia</td>
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<td>Hyperarousal slope</td>
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<td>Amnesia</td>
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<td>Intrusion slope</td>
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<tr>
<td>Intercept</td>
<td>.21</td>
<td>.04</td>
<td>.00</td>
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Intra-Individual N = 1267 units
Inter-Individual N = 386 units

Note. For Inter-individual models males and individuals with full memory of their MVA are the comparison group. The intercept represents the average level of the outcome at the in-hospital assessment for males of a mean age with full memory of their MVA. The slope equations represent the relationships between hyperarousal and intrusive symptoms and the outcome (avoidance) for each individual’s observation.
however, this significant relationship was only present among individuals with a full memory for their MVA. Contrary to our predictions individuals with little to no memory for their MVA demonstrated a .17 increase in avoidance with each incremental increase in occasion. Further examination of the slope of the relationship between avoidance and hyperarousal indicated that for each unit increase in hyperarousal, avoidance increased significantly by .32 units for individuals with a full memory of their MVA, and increased significantly by .48 units for individuals with little to no memory, both supporting the hypothesis that hyperarousal symptoms were likely to influence change in other symptom clusters. Results also indicated that there was a significant slope for intrusion such that for each unit increase in mean intrusion scores there was a .21 increase in mean avoidance. The deviance score for the final model was lower (8191.84) than the unconditional model (8609.28) and results of a chi-square difference test indicated ($\Delta\chi^2[3] = 417.44, p < .005$) that the final model was a better fit.

*Intrusion.* Additional HLM analyses were conducted to examine the average within person change in intrusion symptoms given an increase in occasion, avoidance symptoms, and hyperarousal symptoms. The original model included occasion, avoidance, and hyperarousal as level-1 independent variables. Gender, ISS, age, and race were then added as level-2 moderator variables to explore and control for their effects on the relationship between intrusion symptoms and the level-1 predictors. In-hospital intrusion was the only variable that was significantly impacted by the inclusion of gender, age, and race. Thus, ISS, gender, age, and race were dropped from subsequent slope equations. Results of the final model (see Table 5) indicated that the average intrusion
score at the in-hospital assessment significantly differed by age, race, and gender. Specifically, females (M = 9.92), minorities (M = 8.50), and younger individuals (M = 7.03 + .07 for every year that the individual is younger) scored higher on initial intrusion scores compared to their older, Caucasian male counterparts (M = 7.03). As predicted, intrusion symptoms significantly decreased with the passage of time by 1.52 for every increase in occasion and significant slopes for hyperarousal and for avoidance indicated that for each unit increase in hyperarousal and avoidance, intrusion increased .24 units and .16 units respectively. The deviance score for the final model was lower (7944.65) than the unconditional model (7977.92) and results of a chi-square difference test indicated ($\Delta \chi^2 [3] = 33.27, p < .005$) that the final model was a better fit. Due to the small percentage of minorities (13%) included in the sample results yielding significant differences by race should be interpreted with caution.

Hyperarousal. In addition, HLM analyses were conducted to examine the average within person change in hyperarousal symptoms given an increase in occasion, avoidance symptoms and intrusion symptoms. The model was built by entering occasion, avoidance, and intrusion as level-1 independent variables. Next, gender, ISS, and age were entered as level-2 moderator variables to control for and examine their effect on the relationship between hyperarousal and the level-1 predictors. Upon running this model, results indicated (see Table 6) that mean hyperarousal did not significantly vary by ISS and that ISS, age, and gender did not significantly contribute to within individual change in hyperarousal for any of the level-1 independent variables, hence, these variables were
Table 5

Effect of Time, Hyperarousal, and Avoidance on Intrusion Symptoms

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intra-Individual</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Intrusion (Intercept)</td>
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<tr>
<td>Occasion slope</td>
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<td>.00</td>
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<tr>
<td>Hyperarousal slope</td>
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<td>.04</td>
<td>.00</td>
</tr>
<tr>
<td>Avoidance slope</td>
<td>.16</td>
<td>.03</td>
<td>.00</td>
</tr>
<tr>
<td><strong>Inter-Individual</strong></td>
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<tr>
<td>Intrusion (Intercept)</td>
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<td>.00</td>
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<td>Gender</td>
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<tr>
<td>Race</td>
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<tr>
<td>Intercept</td>
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<td>Hyperarousal slope</td>
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<tr>
<td>Intercept</td>
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<td>.04</td>
<td>.00</td>
</tr>
<tr>
<td>Avoidance slope</td>
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</tr>
<tr>
<td>Intercept</td>
<td>.16</td>
<td>.03</td>
<td>.00</td>
</tr>
</tbody>
</table>

Intra-Individual N = 1267 units
Inter-Individual N = 386 units

Note. For Inter-individual models males and Caucasians are the comparison group. The intercept represents the average level of the outcome at the in-hospital assessment for Caucasian males of a mean age. The slope equations represent the relationships between hyperarousal and avoidance symptoms and the outcome variable (intrusion) for each individual’s observation.
Table 6
Effect of Time, Avoidance, and Intrusion on Hyperarousal Symptoms

<table>
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<tr>
<th>Variable</th>
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<th>SE</th>
<th>p-value</th>
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<td><strong>Intra-Individual</strong></td>
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<tr>
<td>Hyperarousal(Intercept)</td>
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<td>Avoidance slope</td>
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<td>.03</td>
<td>.00</td>
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<tr>
<td>Intrusion slope</td>
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<td>.03</td>
<td>.00</td>
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<tr>
<td><strong>Inter-Individual</strong></td>
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<td>Hyperarousal(Intercept)</td>
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<td>Intrusion slope</td>
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<tr>
<td>Intercept</td>
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<td>.03</td>
<td>.00</td>
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Intra-Individual N = 1267 units
Inter-Individual N = 386 units

Note. For Inter-individual models males are the comparison group. The intercept represents the average level of the outcome (hyperarousal) at the in-hospital assessment for males of a mean age. The slope equations represent the relationships between avoidance and intrusive symptoms and the outcome (hyperarousal) for each individual’s observation.
dropped from the model to improve fit. Thus, a final more conservative model was conducted and the final estimation of fixed effects with robust standard errors revealed that the mean hyperarousal score reported in-hospital was higher among participants that were female (M = 8.63) and/or young (M = 6.11 + .06 for every year that the individual is younger) compared to older male counterparts (M = 6.11). There was a marginally significant relationship between occasion and mean hyperarousal scores (p = .07) indicating that for each unit increase in occasion hyperarousal increased by .20 units, in other words hyperarousal symptoms increased with time. Mean avoidance and intrusion scores also significantly influenced within individual change in hyperarousal scores such that for every unit increase in avoidance and intrusion symptoms, hyperarousal increased by .29 and .24 units respectively. The deviance score for the final model was lower (7813.37) than the unconditional model (7836.38) and results of a chi-square difference test indicated ($\Delta \chi^2 [3] = 23.01, p < .005$) that the final model was a better fit.

Summary. HLM growth models partially supported the hypothesis that all symptom clusters would be elevated at the in-hospital assessment and gradually improve with time. Intrusion was the only symptom cluster to demonstrate improvement over time and did not significantly deviate with the inclusion of moderator variables. Avoidance symptoms did demonstrate the hypothesized decline over time but only within individuals that had a full memory for their MVA. Hyperarousal did not demonstrate a significant change over time but was suggestive of a trend indicating an increase in hyperarousal with the passage of time (See Figure 1). When comparing the rate at which all the symptoms recovered with time intrusion demonstrated the fastest rate of decline
Figure 1. Change in posttraumatic stress symptoms over time
and hyperarousal demonstrated the slowest rate of recovery, supporting our hypothesis that hyperarousal be the symptom cluster least likely to improve with time. In addition, results supported the hypothesis that hyperarousal was strongest predictor of change in intrusion and avoidance over time. While hyperarousal was the strongest predictor of change in the remaining symptom clusters, all symptoms impacted or predicted change in all the remaining symptom clusters, suggesting a reciprocal relationship between all PTSS (See Figure 2).

**Panel Analyses Predicting Chronic PTSS from Acute In-Hospital PTSS**

Hierarchical linear regressions or panel analyses were conducted to examine whether in-hospital assessments of each symptom cluster were predictive of subsequent chronic PTSD symptoms. Linear regressions yield results representative of an overall average across individuals at a given time point or an estimation of a group trajectory. A total of nine hierarchical linear regressions were conducted; 3 analyses for each symptom cluster predicting subsequent assessments conducted at 3 months, 6 months, and 1-year post-MVA. All analyses were 2-step models with control variables entered into the first step and in-hospital intrusion, avoidance, and hyperarousal added in the second step. However, each model had different control variables based on the results of the preliminary analyses discussed above.

**Avoidance.** Hierarchical linear regression analyses were conducted investigating the prediction of acute symptom clusters on chronic avoidance scores after controlling for gender (at 3 and 6 months), race (for predictions at 1 year), and amnesic status (for
Figure 2. Reciprocal relationship between all posttraumatic stress symptoms
predictions at 6 months and 1 year). The regression model was significant at all 3 time points (3 months, F[4, 202] = 11.11, p = .00; 6 months, F[5, 188] = 9.98, p = .00; 1 year, F[5, 168] = 7.31, p = .00). The amount of variance explained by each model was 18%, 21%, and 17.9% respectively (see Table 7). Further, individual variable contributions to the overall model revealed that gender and avoidance significantly contributed to the overall model at the 3-month follow-up. Gender, amnesic status, and hyperarousal significantly added to the model at the 6-month follow-up. Amnesic status and hyperarousal significantly added to the model at the 1-year follow-up. The significant contribution of amnesic status at the 6-month and 1-year assessments suggests that individuals with little or complete accident-specific memory loss scored higher on avoidance subscales compared to those with full memory of their accident.

_Intrusion._ Similar hierarchical linear regression analyses were conducted to examine the extent to which in-hospital subscale scores predicted chronic intrusion scores after controlling for gender (in all regressions) and ISS (for predictions at 3 months) and age (for predictions at 6 months). The regression model indicated that the group trajectory, across individuals, was significant at all 3 time points (3 months, F[5, 201] = 8.88, p = .00; 6 months, F[5, 188] = 10.60, p = .00; 1 year, F[4, 169] = 9.66, p = .00). The amount of variance explained by each model was 18.1%, 22%, and 18.6% respectively (see Table 8). Further individual variable contributions to the overall model revealed that gender and hyperarousal were the only predictors that significantly added to the estimated group trajectory for all 3 time points.
Table 7

Hierarchical Regression Predicting Intrusion

<table>
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<th>Step</th>
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<th>β</th>
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<th>S E B</th>
<th>ΔR²</th>
<th>F of ΔR²</th>
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<td>Predicting Intrusion at 6 months (N=208)</td>
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</tr>
<tr>
<td>1. Gender</td>
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<td>.18*</td>
<td>2.01</td>
<td>.83</td>
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<td>5.90*</td>
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<tr>
<td>2. In-hospital Hyperarousal</td>
<td>.19</td>
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<td></td>
<td>9.66**</td>
<td></td>
</tr>
<tr>
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<td>.35</td>
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<td>.15</td>
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</table>

**p<.01,*p<.05
Table 8

Hierarchical Regression Predicting Avoidance

<table>
<thead>
<tr>
<th>Step</th>
<th>R²</th>
<th>β</th>
<th>B</th>
<th>S E B</th>
<th>ΔR²</th>
<th>F of ΔR²</th>
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</tr>
<tr>
<td>1. Gender</td>
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<td>3.67</td>
<td>1.07</td>
<td>.05</td>
<td>11.74**</td>
</tr>
<tr>
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<td>.11</td>
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<td>.17</td>
<td>.13</td>
<td></td>
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</tr>
<tr>
<td>Avoidance</td>
<td>.18*</td>
<td>.22</td>
<td>.09</td>
<td></td>
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</tr>
<tr>
<td>Amnesic Status</td>
<td>.31**</td>
<td>5.16</td>
<td>1.13</td>
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<td>2. In-hospital</td>
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<td>.13</td>
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<td>.33</td>
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<td>.12</td>
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<tr>
<td>Predicting Avoidance at 1 year (N=189)</td>
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</tr>
<tr>
<td>1. Race</td>
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<td>-.23</td>
<td>1.53</td>
<td>.09</td>
<td>8.26**</td>
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<td>Amnesic Status</td>
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<td>2. In-hospital</td>
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<td>7.31**</td>
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<tr>
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<td>.13</td>
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<tr>
<td>Hyperarousal</td>
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<td>.34</td>
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<td>.01</td>
<td>.13</td>
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</tr>
</tbody>
</table>

**p<.01,*p<.05
Hyperarousal. Additional regression analyses were conducted to examine the extent to which in-hospital subscales predicted chronic hyperarousal after controlling for gender (for all regressions) and ISS (for the 3-month follow-up only). Results indicated that all regression models were significant at all time points (3 months, F[5, 201] = 12.0, p = .00; 6 months, F[4, 189] = 14.88, p = .00; 1 year, F[4, 169] = 6.95, p = .00). The amount of variance explained by each model was 26.6%, 24%, and 14.1% (see Table 9). The contribution of ISS scores to the overall model suggests that individuals with low ISS scores were more likely to score higher on the hyperarousal subscale at 3 months. These results represent an estimation of an overall average across individuals at a given time point and they are estimations of group trajectories.

Table 9
Hierarchical Regression Predicting Hyperarousal

<table>
<thead>
<tr>
<th>Step</th>
<th>R²</th>
<th>β</th>
<th>B</th>
<th>S E B</th>
<th>ΔR²</th>
<th>F of ΔR²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Predicting Hyperarousal at 3 months (N=223)

1. ISS .10 -.13* -.13 .07 .10 11.99**
       Gender .27 .27* 3.67 .84
2. In-hospital Intrusion -.01 -.01 .08
       Avoidance .05 .05 .07
       Hyperarousal .38* .41 .11

Predicting Hyperarousal at 6 months (N=208)

1. Gender .20 .20* 3.18 1.10 .04 8.40**
2. In-hospital Intrusion -.01 -.01 .10
       Avoidance .02 .03 .09
       Hyperarousal .45** .60 .14

Predicting Hyperarousal at 1 year (N=189)

1. Gender .01 .08 1.29 1.17 .01 1.20
2. In-hospital Intrusion .08 .08 .11
       Avoidance .01 .02 .11
       Hyperarousal .30** .40 .15

**p<.01
Summary. Results of the hierarchical linear panel analyses consistently indicated that in-hospital PTSS symptoms predicted chronic PTSD symptoms at 3-, 6-, and 12-months post MVA. With the exception of in-hospital avoidance predicting avoidance at 3-months, hyperarousal was the only symptom cluster to significantly contribute to the overall regression models for all 3 symptom clusters, supporting the hypothesis that hyperarousal is the one symptom cluster most likely to predict change in all PTSD symptom clusters. Furthermore, gender also consistently contributed significantly to the majority of the models, suggesting that gender may play a significant role in symptom presentation and change.

Hierarchical linear panel regressions were conducted in addition to HLM growth models to allowed for an examination of the effect of each in-hospital assessment on each isolated assessment of chronic symptoms rather than an over all trajectory. However, because regressions do not have the advantage of taking into account the interdependence of observations over time and yield results that represent within individual change over time HLM growth models were conducted to examine within individual change over time and the moderation of group membership on within individual change in each PTSS.

Lagged HLM Growth Models Predicting Chronic PTSS from Acute In-Hospital PTSS Symptoms

To test the hypothesis that earlier PTSS would predict later, more chronic, PTSS at the follow-up assessments three new acute variables were created. The purpose of creating acute variables was to examine and control for the impact of the in-hospital assessment, thus providing a model that would allow for the prediction of subsequent
symptoms by earlier symptoms. Aside from hyperarousal, intrusion, and avoidance, three additional variables, acute avoidance, acute intrusion, and acute hyperarousal were created using the existing data from the original data set used for previous HLM growth model analyses. The values of new data set were identical to that of the original data set; however, the first two time points represented for each acute PTSS were identical to the first time point in the original data set. For example an individual that scored a 3, 3, 2, 1, and 0, respectively, on hyperarousal assessments from in-hospital to 1-year post-accident would have an acute variable that would read 3, 3, 2, and 1. The last value from the original hyperarousal variable, 0, is dropped and is adequately accounted for by HLM. All acute variables were used as level I predictors. Level-2 moderators used for each lagged model were based on preliminary analyses and thus were different for each symptom cluster.

Avoidance. HLM analyses were conducted to examine the average within person change in later, more chronic avoidance symptoms when predicted by occasion and earlier PTSS. The model included occasion, acute intrusion, acute hyperarousal, and acute avoidance as level-1 independent variables. Next gender, age, and, amnesic status were entered as level-2 control variables and chronic avoidance was the only variable that significantly differed by these variables. The final estimation of fixed effects with robust standard errors (see Table 10) indicated that the average chronic avoidance scores differed by gender, age, and amnesic status such that females (M = 8.13), individuals with little or no memory (M = 8.76), and younger individuals (M = 4.96 + .04 for every year the person is younger) had significantly higher chronic avoidance symptoms.
Table 10

Effect of Time and Acute PTSS on Chronic Avoidance Symptoms

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intra-Individual</strong></td>
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<td></td>
</tr>
<tr>
<td>ChronicAvoidance(Intercept)</td>
<td>8.92</td>
<td>.35</td>
<td>.00</td>
</tr>
<tr>
<td>Occasion slope</td>
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<td>.57</td>
</tr>
<tr>
<td>Acute Avoidance</td>
<td>.06</td>
<td>.05</td>
<td>.15</td>
</tr>
<tr>
<td>Acute Hyperarousal slope</td>
<td>-.15</td>
<td>.05</td>
<td>.00</td>
</tr>
<tr>
<td>Acute Intrusion slope</td>
<td>.12</td>
<td>.05</td>
<td>.02</td>
</tr>
<tr>
<td><strong>Inter-Individual</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ChronicAvoidance(Intercept)</td>
<td>4.96</td>
<td>.50</td>
<td>.00</td>
</tr>
<tr>
<td>Intercept</td>
<td>-.04</td>
<td>.01</td>
<td>.02</td>
</tr>
<tr>
<td>Gender</td>
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<td>.67</td>
<td>.00</td>
</tr>
<tr>
<td>Amnesic</td>
<td>3.80</td>
<td>.52</td>
<td>.00</td>
</tr>
<tr>
<td>Occasion slope</td>
<td>.05</td>
<td>.18</td>
<td>.78</td>
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<td><strong>Acute Avoidance</strong></td>
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</tr>
<tr>
<td>Intercept</td>
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<td>.05</td>
<td>.20</td>
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<tr>
<td><strong>Acute Hyperarousal slope</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-.15</td>
<td>.06</td>
<td>.00</td>
</tr>
<tr>
<td><strong>Acute Intrusion slope</strong></td>
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</tr>
<tr>
<td>Intercept</td>
<td>.12</td>
<td>.05</td>
<td>.02</td>
</tr>
</tbody>
</table>

Intra-Individual N = 1267 units
Inter-Individual N = 386 units

Note. For Inter-individual models males and individuals with full memory of their MVA are the comparison group. The intercept represents the average level of the outcome (chronic avoidance) at the 6 week assessment for males of a mean age with full memory of their MVA. The slope equations represent the relationships between acute PTSS and the outcome (chronic avoidance) for each individual’s observation.
compared to their older male counterparts that had full memory of their MVA (M = 4.96). Contrary to our hypothesis, early avoidance did not predict a significant within individual change in average chronic avoidance. However, early symptoms of hyperarousal and intrusion did predict a significant change in avoidance symptoms at subsequent time points. For every increase in acute hyperarousal, chronic avoidance symptoms decrease by .15 units and for every unit increase in acute intrusion symptoms, avoidance symptoms increased by .12 units, suggesting that while acute hyperarousal appeared to attenuate within individual change in chronic avoidance, acute intrusion symptoms help to maintain chronic avoidance. The deviance score for the final model was lower (8230.58) than the unconditional model (8295.22) and results of a chi-square difference test indicated ($\Delta \chi^2 [2] = 64.64, p < .005$) that the final model was a better fit.

*Intrusion.* Another HLM analysis examined the average within individual change in later, more chronic intrusion symptoms using occasion, acute avoidance, acute hyperarousal, and acute intrusion as level-1 predictor variables. Next, gender, ISS, age, and race were entered as level-2 moderator variables to control for and examine their effect on the relationship between chronic intrusion symptoms and the level-1 predictors. Because chronic intrusion symptoms and all acute PTSS did not significantly differ by these control variables they were dropped from the model. The final estimation of fixed effects with robust standard errors for this model (see Table 11) indicated that chronic intrusive symptoms significantly decreased across occasions such that for every increase in occasion, intrusion symptoms decreased by 1.6 units. All other relationships between acute PTSS predictors and chronic intrusion symptoms were not significant.
Table 11

Effect of Time and Acute PTSS on Chronic Intrusion Symptoms

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-Individual</td>
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</tr>
<tr>
<td>ChronicIntrusion(Intercept)</td>
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<td>Occasion slope</td>
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<td>Acute Intrusion slope</td>
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<td>Acute Hyperarousal slope</td>
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<td>.04</td>
<td>.13</td>
</tr>
<tr>
<td>Acute Avoidance slope</td>
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<td>.13</td>
</tr>
<tr>
<td>Inter-Individual</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results remained insignificant

Intra-Individual N = 1267 units
Inter-Individual N = 386 units

Note. The intercept represents the average level of the outcome (chronic intrusion) at the 6 week assessment. The slope equations represent the relationships between acute PTSS and the outcome variable (chronic intrusion) for each individual’s observation.

Hyperarousal. Additional HLM analyses were conducted to predict the average within individual change in chronic hyperarousal symptoms. This model was built by entering occasion, acute avoidance, acute hyperarousal and acute intrusion as level-1 independent variables. Next, gender, and age were entered as level-2 moderator variables to control for and examine their effect on the relationship between chronic hyperarousal symptoms and the level-1 predictors.

Upon running this model, results indicated that age and gender did not significantly contribute to within individual change for any of the level-1 independent variables; hence, these variables were dropped from the model to improve fit. Thus, a final more conservative model was conducted and the final estimation of fixed effects
with robust standard errors revealed that chronic hyperarousal was higher among participants that were female (M = 8.61) and/or young (M = 6.17 + .05 for each year the person is younger) compared to older male counterparts (M = 6.17). Occasion and acute avoidance did not significantly predict chronic hyperarousal. However, for every unit increase in acute hyperarousal, chronic hyperarousal decreased by .14 units and for every unit increase in acute intrusion, chronic hyperarousal symptoms increased by .20 units. The deviance score for the final model was lower (7815.77) than the unconditional model (7834.27) and results of a chi-square difference test indicated ($\Delta \chi^2 [2] = 18.40, p < .005$) that the final model was a better fit (see Table 12 for results).

Summary. In sum, early avoidance did not predict within individual change in any of the PTSS at the later time points. However, chronic avoidance was significantly predicted by early symptoms of intrusion and hyperarousal but in opposite directions. Consistent with previous findings, early intrusive symptoms slowed down the rate of recovery in chronic avoidance symptoms. However, results indicated that acute hyperarousal attenuated the within individual change in avoidance and in hyperarousal. Early intrusion symptoms also caused the rate of recovery of chronic hyperarousal symptoms to slow down. While intrusion symptoms still demonstrated a significant change over time such that within individual change in intrusion symptoms recovered with each occasion, none of the acute PTSS predicted within individual change in chronic intrusion symptoms.
Table 12

Effect of Time and Acute PTSS on Chronic Hyperarousal Symptoms

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intra-Individual</strong></td>
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</tr>
<tr>
<td>ChronicHyperarousal(Intercept)</td>
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<td>.00</td>
</tr>
<tr>
<td>Occasion slope</td>
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<td>Acute Hyperarousal slope</td>
<td>-.14</td>
<td>.04</td>
<td>.00</td>
</tr>
<tr>
<td>Acute Avoidance slope</td>
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<td>.04</td>
<td>.73</td>
</tr>
<tr>
<td>Acute Intrusion slope</td>
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<td>.04</td>
<td>.00</td>
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<tr>
<td><strong>Inter-Individual</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>ChronicHyperarousal(Intercept)</td>
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<td>.35</td>
<td>.00</td>
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<tr>
<td>Intercept</td>
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<td>.02</td>
<td>.00</td>
</tr>
<tr>
<td>Gender</td>
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</tr>
<tr>
<td>Occasion slope</td>
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<tr>
<td>Intercept</td>
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<td>.04</td>
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</tr>
<tr>
<td>Acute Avoidance slope</td>
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<td>.72</td>
</tr>
<tr>
<td>Intercept</td>
<td>.20</td>
<td>.04</td>
<td>.00</td>
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</tbody>
</table>

Intra-Individual N = 1267 units
Inter-Individual N = 386 units

Note. For Inter-individual models males of a mean age are the comparison group. The intercept represents the average level of the outcome (chronic hyperarousal) at the 6 week assessment for males of a mean age. The slope equations represent the relationships between acute PTSS symptoms and the outcome (chronic hyperarousal) for each individual’s observation.
HLM Linear Growth Models Examining Whether Urinary Hormones Predict Change in Subscale Scores Over Time

HLM growth models were conducted to test whether both cortisol and catecholamines would predict the average within individual change in PTSD symptom clusters. Each model included occasion, the remaining 2 symptom clusters, and cortisol and or catecholamines as level-1 predictor variables. All moderator variables were entered at level-2 to control for and examine their effect on the relationship between each symptom cluster and the level-1 predictors. Level-2 moderators were identical to the first set of HLM growth models reported above. Each HLM model was conducted 3 different ways using only the 0-5 hr urine specimen, only the 5-10 hr urine specimen, and using an average of the two specimens to represent the in-hospital assessment of cortisol and catecholamines. All 3 types of analyses were conducted using the entire sample (N=386) and samples that excluded individuals with contraindications for cortisol (N=324) and catecholamines (N= 306). All analyses using urinary stress hormones to predict intra-individual change in mean PTSS produced no significant findings, failing to support the study hypothesis that cortisol and/or catecholamine levels would predict the onset and temporal progression of PTSS. Descriptive statistics for cortisol, epinephrine, and norepinephrine at each time point are reported in Table 13 and a representation of changes in urinary stress hormones over time is illustrated in Figure 3.

In addition, hierarchical linear regression analyses were conducted to test whether cortisol and catecholamine levels at each time point predict PTSS at subsequent time points and all relationships were non-significant (p>.05).
Table 13

Means and Standard Deviations for Urinary Stress Hormones at Each Time Point

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
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</thead>
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<td><strong>Inhospital</strong></td>
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</tr>
<tr>
<td>0-5hr cortisol</td>
<td>302</td>
<td>34.90</td>
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<tr>
<td>5-10hr cortisol</td>
<td>288</td>
<td>37.41</td>
<td>81.98</td>
</tr>
<tr>
<td>0-5hr epinephrine</td>
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<td>27.94</td>
<td>33.23</td>
</tr>
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<td>17.77</td>
</tr>
<tr>
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<tr>
<td>5-10hr norepinephrine</td>
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<td><strong>3 month assessment</strong></td>
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<tr>
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<td>7.72</td>
</tr>
<tr>
<td>norepinephrine</td>
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<td>29.88</td>
<td>17.16</td>
</tr>
<tr>
<td><strong>6 month assessment</strong></td>
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<td>22.46</td>
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<tr>
<td>epinephrine</td>
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<td>4.20</td>
</tr>
<tr>
<td>norepinephrine</td>
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<td>14.09</td>
</tr>
<tr>
<td><strong>1 year assessment</strong></td>
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<tr>
<td>cortisol</td>
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<td>epinephrine</td>
<td>80</td>
<td>3.97</td>
<td>3.94</td>
</tr>
<tr>
<td>norepinephrine</td>
<td>79</td>
<td>29.29</td>
<td>15.96</td>
</tr>
</tbody>
</table>

units of measurement for cortisol were µg/dL
units of measurement for epinephrine and norepinephrine were µg/g creatinine
Figure 3. Change in urinary stress hormones over time
HLM Linear Growth Models Examining Whether Change in Urinary Stress Hormones Over Time Differs by Chronic PTSS Status

HLM analyses were conducted to test whether individuals with greater chronic PTSS would have lower urinary cortisol and higher catecholamine levels immediately post-MVA and would continue to have lower cortisol and higher catecholamine levels throughout recovery compared to MVA survivors with little to no PTSS. Prior to running these analyses, a total of the 3-month, 6-month, and 1-year assessments were computed for each individual subscale and a median split was computed for each subscale total score resulting in high and low groups for each PTSD symptom cluster. All HLM analyses were conducted with all of the original 386 participants included in the study; however, all models were nonsignificant for each urinary stress hormone by each subscale median split. Furthermore, participants’ records were screened for medications or physical illness that could potentially interfere with the urinary stress hormone levels under investigation and histograms and box-and-whisker plots were created to identify potential outliers. Subsequent analyses were conducted using 324 participants for analyses that examined only cortisol as an outcome variable, and 306 individuals for analyses that examined only catecholamine levels as an outcome.

Cortisol. The model included occasion as the only level-1 predictor variable and chronic high/low status as the level-2 moderator variable. Results of the HLM growth models examining cortisol over time by high and low subscale groups indicated that change in cortisol over time did not significantly differ by chronic intrusion or avoidance. Cortisol levels did differ by hyperarousal groups on the day of the accident (β = -.28, S.E.
= .13, p = .035) and over time (β = .26, S.E. = .09, p = .00) such that individuals that scored high on chronic hyperarousal had lower mean cortisol levels (high group M= 2.90 vs. low group M = 3.18) on the day of their MVA and had a slower rate of decline in cortisol over time compared to individuals that scored lower on chronic hyperarousal (low group β = -1.00, S.E. = .07, p = .00). The HLM growth model looking at cortisol over time by high/low hyperarousal scores yielded a lower deviance score than the unconditional model, the chi-squared difference test yielded nonsignificant results (p > .1). Hence, there were no significant difference in fit between the unconditional model and the conditional model.

*Catecholamines.* Neither epinephrine nor norepinephrine levels significantly differed by high/low hyperarousal, avoidance, or intrusion groups (all p’s > .1).
The purpose of the present study was to prospectively examine the relationships between and among physiological and psychological responses to trauma, beginning shortly after a motor vehicle accident (MVA) and continuing until a 1-year follow-up. Based on prior research that examined symptom cluster change over time (Marshall et al., 2006; Schell et al., 2004), the present study hypothesized that PTSS would be highest shortly following a MVA and would gradually decline over time, indicating symptom improvement. Unlike Schell and colleague’s (2004) previously reported decline in all symptom clusters over time, this hypothesized trajectory was not consistently supported in all symptom clusters in the present study. Symptoms of intrusion and symptoms of avoidance, only among individuals with a full memory of their MVA, were elevated at the in-hospital assessment and declined with the progression of time. Conversely, avoidance symptoms among individuals with little to complete memory loss increased with time. In addition, a marginally significant increase in hyperarousal symptoms suggested little change and no recovery over time.

Based on the vast literature examining the effects of memory on PTSD there may be many explanations that support the unexpected increase in avoidance symptoms over time, among amnesic individuals. While some research suggests that memory loss may
protect against the development of PTSS and subsequent PTSD diagnosis (Gil, et al., 2005), others suggests that increases in avoidance symptoms over time may be attributed to the disorganized and fragmented nature of trauma-related memories (Foa & Riggs, 1993). During a traumatic event, experiencing feelings of intense helplessness and horror may interrupt the integration and normal processing of new information, resulting in the formation of highly salient but fragmented memories (Brewin, 2001). Research emphasizing the ameliorating effects of exposure therapy lends support to the notion that memory fragmentation, as a result of trauma exposure, results in increases in PTSS. Trauma exposure therapy works by systematically exposing individuals to traumatic memories with the intension of helping the trauma survivor produce a more organized representation of their traumatic event (Foa & Meadow, 1997; Foa et al., 1995). Thus is it likely that individuals with amnesia may have difficulty processing or making sense of trauma-related information due to fragmented memories causing the development and/or maintenance of avoidance symptoms over time.

Alternatively, study participants with little to complete memory loss for their MVA may have scored higher on the avoidance subscale because they have no memory, rather than because they are actively avoiding thoughts or feelings related to their MVA. Or, loss of memory for their traumatic MVA may not be attributed to post-traumatic stress but may be a result of an accident-related injury such as a head trauma. Results of the present study underscore the importance of considering the impact of amnesia or memory.
The present study’s inability to replicate Schell and colleague’s decline in hyperarousal symptoms over time may have been due to the difference in sample characteristics between both studies. Schell and colleagues (2004) sample consisted of minority men that had been victims of community, which necessitated surgery for incurred injuries. Compared to the present study, the interpersonal nature of the trauma as well as the potential involvement of more severe injuries sustained by the participants, it is probable that initial symptoms of hyperarousal may have been more extreme resulting in a more significant decline in symptom expression over time. Alternatively, given that the present sample included a very small amount of individuals that were subsequently diagnosed with PTSD; this may suggest that individuals that do not develop PTSD do not demonstrate a specified hyperarousal pattern over time. Furthermore, these results may highlight the significance of examining hyperarousal from a more curvilinear perspective. The present study’s examination of linear symptom trajectories may have underscored the importance of symptom fluctuation with time.

The present study also hypothesized that hyperarousal would be the most likely symptom cluster to demonstrate the least amount of symptom improvement. In support of this hypothesis we found that hyperarousal symptoms demonstrated the least amount of change with time, in comparison with avoidance and intrusion symptoms. The results of the present study indicating that hyperarousal is the symptom cluster least likely to show improvement with the progression of time has important ramifications for clinical approaches to posttraumatic stress treatment. It may be that hyperarousal symptoms are the most consistent of the three symptom clusters, suggesting that they may be the most
difficult to recover from and ultimately the most important symptom cluster to be targeted through therapeutic or pharmacological intervention.

Results of HLM analyses also provided insight into the reciprocal relationship between all the symptom clusters over time. In support of the proposed hypothesis and in accordance with previous research, all symptom clusters were associated with maintenance in PTSS over time. More specifically, results indicated that hyperarousal was the strongest predictor of change in intrusion and avoidance symptoms over time. These results provide important insights into PTSD course and suggest a variety of treatment and therapy options that might help to prevent the development of PTSD following a traumatic experience. Given that hyperarousal was found to be the most significant predictor of the symptom clusters, pharmacological or psychological interventions specifically addressing hyperarousal symptoms may be efficacious at reducing PTSD symptoms. For example, primary intervention strategies might include the use of meditation or relaxation techniques to provide trauma survivors with the adequate tools to cope with their hyperarousal symptoms. In addition, these results also lend support to secondary intervention studies (Pitman et al., 2002; Vaiva et al., 2003) that use pharmacological interventions such as beta-blockers to reduce the anxiety of trauma-related memories thereby, preventing the subsequent development of PTSD.

While hyperarousal influenced the most change in intrusion and avoidance symptoms over time, our findings also indicated that both intrusion and avoidance also contributed to the slowed recovery and ultimate maintenance of the remaining PTSS over time, however to a lesser degree than was indicated by hyperarousal. These results
provide little support for any one theory suggesting that either intrusion or avoidance alone are predominantly influence the remaining symptom clusters. The present study’s results were partially supported by Schell and colleagues (2004) findings that indicated that intrusion symptoms had a small but significant effect on change in PTSS over time, but were contrary to the findings that avoidance did not contribute to PTSS change over time. Results of the present study were also supported by Horowitz’s theory (2001) that suggested that avoidance symptoms emerge first, following a traumatic event and are subsequently followed by intrusion symptoms and Creamer’s theory (1992) that suggested that intrusion symptoms appear first, which lead to avoidance symptoms. Or still yet, our results could support the theory that intrusion and avoidance symptoms co-exist in a cyclical pattern, each impacting a change in the other (Horowitz, 1986; Foa et al., 1995). Due to the strength of initial hyperarousal symptoms evident at the in-hospital assessment it probable that, like that of Bremner, et al., 1996, hyperarousal symptoms precede avoidance and intrusion symptoms and as time progresses more hyperarousal symptoms are produced as a result of intrusion and avoidance symptoms, creating a dynamic cycle.

The present study also proposed that acute PTSS, reported in-hospital, would predict chronic PTSS. Results of regression analyses indicated that in-hospital hyperarousal was the most significant predictor chronic hyperarousal, intrusion, and avoidance symptoms at the 3-, 6-, and 12-month follow-up assessments. Furthermore, regression analyses indicated that neither in-hospital intrusion nor avoidance contributed to the prediction of chronic hyperarousal at any of the later time points. Because these
panel analyses represent an overall average across individuals at a specific time point, and are not able to look at overall averages within each individual across time, additional HLM analyses were conducted to examine overall averages within each individual across time as well as between group variability, within each individual over time.

As previously explained, HLM lagged models allow for the examination and control for the impact of earlier assessments, thus providing a model that would allow for the prediction of subsequent symptoms by earlier symptoms. Results of these lagged analyses indicated that while chronic intrusion symptoms significantly decreased with time, chronic avoidance and hyperarousal did not. Upon comparing these results with our previous analyses that looked only at change over time in PTSS, the relationships between occasion and intrusion and occasion and hyperarousal were consistent with earlier models.

Additionally, early hyperarousal symptoms attenuated the within individual change in mean chronic avoidance and mean chronic hyperarousal, suggesting that individuals with higher early hyperarousal symptoms were likely to have a faster rate of recovery in later, more chronic avoidance and hyperarousal. This relationship may suggest that individuals that have more hyperarousal at the time of their MVA should recover more quickly or potentially be at less risk of receiving a subsequent PTSD diagnosis (Ozer et al., 2003). While this result contradicts previous HLM growth model analyses, this inconsistent finding is supported by prior research that suggests the opposite relationship; that individuals that have a blunted physiological response to their traumatic event during or immediately following their trauma are at increased risk for
developing PTSD (Delahanty et al., 2003; Griffin, Resick, & Mechanic, 1997).

Individuals that might likely fall into this category of low physiological responders may be individuals that dissociate during or immediately following their trauma. Laboratory and naturalistic studies have demonstrated that peri-traumatic dissociative symptoms are associated with lower physiological arousal during trauma or to trauma cues (Delahanty et al., 2003; Griffin, Resick, & Mechanic, 1997). Future studies that examine the prospective relationship between PTSD symptom clusters over time would benefit from the inclusion of peritraumatic dissociation as a predictor and/or moderator of change in PTSS.

In addition HLM lagged models revealed that acute intrusion symptoms predicted an increase in chronic avoidance and chronic hyperarousal symptoms, suggesting that acute intrusion symptoms predicted the course of chronic hyperarousal and avoidance symptoms. Considering this finding in addition to the finding that acute avoidance did not predict chronic PTSS, our results might suggest that intrusion symptoms are more likely to emerge first, immediately following a traumatic event with avoidance symptoms to follow (Creamer et al., 1992).

As an extension of the current literature (Marshall et al., 2006; O’Donnell et al., 2007; Schell et al, 2004), it was hypothesized that both cortisol and catecholamines, a manifestation of physiological hyperarousal, would predict the formation of PTSD symptom clusters over time. We were unable to find support that any of the urinary stress hormones (cortisol, epinephrine, or norepinephrine) contributed to the onset or temporal progression of PTSS. Inability to find support for this hypothesis was likely due to small
sample size and inadequate power; however, it is also likely that these results suggest that urinary stress hormone levels are correlates rather than predictors of posttraumatic stress.

In addition, it was hypothesized that change in cortisol and catecholamines over time would differ by individuals that scored high or low on chronic PTSS, based on research suggesting that individuals subsequently diagnosed with PTSD have a specific neuroendocrine profile. The results did not fully support the propose hypothesis, such that change in cortisol over time did not differ by high/low chronic intrusion or avoidance groups, but did differ by high/low hyperarousal groups. Results indicated that individuals that scored high on chronic hyperarousal had lower mean cortisol levels on the day of their MVA and had a slower rate of recovery over time compared to individuals that scored lower on chronic hyperarousal. Additionally, the present study failed to find support for the hypothesis that change in catecholamines over time would differ significantly by high or low chronic PTSS groups.

Limitations of the Present Study

A number of limitations to the present study suggest caution in interpreting the findings. The current study sample consisted of a relatively homogenous group of severely injured, Caucasian MVA survivors. Only 11 MVA survivors were subsequently diagnosed with PTSD, potentially contributing to our inability to support or replicate previous research findings that were based on a larger population of PTSD diagnosed individuals. While the examination of acute symptoms as well as symptom trajectories within nonPTSD diagnosed individuals are as important as examining chronic PTSS and subsequent diagnosis, the present study may have benefited from a closer examination of
individuals that have some but not all the symptoms of PTSD; individuals with subthreshold PTSD. Furthermore, our homogeneous sample made comparisons among racial/ethnic backgrounds and types of trauma difficult and questioned the ability to generalize our results to other populations.

Additionally, because the present study was part of a larger grant study conducted to primarily investigate acute PTSD and biological correlates of PTSD, it was not designed with the intention of examining more chronic PTSS. Thus, administration of the same measure of PTSD symptomatology was not consistent throughout all time points. While it was not appropriate to give the CAPS in the immediate aftermath of a traumatic event due to the inability to diagnose an individual with PTSD that soon after a trauma, the present study would have benefited from the inclusion of the CAPS at the 3-month follow-up, either in place of or in addition to IES-R self-report measure. The CAPS was not given at the 3-month follow-up because this time point was designated as a time for the collection of physiological samples. Given the amount of time the participant was required to invest in collecting physiological samples and completing a battery of self-report questionnaires, it did not seem feasible to conduct another clinician-guided interview at this time point. However, in order to have enough statistical power to test the hypothesized relationships, the present study had to use both self-report measures as well as clinician administered measures to compile enough time points. Thus, differing assessment modalities may have affected the ability to detect significant differences in symptom clusters over time.
Additionally, for ease of interpretation the present study implemented the use of time points or occasions to measure change over time. This choice may have limited the variability in our results, as not all subjects were assessed exactly at the 6-week, and 3-, 6-, and 12-month periods. Future research would benefit from the inclusion of days and assessment time points as a unit of time to more accurately assess change in PTSS over time.

Another limitation of the study is the small sample used for the HLM analyses that examined change in urinary stress hormones over time. Our limited sample was primarily due to a change in the conduct of biological assays. The change in assay procedure yielded results that were inconsistent with the original procedure, which prompted the disposal of a substantial amount of urine specimens. Thus, due to the limited amount of urinary stress hormone data available, analyses investigating the growth trajectory of cortisol and catecholamines did not include control variables or covariates, so as to not further jeopardize the power of these statistical tests. Imputation was considered; however, given that current literature is largely mixed on the relationship between PTSS and stress hormones it would have been difficult to decide which variables would make the most theoretical sense on which to base participant matching. Furthermore, since biological analyses were exploratory in nature, the present study chose only to look at the change in urinary stress hormones by a dichotomous representation of each subscale score. The choice to examine change by high/low subscale groupings may have also limited the variability in results.
**Future Directions**

As our findings suggest hyperarousal symptoms are paramount to the onset and progression of PTSS. Specific hyperarousal symptoms such as sleep disturbances, following trauma exposure, have been found to reliably predict PTSS and subsequent PTSD diagnosis (Mellman & Hipolito, 2006). Thus, future research should more closely examine the specific types of hyperarousal (e.g. increased startle response, difficulty sleeping) that might be driving this relationship. As implemented in the present study, more research would benefit from the examination of physiological measures of hyperarousal in addition to self-reports of hyperarousal symptoms. Future research examining the relationship between PTSS and stress hormones associated with these symptoms might utilize a daily-diary design in which individuals would be required to report daily symptoms of avoidance, intrusion, and hyperarousal as well as collect biological samples at various time points throughout the day.

In addition, future research investigating the dynamic interplay between PTSS and between PTSS symptoms and biological alterations associated with PTSS would benefit from a more complete model that might include additional moderator variables, such as personal trauma history, individual coping strategies utilized to pacify unwanted recollections of a traumatic event, and the availability of social support networks, which may account for discrepancies found regarding the onset and progression of PTSS over time. Additionally, prior research has suggested that PTSS can increase, decrease, or consistently fluctuate with time. Hence, future research should recognize that PTSD symptom progression is not always a linear trajectory. Thus other non-linear and
curvilinear trajectories, as previously examined by O’Donnell and colleagues (2007), should be used when prospectively examining changing PTSD symptom clusters and physiological correlates over time.

In summary, we used a variety of hierarchical linear models as well as linear regression analyses to examine the reciprocal relationships between PTSS and between PTSS and urinary stress hormones. Results indicated that intrusion, avoidance, and hyperarousal symptoms interact with each other to influence symptom presentation and course. Hyperarousal consistently demonstrated the most influence on itself as well as symptoms of intrusion and avoidance. Results were unable to determine whether urinary stress hormones predict or change the onset and course of individual symptom clusters over time. These findings highlight the important role that psychological symptoms of hyperarousal play in posttraumatic stress and suggest that future research that examines the physiological expression of hyperarousal over time may provide more insight into the mechanisms by which hyperarousal predicts and influences symptom progression and maintenance over time.
REFERENCES


catecholamine excretion and severity of PTSD symptoms in Vietnam combat


negative feedback inhibition as examined using the ACTH response to cortisol
administration in PTSD. *Psychoneuroendocrinology, 31,* 447-451.
APPENDIX A

MINI MENTAL STATE EXAMINATION (MMSE)
MINI MENTAL STATE EXAMINATION (MMSE)

1.) What is the date?  Probe for: (year) (date) (day) (month) (season)
   1 point for each. **Max score is 5**
   ________

2.) Can you tell me where we are right now?  Probe for: (country) (state)
   (county) (city) (hospital)
   1 point for each. **Max score is 5**
   ________

3.) I'm going to name three objects. After I have said them, I want you to
   repeat them. Remember what they are because I am going to ask you to
   name them again in a few minutes. Say 1 work per second: APPLE,
   TABLE, PENNY (repeat until they hear all three). Please repeat the
   names for me
   1 point per word. **Max score is 3**
   ________

4.) Subtract 7 from 100, and keep subtracting 7 from each answer. (93, 86,
   79, 72, 65). If the patient refuses or cannot do this at all: Now spell
   this word forwards and backwards. The word is WORLD. First spell it
   forward (if able to do this) Now spell it backwards
   (record response :_________)
   1 point per number; or for DLROW, count 1 error for each omission,
   transposition, and insertion of letters (i.e. DLOW=4 (omission);
   DLTOW=3(omission and insertion); DLORW=4 (transposition).
   **Max score is 5**
   ________

5.) Ask the patient to recall the three words that you told them once again.
   (Apple, table, penny)
   **Max score is 3**
   ________

6.) Show the patient a wristwatch and ask him/her what it is. Do the same
   with a pen/pencil.
   **Max score is 2**
   ________

7.) Read the words on this page, then do what it says ("Close your eyes";
   written on back of form)
   **Max score is 1**
   ________

8.) Repeat this phrase after me: "no if's, and's or but's".
   **Max score is 1**
   ________

Score
APPENDIX B

STUDY CONSENT FORM
STUDY CONSENT FORM

Project Title:  Peritraumatic psychophysiological predictors of well-being following motor vehicle accidents

Investigators:  Douglas L. Delahanty, PhD, Kent State University  
Jay Raimonde, MD, Summa Health Systems  
Eileen Spoonster, RN, Summa Health Systems

INTRODUCTION: You are being asked to participate as one of approximately 400 subjects in a research study examining peoples’ responses to motor vehicle accidents. All subjects will have been involved in a motor vehicle accident and will have been seen by a Summa Health System trauma team due to injuries suffered in the accident. We have previously found that initial thoughts, feelings, behaviors, and physiological responses can predict later well-being, and we would like to examine your initial and later responses to your specific accident.

YOUR PARTICIPATION: If you decide to take part in this experiment, one of the members of our research team will ask you a few questions now, call you and ask you a few questions in 2 weeks, and meet with you 6 weeks after your accident, and then 3, 6 and 12 months after your accident. Each subsequent meeting will last approximately 1 - 2 hours and will be scheduled at a convenient time in your home. During the first assessment we will ask you to fill out a few questionnaires and we will take two-60ml samples of your urine from the urine that the hospital is collecting. The urine samples will be used to measure levels of hormones in your body -- the sample will not be used for any alcohol or drug testing. Two weeks after your accident we will call you and ask you a few questions over the phone. At this time we will ask you to provide us with two saliva samples which will also be used only for measuring hormones. During each subsequent assessment we will come to your house and ask you questions about what you remember of your accident. To ensure that we don’t miss anything, your answers will be audiotaped. We will also be asking you to fill out a variety of questionnaires and to participate in an interview designed to measure your thoughts, feelings, and reactions to your accident. In addition, at the fourth, fifth, and sixth assessments you will be asked to provide a urine sample (to measure hormone levels), and we will draw one tube of blood to measure immune levels. Your blood will be drawn by a person trained to minimize any discomfort, and the amount we take is approximately 4-7 teaspoons. If you are uncomfortable having your blood drawn, you may skip this part of the study. We will also need to look at your medical records to determine what specific injuries you may have suffered in your accident. By signing below, you are giving us permission to look at these records.

BENEFITS: You personally may not receive any direct benefit from your participation in this study. Your participation in this study may enable us to help future victims of motor vehicle accidents.

_________ Subject’s initials                                      106                                      _________ Date
**RISKS:** Some of the questions we ask will require you to remember aspects of your accident, and this may lead to increases in distress. The long-term effects of discussing your memories is unknown, but it is possible that some of the questions may provoke stressful memories. In addition, as the long-term effects of early memory recall is unknown, participating in the present study may have no effect on your levels of distress, may lead to longer-lasting distress, or may reduce your levels of distress. Risks associated with having your blood drawn include slight discomfort and bruising at the site. If any part of the study causes you to become distressed (symptoms of distress and/or depression include sleep disruption, concentration problems, changes in appetite, and similar disruptions in normal functioning), please call Dr. Jay Raimonde at (330) 253-5030 for an appropriate referral during office hours. After office hours you can call the Community Support Services in your county using the number we have provided.

**CONFIDENTIALITY:** All data collected in this study will be kept strictly confidential within the limits of the law. This means that your data will only be revealed if we are subpoenaed by an attorney. The information you provide us with will be identified only by a subject number, and will be examined only by Dr. Delahanty and qualified members of his research team. The only copies of the data will remain in a locked file. After the study, data will be published in scientific journals, but data will not be published in any manner that can identify you.

**VOLUNTARY PARTICIPATION:** Your participation in this study is voluntary and you may decline to participate in it without loss of any future services or benefits to which you may be entitled. Should you choose to participate, you may voluntarily withdraw from it at any time. By signing this form you are indicating that you have been informed about the research study in which you are agreeing to participate, and have had all of your questions satisfactorily answered. You will receive a copy of this form for your records.

**RESEARCH-RELATED INJURIES:** You should also be aware that there are no Federal, State or private programs established to provide research subjects with compensation and/or medical treatment or other financial losses due to physical injuries resulting from research procedures such as the one in which you are being asked to participate.

**COSTS:** You are not responsible for any costs above those of your standard or routine care. Twenty-five dollars at the initial session and each following session ($150.00 total) will be provided to you to compensate you for your time.

**QUESTIONS:** If you have any questions now, during or following your participation regarding this study and its associated risks, please contact Douglas L. Delahanty at (330) 672-2395. This project has been approved by Summa Health System. If you have questions about Summa Health System’s rules for research, please call the Summa Health System Institutional Review Board, telephone (330) 375-4045.

**SIGNATURE LINES:** By signing this form I acknowledge that I have read it, understand it, and have had any questions regarding the risks and benefits of this study satisfactorily answered, and I am voluntarily consenting to participate in this study. Further, I realize that by signing this form I do not waive any of my legal rights.

Date: ___________ Subject Signature:
Date: ___________ Witness Signature:
APPENDIX C

DEMOGRAPHIC QUESTIONNAIRE
DEMOGRAPHIC QUESTIONNAIRE

1. Age: _______

2. Sex: Male Female

3. Race/Ethnicity: _______________________

4. How long have you been driving? ____________ years.

5. How would you characterized where you live now?
   _____ Rural community
   _____ Urban Neighborhood
   _____ Small town
   _____ Other (specify) _________________________
   _____ Suburban neighborhood

6. What is your marital status, and how long has this been the case?
   _____ Single
   _____ Long-term Live-in How long ________
   _____ Separated How long ________
   _____ Divorced How long ________
   _____ Married How long ________
   _____ Widowed How long ________

7. What is the highest educational level you have completed?
   _____ Elementary
   _____ Jr. High
   _____ GED
   _____ High School
   _____ Trade School (Years beyond HS: __________)
   _____ Some College or 2-year Degree
   _____ 4 Year Degree
   _____ Advanced College Degree

8. What is your approximate annual income?
   _____ Under $10,000/year
   _____ $10,000 - $15,000/year
   _____ $15,001 - $20,000/year
   _____ $20,001 - $30,000/year
   _____ $30,001 - $40,000/year
   _____ $40,001 - $50,000/year
   _____ $50,001 - $60,000/year
   _____ $60,001 - $70,000/year
   _____ Over $70,001/year
9. What is your occupation? ________________________________

10. What is your spouse's occupation? ______________________

11. Is there someone available to help you with any medical care that you might need?
   Yes     No     Doesn't apply

12. Is there someone available to drive you on errands or to work, if you are unable to do this for yourself?
   Yes     No     Doesn't apply
APPENDIX D

IMPACT OF EVENTS SCALE- REVISED (IES-R)
IMPACT OF EVENTS SCALE- REVISED (IES-R)

Sometimes, after a serious accident such as the one you were in, people find themselves having thoughts about the accident that suddenly pop into their heads even when they are not trying to think about the accident. These thoughts are called intrusive thoughts. Please answer the following questions based on any intrusive thoughts you have had about your accident.

Have you experienced intrusive thoughts in the last week?
Yes  No  Don’t Know

What do you see/hear/smell/taste while experiencing intrusive thoughts:

Below is a list of comments made by people after stressful life events. Please check each item, indicating how frequently these comments were true for you SINCE THE ACCIDENT. If they did not occur during that time, please mark the “not at all” column.

Please think of your car accident when filling out this questionnaire.

<table>
<thead>
<tr>
<th>Comment</th>
<th>Not at all</th>
<th>A little bit</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Any reminder brought back feelings about it</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. I had trouble staying asleep</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. Other things kept making me think about it</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. I felt irritable and angry</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. I avoided letting myself get upset when I thought about it or was reminded of it</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. I thought about it when I didn’t mean to</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7. I felt as if it hadn’t happened or wasn’t real</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8. I stayed away from reminders about it</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9. Pictures about it popped into my mind</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not at all</td>
<td>A little bit</td>
<td>Moderately</td>
<td>Quite a bit</td>
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<td>------------</td>
<td>--------------</td>
<td>------------</td>
<td>-------------</td>
</tr>
<tr>
<td>11. I tried not to think about it</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>12. I was aware that I still had a lot of feelings about it, but I didn’t deal with them</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>13. My feelings about it were kind of numb</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>14. I found myself acting or feeling like I was back at that time</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>15. I had trouble falling asleep</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>16. I had waves of strong feelings</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>17. I tried to remove it from my memory</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>18. I had trouble concentrating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>19. Reminders of it caused me to have physical reactions, such as sweating, trouble breathing, nausea, or a pounding heart</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>20. I had dreams about it</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>21. I felt watchful and on-guard</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>22. I tried not to talk about it</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
APPENDIX E

FOOD CHECKLIST
FOOD CHECKLIST

Please circle any of the following items which you consumed the day of the accident:

Brewed Coffee: number of cups: ____________
Instant Coffee: number of cups: ____________
Tea: number of cups: ____________
Cola: number of cups: ____________

Decaffeinated Coffee, cocoa, wine, beer, other alcoholic beverages

Chocolate, walnuts, chocolate or coffee flavored candies, candy with walnuts, vanilla.

Breads containing fruits (raisins, prunes, orange peel, banana, pineapple), cheese bread

Banana, avocado, pineapple, canned figs, raisins, plums, prunes, oranges or orange juice, fruit cocktail with pineapple

Tomatoes or tomato sauce, catsup, chili sauce, olives, broad beans (fava beans), eggplant, any vegetables in cheese sauce.

Chicken liver, aged cheese, sour cream, anchovies, herring, smoked or pickled fish, brain.

Cheese omelet, macaroni and cheese, spaghetti in tomato sauce.

If you are not sure if a food that you ate during this period matches one of the categories listed above, please write it down here:

________________________________________________________________________

Do you smoke? Yes No

If you smoke, approximately how many cigarettes have you smoked the day of the accident: ______________

Please list any medications, over-the-counter medications, or drugs that you are currently taking.

Height: ______________
Weight: ______________
APPENDIX F

CLINICIAN ADMINISTERED PTSD SCALE (CAPS)
**CLINICIAN ADMINISTERED PTSD SCALE (CAPS)**

* Given that the CAPS is a lengthy interview the CAPS summary score sheet is provided below. If you would like a full copy of the CAPS please let me know

**CAPS-DX Summary Sheet**

Subject #_______________ Interviewer ________________ Date ________________

<table>
<thead>
<tr>
<th>A. Traumatic Event:</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. Reexperiencing symptoms</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1. Intrusive recollections</td>
</tr>
<tr>
<td>2. Distressing dreams</td>
</tr>
<tr>
<td>3. Acting or feeling as if event were recurring</td>
</tr>
<tr>
<td>4. Psychological distress at exposure to cues</td>
</tr>
<tr>
<td>5. Physiological reactivity on exposure to cues</td>
</tr>
<tr>
<td><strong>B subtotals</strong></td>
</tr>
<tr>
<td><strong>Number of Criterion B symptoms (need 1)</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C. Avoidance and numbing symptoms</th>
<th>Current</th>
<th>Lifetime</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Freq</td>
<td>Int</td>
</tr>
<tr>
<td>6. Avoidance of thoughts, feelings, or conversations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Avoidance of activities, places, or people</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Inability to recall important aspects of trauma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Diminished interest or participation in activities</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

117
<table>
<thead>
<tr>
<th>Criteria</th>
<th>Current</th>
<th>Lifetime</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>D. Hyperarousal symptoms</strong></td>
<td>Freq</td>
<td>Int</td>
</tr>
<tr>
<td>13. Difficulty falling or staying asleep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. Irritability or outbursts of anger</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Difficulty concentrating</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. Hypervigilance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. Exaggerated startle response</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>B subtotals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Number of Criterion B symptoms (need 1)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C subtotals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Number of Criterion C symptoms (need 1)</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>