The utility of hair cortisol concentrations in the prediction of PTSD symptoms following traumatic physical injury

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ABSTRACT

Rationale: Although cortisol alterations have been associated with posttraumatic stress disorder (PTSD) and PTSD symptoms (PTSS), the direction of association is mixed. Cortisol which is measured in blood, saliva, or urine is subject to transient factors that may confound results. Recent advances in cortisol sampling techniques provide novel opportunities to address these inconsistencies. Hair cortisol sampling is a non-invasive method for the retrospective assessment of long-term integrated cortisol, yet its utility at predicting PTSS has not been assessed in acute injury victims.

Objective: The aim of this prospective study was to examine whether higher levels of hair cortisol concentrations (HCC) were associated with increases in PTSS following traumatic physical injury.

Method: From January 2012 to May 2013, injury victims admitted to a level-1 Midwestern trauma center were recruited during their routine trauma clinic appointment within 30-days post-injury. Thirty participants had sufficient hair length to obtain 3-cm hair samples for cortisol assay. These participants completed PTSS assessments in relation to their recent injury at both the baseline and follow-up assessments (within 30- and 60-days post-injury, respectively).

Results: Hierarchical regression analyses — which controlled for baseline PTSS, age, and sex — revealed that higher HCC predicted significant increases in overall PTSS at follow-up. Higher HCC also predicted increases in the avoidance/numbing subscale symptoms of PTSS. Dividing the avoidance symptoms and numbing symptoms into two separate clusters (consistent with the 4-factor DSM-5 model of PTSD) revealed that HCC was only marginally associated with numbing, but not with avoidance symptoms.

Conclusion: Hair sampling is a feasible method for assessing integrated cortisol levels soon after traumatic physical injury. This study suggests that elevated HCC may serve as a biomarker of risk for the development of posttraumatic symptomatology, and identifies specific symptoms that may be targeted for intervention in those with high HCC in the aftermath of injury.

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1. Introduction

Altered cortisol levels are associated with the development of posttraumatic stress disorder (PTSD) and PTSD symptoms (PTSS) following trauma exposure (Lehrner et al., 2016; Morris et al., 2012; Yehuda et al., 2002). Despite numerous attempts over recent decades to clarify inconsistent findings regarding the direction of these alterations, the relationship between post-traumatic sequelae and cortisol remains unclear (Miller et al., 2007; Morris et al., 2012). Generally, patterns of hypocortisolism typically
characterize the presence of PTSD and PTSS (for review, see (Morris et al., 2012)), which is in part due to habituation to trauma cues and blunted reactivity of the hypothalamic–pituitary adrenal (HPA) axis. Still, individual differences and patient characteristics (e.g., gender), trauma-related factors (e.g., abuse-related trauma, lack of consideration of prior trauma, and time since traumatization), and sampling timeframe (e.g., afternoon-based samples) are important qualiﬁers of this relationship (for review, see (Meewisse et al., 2007; Steudte-Schmiedgen et al., 2016)). As such, numerous studies have found PTSD/PTSS to be associated with hypercortisolism (Friedman et al., 2007; Inslicht et al., 2006; Young and Breslau, 2004). Notably, existing research has typically relied on urine, blood serum, and saliva sampling to assess cortisol levels, although these measures provide small assessment windows (averaging levels over minutes to hours) and are greatly inﬂuenced by factors occurring during sampling (e.g., pain, medication and smoking status, activities, ultradian and circadian rhythmicity etc.) (Kirschbaum et al., 1993; Rasmussen et al., 2003; Weitzman et al., 1971; Young et al., 2004).

A considerable advancement is the relatively novel and non-invasive technique of measuring cortisol in human scalp hair, which acts as a retrospective marker of long-term integrated cortisol concentrations (HCC). Hair cortisol concentration (HCC) is a robust, non-invasive sampling technique that provides details of cortisol secretion from across the previous 30 days, hair from 1 to 2 cm from the scalp corresponds to 30- to 60-days prior and so on (Gow et al., 2010). This feature allows for the unique opportunity to obtain estimates of two things. First, the integrated pre-trauma cortisol activity can be estimated in survivors of acute trauma, as strands of hair sampled in the immediate aftermath of injury — within 1-day — reﬂect pre-trauma levels. Second, the integrated pre-, peri-, and post-trauma cortisol concentrations, reﬂected in hair sampled during the acute phase of injury, can be estimated (e.g., within 30-days post-injury) (Steudte-Schmiedgen et al., 2016).

Though hair sampling has provided an advantageous and novel avenue for assessing cortisol concentrations relative to stress disorders, prospective studies are rare (for exceptions, see (Gao et al., 2014; Luo et al., 2012; Steudte-Schmiedgen et al., 2015)), and ﬁndings in relation to traumatic stress-related disorders are inconclusive (see (Vives et al., 2015)). A critical distinction to make between HCC and PTSD/PTSS is the timing of the hair sampling in relation to the traumatic event. Speciﬁcally, prior research suggests that trauma-related cortisol responses are time-dependent: Elevated levels characterize the initial post-trauma response, while blunted levels are evident in the chronic phase among those experiencing psychological disturbances (Miller et al., 2007; Morris et al., 2012; Steudte-Schmiedgen et al., 2016). Indeed, while the general literature supports lower HCC in relation to chronic stress exposure and in those who have been suffering from chronic levels of PTSD/PTSS (Steudte-Schmiedgen et al., 2015; Steudte et al., 2013), studies focused on more recent traumatization reveal the opposite pattern. Speciﬁcally, Luo and colleagues (Luo et al., 2012) reported elevated HCC related to PTSD during the ﬁrst few months following the Wenchuan earthquake in China. Yet, as time progressed past the acute phase, blunted HCC became predictive of PTSD. Similarly, in a sample of recently traumatized Ugandan individuals (with continued ongoing stress), elevated HCC was associated with both PTSD and the number of stressful events in their lifetimes (Susann Steudte et al., 2011). This latter research parallels ﬁndings derived from traditional cortisol collection strategies, in that elevated cortisol levels collected in the acute trauma phase predict PTSS (Miller et al., 2007; Pervanidou et al., 2007). Thus, the timing of assessment relative to the trauma appears to be critically important (Miller et al., 2007; Steudte-Schmiedgen et al., 2016).

Given the variable nature of trauma, it can be challenging to obtain cortisol samples in close proximity to traumatic events. Nonetheless, survivors of single-incident traumatic physical injury are ideal candidates to study the acute trauma phase with, as they often seek emergency care for acute injuries in a research-supported medical environment. Traumatic injury is also the leading cause of morbidity and mortality in people between the ages of 1 and 46 (Centers for Disease Control and Prevention, 2015; National Trauma Institute, 2016), and up to 24% of trauma patients exhibit a new-onset psychiatric disorder at 12-months post-injury (with PTSD being one of the most common disorders (Bryant, 2010)). Further, 40% of acute trauma patients develop signiﬁcant PTSS (Petrie and Zatzick, 2010), which causes functional impairment that is comparable to meeting criteria for full PTSD (Cukor et al., 2010; Marshall et al., 2001). Such psychiatric symptoms serve as stronger predictors of disability at 12-months compared to trauma-related injury-related physical factors (O'Donnell et al., 2013). Nonetheless, there are no standards for acute mental health screening or prevention in injury survivors, as only 7% of trauma centers even screen for PTSD (Love and Zatzick, 2014). Early assessment of a biomarker predicting risk for post-traumatic distress development would aid in identifying at-risk individuals and developing targeted intervention approaches. Although HCC are valid and reliable biomarkers, no study has examined whether HCC predict the development of PTSS in civilian victims of single incident physical injury. To our knowledge, only one proof-of-concept study collected hair samples from 10 injured trauma patients (whiplash or fall victims) within 4-weeks post-injury, and reported solely on pain and disability outcomes for hair-normalized values of the cortisol waking response (compared to raw HCC) (Walton et al., 2013). To date, only one cross-sectional study has examined whether HCC are differentially associated with development of the speciﬁc PTSD symptom clusters. Speciﬁcally, Steudte and colleagues (Steudte et al., 2013) observed a negative association between HCC and intrusion symptoms, and between HCC and avoidance symptoms using DSM-IV criteria (Steudte-Schmiedgen et al., 2014).

The majority of extant literature regarding the relationship between HCC and PTSD/PTSS has been conducted in non-civilian samples (Steudte-Schmiedgen et al., 2015), treatment-seeking samples (Steudte et al., 2013), individuals undergoing chronic or ongoing stress exposure (e.g., severely traumatized Ugandan individuals (Steudte et al., 2011)), and victims of mass disaster (earthquakes (Gao et al., 2014; Luo et al., 2012)). This heterogeneity may introduce confounding and may limit generalization to civilian injury victims. Further, existing studies have typically examined single sex samples: female adolescents (Luo et al., 2012), male adolescents (Gao et al., 2014), and male soldiers (Steudte-Schmiedgen et al., 2015).

1.1. The present study

To address these gaps and expand upon prior research, the current prospective study sought to examine whether HCC, sampled in the acute phase of injury, predicted total PTSS and the DSM-IV deﬁned subscales of re-experiencing, avoidance/numbing, and hyperarousal. Speciﬁcally, we obtained 3-cm hair samples within 30-days post-injury (reﬂecting HCC in the 90-days prior to sampling; i.e., integrated pre-injury, peri-injury, and post-injury


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