Chronic stress predicts post-traumatic stress disorder symptoms via executive function deficits among urban American Indian children

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ABSTRACT
Little is known about how chronic exposure to stress affects mental health among American Indian (AI) children. The current study aimed to fill this gap by exploring if hair cortisol concentration (HCC), an indicator of chronic stress, predicted post-traumatic stress disorder (PTSD) symptoms through deficits in executive function (EF) skills commonly referred to as inhibitory control, working memory, and cognitive flexibility. A total of 163 urban AI children between 8- and 15-years old participated in the study (92 girls, 56.4%; $M_{\text{age}} = 11.19$, $SD = 1.98$). Chronic stress was measured as the concentration of cortisol in children’s hair. EF deficits and PTSD symptoms were reported by primary caregivers using the Behavior Rating Inventory of Executive Function and the Trauma Symptom Checklist for Young Children. The results demonstrated that higher HCC was indirectly associated with more PTSD symptoms through deficits in EF skills. Specifically, higher levels of HCC were related to more symptoms of PTSD arousal through impaired working memory, and more symptoms of PTSD avoidance and Intrusion through deficits in cognitive flexibility. The findings suggest interventions that reduce or buffer chronic stress, or that focus on improving EF skills, may promote not only cognitive development but also the mental health of Al children.

Indigenous groups are more likely to suffer from the negative effects of toxic stress due to the long-term and pervasive effects of colonization which include high levels of exposure to violence, poverty, discrimination, and systemic racism (Bassett et al., 2014; Duran et al., 2004; Gone & Trimble, 2012; Goodkind et al., 2010; Thayer et al., 2017). This fact, in combination with the growing body of evidence illustrating the disruptive impact of toxic stress on the development of both physical and mental health motivated this study (see Shonkoff et al., 2012 for a review). Indeed, Sarnyai et al. (2016) and Ketheesan et al. (2020) proposed a comprehensive model exemplifying how dysregulation of the stress response system due to colonization could mediate the mental health disparities found in Indigenous Australians.

A large body of research has demonstrated that the prefrontal cortex is particularly vulnerable to toxic stress with damage to the prefrontal cortex negatively impacting children’s executive function (EF) skills (Blair, Granger et al., 2011; Blair, Raver et al., 2011; Pechtel & Pizzagalli, 2011; Watt et al., 2017). EF is an umbrella term referring to higher-order, top-down cognitive processes that manage and control thoughts, emotions, and behaviors in novel or complex situations (Diamond et al., 2007; Gioia et al., 2000). EF is commonly referred to as a set of three separable, but related components that allow individuals to process multiple sources of information at once (working memory), inhibit prepotent thoughts and responses (inhibitory control), and shift between task sets (cognitive flexibility) (Best & Miller, 2010; Diamond, 2013; Miyake et al., 2000). EF is important for children’s well-being as deficits in EF have been consistently linked to poorer academic achievement (Best et al., 2011; Willoughby et al., 2019) and greater risk for psychopathology symptoms (Trossman et al., 2021).

Given that 22% of American Indian (AI) youth experience post-traumatic stress disorder (PTSD) which is triple the rate of the general population (Lechner et al., 2016), we focused specifically on pathways among toxic stress, EF deficits, and PTSD. Although research has found that PTSD predicts impaired EF skills in adults (Marin et al., 2011; Woon et al., 2017), developmental research in children strongly supports a model in which chronic stress predicts deficits in EF skills (Blair & Raver, 2012; Watt et al., 2017) with these deficits then predisposing children to be more vulnerable to stress-associated mental illnesses (Turner et al., 2020; Watt et al., 2017). For example, a review of twin studies and both cross-sectional and longitudinal research by Aupperle and colleagues (2012) found impairments in EF skills served as risk factors for the development and severity of PTSD symptoms with...
impairments in EF skills related to dysfunction within the prefrontal cortex. A longitudinal epidemiological study conducted by Parslow and Jorm (2007) found that deficits in EF were a robust risk factor for developing symptoms of PTSD. Additional studies revealed that cognitive control, which is closely related to EF, mediated the relations among chronic stress, depression, and anxiety (Quinn & Joormann, 2015, 2020; Tsai et al., 2020). Researchers have suggested that EF deficits contribute to the development of PTSD symptoms due to resulting difficulties with regulating attention and inhibiting responses to emotional or trauma-related stimuli leading to the development of potentially maladaptive coping mechanisms (Aupperle et al., 2012; Ben-Zion et al., 2018; Jagger-Rickels et al., 2021).

A growing body of research demonstrates that cortisol extracted from hair samples (i.e., hair cortisol concentration; HCC) can reliably index free cortisol across 3 months (Groeneveld et al., 2020; Sauvé et al., 2007; Stalder & Kirschbaum, 2012; van den Heuvel et al., 2020) and reveals consistent relations between perceived stress and HCC (O’Brien et al., 2013, 2017; Pereg et al., 2011; Van Uum et al., 2008; Yamada et al., 2007; Yip et al., 2021). Although cortisol concentrations in saliva have been linked to disproportionately high levels of PTSD among AI adults (Laudenslager et al., 2009), this is the first study to use HCC as a measure of chronic stress in ALs. Research on HCC and EF, in non-Al samples, found that higher HCC was associated with poorer inhibitory control in third graders (Groeneveld et al., 2020) and poorer working memory skills amongst preschoolers (Hennessey et al., 2020). In addition, research using salivary cortisol concentrations found higher levels of cortisol predicted poorer EF in early childhood (Blair, Granger et al., 2011).

We are the first to test if deficits in EF skills are central in the process linking HCC to PTSD symptomology among urban AI children. Due to the scarcity of research including biological measures of chronic stress and assessments of EF deficits among AI children, this study was exploratory.

Method

Participants

A community sample of 163 urban AI children (92 girls, 56.4%) ages 8-15 years \( (M = 11.19 \text{ years}, SD = 1.98 \text{ years}) \) and their primary caregivers participated in the study. Approximately half of the primary caregivers were biological mothers (52.1%), 7.4% were grandmothers, and 6.1% were biological fathers. The remaining caregivers were adoptive parents, stepparents, or other relatives. The average annual income was $42,648 \( (SD = 29,731) \) with a range of $0–$160,000.

Through collaboration with the directors of the Native American Education Program (NAEP), invitation letters for an informational meeting about the study were sent out to the primary caregivers of urban-based AI children in 3rd through 8th grades. The research team also sent letters to principals of elementary schools where the enrollment rate of urban AI students was high, explaining the study and requesting permission to distribute letters to urban AI students directly inviting them to participate in the study. The study was approved by both the participating school district and the Institutional Review Board of the primary investigator’s university. This university’s IRB has a special panel that reviews all Indigenous research to ensure proper cultural protocols are followed in addition to the main IRB review. All participants consented to participate in the study after being informed that they had the right to refuse and would still receive the promised monetary gift ($50 for the primary caregiver and $50 for the child) just for meeting with the research team. Additionally, the children were told that they had the right to refuse to participate even if their primary caregiver gave permission, and they would still receive the promised monetary gift. Finally, the primary caregivers and children were told that they did not have to give a hair sample to participate in the study; consent from both the primary caregiver and the child was needed in order for the hair sample to be collected.

Measures

Hair cortisol assessment

Hair was cut using stylist shears close to the scalp at the posterior vertex. Thinning shears were used for children who had short hair to ensure the cut was not noticeable. The primary researcher and two assistants underwent training on how to cut the hair using videos produced by Dr Mark Laudenslager and his team at the University of Colorado, Denver where the hair was sent for processing. Dr Laudenslager’s laboratory utilized quality control programs established by Salimetrics and the Society for Hair Testing. Hair length was measured after aligning the strands with the proximal 3 cm of hair ground and analyzed using the method described by Hoffman et al. (2017). Cortisol levels were determined using a commercial high sensitivity enzyme-linked immunoassay (EIA) kit (Salimetrics LLC, State College, PA) per manufacturer’s protocol. Inter-assay coefficients of variation (CV) were 12.1% for high hair control and 13% for low hair control. The intra-assay CV on duplicates was 2.3%. In keeping with the standard practice for distributions with substantial positive skewness, results were log-transformed to better fit the normal curve (M. Laudenslager, personal communication, 8/01/2017; Tabachnick & Fidell, 2007) but were initially reported as pg/mg hair. All hair samples were destroyed once the cortisol readings were obtained.

Executive function deficits

The Behavior Rating Inventory of Executive Function (BRIEF; Gioia et al., 2000) assesses aspects of EF in children. The BRIEF contains 80 items within eight subscales (Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor). Items are rated on a 3-point scale (1 = never, 2 = sometimes, 3 = often). The present study asked the primary caregiver to rate the child on three subscales – Inhibit, Working Memory, and Shift, which are consistent with the three major components of EF – inhibitory control, working memory, and cognitive flexibility,
respectively. The Inhibitory Control subscale evaluates children’s ability to control impulses and behavior (e.g. “Acts too wild or ‘out of control’”; 13 items). Working Memory measures the capacity to hold information in mind for problem solving (e.g. “Has trouble concentrating on chores, schoolwork, etc.”; 12 items). The Cognitive Flexibility subscale assesses how well a child moves from one situation or activity to another (e.g. “Becomes upset with new situations”; 10 items). Scores were summed across all items in each subscale, with higher scores indicative of a deficit in that domain. The internal reliabilities (Cronbach’s alpha) of all three subscales were high: .90 for Inhibitory Control, .94 for Working Memory, and .78 for Cognitive Flexibility.

**Post-traumatic stress disorder symptoms**

The primary caregiver completed the Trauma Symptom Checklist for Young Children (TSCYC; Briere, 2005), which is a standardized report of trauma symptoms in children. The scale is composed of 90 items within eight subscales (anxiety, depression, anger/aggression, post-traumatic stress-intrusion, post-traumatic stress-avoidance, post-traumatic stress-dissociation, and sexual concerns). The current study used 26 items from the three subscales that are relevant to post-traumatic stress symptoms (i.e. 9 intrusion items, 8 avoidance items, 9 arousal items). Intrusion assesses children’s reexperiencing of traumatic memories (e.g. “Bad dreams or nightmares”), Avoidance measures children’s avoidance of post-traumatic distress (e.g. “Not wanting to go somewhere that reminded him/her of a bad thing from the past”), and Arousal evaluates children’s experience of autonomic hyperarousal (e.g. “Being easily startled”). The primary caregiver rated each item based on the frequency of a symptom during the previous month on a 4-point scale (0 = not at all to 3 = very often). Scores were summed across all items included in each subscale such that a higher score means a higher frequency of displayed PTSD symptoms. Cronbach’s alpha values were .80 for intrusion, .78 for avoidance, and .82 for arousal.

**Covariates**

Covariates in this study included child age and sex (0 = female, 1 = male). Household income reported by primary caregivers was initially considered as a covariate based on prior research (Hackman et al., 2015), but we did not include it in the final model because it was not correlated with any study variables.

**Procedure**

Primary caregivers who agreed to participate in the study were sent a link to the questionnaires through Qualtrics, an online survey system. The link was identified only by the ID number given by e-mail or text message. Primary caregivers who did not have access to a phone, tablet, or computer were provided one to complete the questionnaires. The children’s hair samples were collected in-person in our lab or at the participant’s school.

**Data analytic plan**

We examined the rate of missing data before conducting analyses. The average missing rate was 13.7% across study variables and covariates, with 98 participants with no missing data, 31 participants with missing data on one variable, and 34 participants with missing data on three to seven variables. Results from a sensitivity analysis using complete cases were similar to those using the full sample. Preliminary analyses revealed significant differences in some study variables between participants with and without missing data on HCC, and with and without complete data (see Supplemental Tables 1 and Table 2). Thus, we used full information maximum likelihood (FIML) in Mplus 8.2 (Muthén & Muthén, 1998–2018) to account for missing data (Enders, 2010).

Descriptive statistics and correlations among study variables and covariates were analyzed in SPSS 25.0 (SPSS Inc., Chicago, IL). We tested the hypothesized model in Mplus 8.2 (Muthén & Muthén, 1998–2018) with bootstrapping (1000 resamples) and bias-corrected 95% confidence intervals (CI). We employed multiple model fit indices to evaluate model fit, including the chi-square statistic ($\chi^2$), the root mean square error of approximation (RMSEA) and its 90% CI, the comparative fit index (CFI), and the standardized root mean square residual (SRMR). Model fit is considered good when RMSEA < .050, CFI > .950, and SRMR < .050, and acceptable when RMSEA < .080, CFI > .900, and SRMR < .080 (Little, 2013).

### Table 1. Descriptive statistics and correlations.

| Variables | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | M (SD) | Range |
|-----------|---|---|---|---|---|---|---|---|---|----|--------|-------|
| 1. Sex | N/A | | | | | | | | | | | |
| 2. Age | -.01 | 134.34 (23.81) | | | | | | | | | 96.00–189.00 |
| 3. Income | -.11 | -.09 | .12 | .19 | | | | | | | 42.65 (29.73) | 0–160 |
| 4. HCC | .23* | -.16 | -.06 | | | | | | | | 21.22 (42.29) | 2.50–283.20 |
| 5. IC | -.05 | -.26** | .12 | | | | | | | | 12.97 (4.20) | 8.00–29.00 |
| 6. WM | .03 | -.17 | .09 | .25 | .72*** | | | | | | 14.89 (4.85) | 8.00–29.00 |
| 7. CF | -.02 | -.27** | .10 | .28** | .70*** | .63*** | | | | | 10.62 (3.11) | 6.00–20.00 |
| 8. Intrusion | -.05 | -.01 | .03 | .09 | .19** | .22* | .36*** | | | | 1.36 (1.36) | 0–10.00 |
| 9. Avoidance | .01 | .02 | -.14 | .09 | .25** | .26** | .39*** | .61*** | | | 1.23 (2.08) | 0–16.00 |
| 10. Arousal | .07 | -.10 | -.02 | .24* | .54*** | .69*** | .55*** | .52*** | .52*** | | 3.54 (3.82) | 0–20.00 |

Note. Child sex is coded as 0 = female, 1 = male. Child age is shown in months. Household income is shown in thousands. HCC: hair cortisol concentration; IC: inhibitory control; WM: working memory; CF: cognitive flexibility. Reported means for HCC, intrusion, and avoidance were not log transformed here as they were for the actual statistical analyses.

\*p < .10, \*p < .05, \*\*p < .01, \*\*\*p < .001.
Indirect effects of stress on PTSD symptoms via EF deficits

We estimated a path model to examine whether HCC was indirectly related to PTSD symptoms of intrusion, avoidance, and arousal via inhibitory control, working memory, and cognitive flexibility. Child age and sex were included as covariates. Paths involving covariates were included in the model if significant correlations were observed. The results of the model are shown in Figure 1. The model had good fit to the data: \( \chi^2(N=163, df=10) = 9.71, p = .467, \text{CFI} = 1.00, \text{RMSEA} = 0 \), given the cross-sectional nature of the study, we compared the fits of the hypothesized model (stress \( \rightarrow \) EF \( \rightarrow \) PTSD) and the alternative model (Stress \( \rightarrow \) PTSD \( \rightarrow \) EF) (Supplemental Table 3). Although both models were statistically equivalent with a good fit to the data, we proceeded with the hypothesized developmental model as it was the more strongly supported by the literature given the age of our participants and our community-based sample.

As shown in Figure 1, HCC was positively related to deficits in working memory and cognitive flexibility. In addition, deficits in working memory were positively related to PTSD arousal, whereas deficits in cognitive flexibility were positively related to PTSD avoidance and PTSD intrusion. Analyses of indirect effects showed that HCC was indirectly and positively associated with PTSD arousal through deficits in working memory (\( \beta = .12, 95\% \text{CI} = [.04, .24] \)). Additionally, HCC was indirectly and positively associated with PTSD avoidance (\( \beta = .08, 95\% \text{CI} = [.01, .20] \)) and intrusion (\( \beta = .11, 95\% \text{CI} = [.04, .22] \)).

**Table 2.** Total effects, direct effects, and indirect effects of hair cortisol concentration on PTSD symptoms of arousal, avoidance, and intrusion through deficits in inhibitory control, working memory, and cognitive flexibility.

|                      | \( \beta \) | SE  | \( p \) | 95% CI       |
|----------------------|-------------|-----|---------|--------------|
| HCC \( \rightarrow \) PTSD arousal |               |     |         |              |
| Total effect         | 0.21        | 0.10| 0.039   | [0.02, 0.40] |
| Direct effect        | 0.05        | 0.09| 0.603   | [−0.12, 0.24]|
| Indirect effect      |             |     |         |              |
| Via IC               | 0.00        | 0.03| 0.985   | [−0.05, 0.06]|
| Via WM               | 0.12        | 0.05| 0.023   | [0.04, 0.24] |
| Via CF               | 0.04        | 0.04| 0.337   | [−0.02, 0.14]|
| HCC \( \rightarrow \) PTSD avoidance |               |     |         |              |
| Total effect         | 0.14        | 0.09| 0.103   | [−0.03, 0.29]|
| Direct effect        | 0.03        | 0.09| 0.745   | [−0.15, 0.19]|
| Indirect effect      |             |     |         |              |
| Via IC               | 0.00        | 0.03| 0.968   | [−0.05, 0.05]|
| Via WM               | 0.04        | 0.03| 0.205   | [−0.02, 0.13]|
| Via CF               | 0.08        | 0.04| 0.080   | [0.01, 0.20] |
| HCC \( \rightarrow \) PTSD intrusion |               |     |         |              |
| Total effect         | 0.08        | 0.10| 0.402   | [−0.12, 0.27]|
| Direct effect        | −0.01       | 0.09| 0.908   | [−0.19, 0.17]|
| Indirect effect      |             |     |         |              |
| Via IC               | −0.02       | 0.03| 0.424   | [−0.09, 0.02]|
| Via WM               | 0.01        | 0.03| 0.820   | [−0.06, 0.07]|
| Via CF               | 0.11        | 0.05| 0.018   | [0.04, 0.22] |

HCC: hair cortisol concentration; PTSD: post-traumatic stress disorder; IC: inhibitory control; WM: working memory; CF: cognitive flexibility.
.22]) through deficits in cognitive flexibility. There were no significant associations with inhibitory control (see Table 2).

Discussion

This study contributes to the understanding of how chronic stress gets under the skin by extending findings documenting negative relations among chronically experienced stress, cognitive functioning, and mental health. To our knowledge, we are the first to extend these findings to AI children, an underrepresented group in this growing body of research. Our findings represent an important first step in pinpointing how chronic stress can differentially impact the primary components of EF (i.e. inhibitory control, working memory, and cognitive flexibility) and contribute to variations in PTSD symptomology. As noted by Jagger-Rickels et al. (2021), the clinical and neurobiological heterogeneity of PTSD presents a major obstacle to understanding and treating PTSD, thus it is important to identify specific cognitive impairments and neural pathways that contribute to subtypes of PTSD.

We found that higher HCC in children was associated with greater PTSD arousal symptoms via poorer parent-reported working memory skills. In real-world terms, this means that children with higher levels of chronic stress were more likely to have higher ratings on the PTSD Arousal subscale items such as having trouble concentrating, experiencing sleep difficulties, and being tense because they had more problems processing multiple sources of information at once in working memory.

In addition, higher HCC in children was associated with a higher number of PTSD avoidance and intrusion symptoms via poorer parent-reported cognitive flexibility skills. Thus, children with higher levels of chronic stress were more likely to have higher scores on the PTSD Avoidance and Intrusion subscale items such as having nightmares or being bothered by memories of the past due to more difficulties with behavioral indicators of cognitive flexibility such as finding a different way to solve a problem and easily adapting to new situations.

We did not find significant pathways from HCC to inhibitory control and from inhibitory control to PTSD symptomology. It could be that age was most predictive of the behavioral indicators of inhibitory control. Thus, once we controlled for age, we no longer found a significant correlation with HCC. Indeed, the specific items parents rated their children on for inhibitory control revealed that most were behaviors that are more prevalent in younger children such as being silly, getting out of control more than friends, and needing adult supervision. Alternatively, it could be that inhibitory control is not a significant predictor of PTSD symptomology, either directly or indirectly. Ben-Zion et al. (2018) examined similar pathways from working memory, response inhibition, memory, and cognitive flexibility to PTSD symptomology and found only cognitive flexibility significantly predicted PTSD symptom severity.

Given the mediating role of working memory and cognitive flexibility in linking chronic stress and PTSD symptoms, intervention efforts targeting these EF skills may help buffer AI children from the negative effects of toxic stress. These efforts may be especially beneficial during early childhood and the transition to adolescence, given the plasticity of EF early in development (Hsu et al., 2014; Zelazo & Carlson, 2012). Although findings regarding the effectiveness of EF interventions are mixed (Au et al., 2015), a growing number of studies have shown that short- and long-term training and activities designed to improve EF result in increases in various EF skills in early and late childhood (e.g. Benzing et al., 2019; Tang et al., 2012; Traverso et al., 2015; Zhang et al., 2019). It is important to note, however, that whereas interventions targeting improvements in EF are often successful in obtaining near transfer effects, evidence of far transfer (e.g. EF abilities extending to other contexts) is less robust (Zelazo, 2020). Thus, given the benefits of EF, there is a need to identify procedures designed to facilitate far transfer effects for EF.

It is critical to highlight the educational implications of our results. AI children have disproportionate rates of school discipline including suspension and expulsion (Chin et al., 2018). As illustrated by our results, AI children who had higher HCC were more likely to display the types of behaviors that are likely to get them in trouble at school such as the inability to focus or sit still and being prone to anger. Given that meta-analysis of research on hair cortisol found that higher levels of HCC were indicative of ongoing stress at the time of data collection (Stalder et al., 2017), teachers and school officials should do more to help reduce stress and identify culturally appropriate ways to help students regulate their behavior in class. Moreover, it is important to make sustained efforts at both national and state levels to reduce chronic stress in AI children given that much of the stress AI youth experience is due to inequality created by colonization (Bassett et al., 2014; Duran et al., 2004; Goodkind et al., 2010; Gone & Trimble, 2012; Thayer et al., 2017).

Interestingly, EF deficits were not strongly related to income, despite past research documenting robust relations between lower socioeconomic status and impaired EF (Lawson et al., 2018). However, this study replicates results from a study on the Tohono O’odham reservation with 7- to 12-year-old children that found income was not significantly correlated with tests of working memory and inhibitory control (Tssethlikai, 2011). Income might not have the same influence for AI children as it does for Westernized children because AI families frequently share resources to buffer the negative effects of poverty (Red Horse, 1997).

The current study has important limitations to consider including the use of parent-reported measures of PTSD symptoms and EF. Self-reports, especially for the older children, were desirable; however, the wide age range in the current study precluded including self-reports of EF and PTSD. In addition, performance-based assessments of EF might be better indicators of actual cognitive abilities than behavioral ratings (Buchanan, 2016). However, performance-based measures also have weaknesses in that they have not been validated in AI samples (Walls et al., 2019). One should also consider that performance-based EF measures and ratings-based EF measures are often not significantly correlated (Toplak et al., 2013). Therefore, more research is needed to...
evaluate if the findings presented here will replicate with performance-based assessments.

Given the cross-sectional nature of this study, we cannot make any definitive statements about the direction of the effects. As shown in our test of model fit for the alternative model, both models had good fit. Thus, PTSD symptoms might mediate the relation between chronic stress and EF. Indeed there is some evidence that EF deficits can be outcomes of PTSD (e.g., DePrince et al., 2009; Schoeman et al., 2009). Thus, we can only say that there were significant indirect pathways from chronic stress to PTSD symptoms via EF deficits, consistent with the directions that are strongly supported by developmental models (e.g., Aupperle et al., 2012). Longitudinal research is needed in order to more fully advance this line of research and to identify protective factors that can buffer stress and promote healthy EF development even in high-stress environments.

In conclusion, the results of this study provide support for the primary role of chronic stress as a mechanism contributing to mental health disparities in Indigenous groups and extend this work to urban AI children. The results of this study support the need for more science-informed interventions that reduce trauma, chronic stress, and exposure to violence for urban AI children. In the interest of social justice, and consistent with research demonstrating that cultural continuity buffers Indigenous Canadians from the negative effects of stress (Currie et al., 2019, 2020), interventions that include tribal languages, culture, and spiritual practices are needed.

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