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Adversity Type and Timing Predict Temporal Summation of Pain in African-American Adults

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Abstract

African Americans are disproportionately exposed to adversity across the lifespan, which includes both stressful and traumatic events. Adversity, in turn, is associated with alterations in pain responsiveness. Racial differences in pain responsiveness among healthy adults are well established. However, the extent to which adversity type and timing are associated with alterations in pain responsiveness among healthy African-American adults is not well understood. The present study included 160 healthy African-American adults (98 women), ages 18 to

45. Outcome measures included pain tolerance and temporal summation of pain to evoked thermal pain. Composite scores were created for early-life adversity (childhood trauma, family adversity) and recent adversity (perceived stress, chronic stress burden). A measure of lifetime racial discrimination was also included. Higher levels of recent adversity were associated with higher temporal summation of pain, controlling for gender, age, and education. Neither early-life adversity nor lifetime racial discrimination were associated with temporal summation of pain. The present findings suggest that heightened temporal summation of pain among healthy African-American adults is associated with exposure to recent adversity events. Improved understanding of how recent adversity contributes to heightened temporal summation of pain in African Americans could help to mitigate racial disparities in pain experiences by identifying at-risk individuals who could benefit from early interventions.

Keywords

Racial disparities in pain are well-established, with African-American (AA) adults reporting greater pain severity and pain-related functional disability compared to non-Hispanic Whites for comparable pain conditions (Anderson et al., 2009; Institute of Medicine, 2011). In addition, there are pronounced racial differences in experimental pain responses, with healthy AA adults exhibiting pro-nociceptive alterations when compared to non-Hispanic Whites (Kim et al., 2017; Rahim-Williams et al., 2012). Experimental pain responses predict development of postoperative persistent pain (Arendt-Nielsen et al., 2018; Petersen et al., 2018; Weissman-Fogel et al., 2009; Wylde et al., 2013; Yarnitsky et al., 2008), influence the course of chronic pain (Georgopoulos et al., 2019; Greenspan et al., 2013; Morris et al., 2021a; O'Leary et al., 2017), and exhibit promise as biomarkers of risk for chronic pain among healthy individuals (Fillingim et al., 1998; Staud, 2012). Understanding how and why racial differences in experimental pain responses emerge for healthy individuals could improve pain risk assessment and, ultimately, inform the development of interventions to prevent the transition to chronic pain.

Stress is a key driver of individual differences in pain experiences (Fillingim, 2017). However, "not all forms of stress are created equal" with regard to their impact on health (O'Connor et al., 2021). Theoretical stress frameworks propose that racial disparities in health outcomes may be attributed, in part, to racial minorities being *more* likely to experience social, economic, and race-related stressors (*differential exposure*), and *less* likely to have access to psychosocial and material coping mechanisms needed to buffer against these stressors (*differential vulnerability*) (Kessler, 1979; Myers, 2009). Greater exposure to adversity across the lifespan is associated with alterations in experimental pain responses in predominantly non-Hispanic White (Sherman et al., 2015; Sturycz et al., 2019; Tesarz et al., 2016; You & Meagher, 2016, 2018) and mixed samples of AA and non-Hispanic White adults (Fillingim & Edwards, 2005). Temporal summation of pain is an experimental pain response index that captures increases in perceived pain intensity despite constant intensity of the repeated pain stimulus (Price et al., 1977). Early life stressors such as childhood trauma are linked to greater temporal summation of pain among healthy,

predominantly White individuals (You & Meagher, 2016) and those with chronic pain (Sherman et al., 2015). In addition, more recent stressors such as chronic difficulties (e.g., individual and neighborhood socioeconomic status [SES]) and acute stress levels are linked to alterations in both pain facilitation and inhibition in predominantly White (Geva et al., 2014; Morris et al., 2021b) and mixed samples of Latinx and non-Hispanic White adults (Rassu et al., 2020).

Racial discrimination in particular is associated with a variety of negative health outcomes (Pascoe & Richman, 2009; Williams et al., 2019), including greater clinical pain intensity and pain-related impairment (Burgess et al., 2009; Edwards, 2008; Walker et al., 2016). Pain tolerance is an experimental pain response that captures the point at which a stimulus is terminated because the individual can no longer endure it, and is thought to reflect the affective-motivational dimension of pain (Geva & Defrin, 2013). Greater racial/ethnic discrimination has also been linked to lower cold pain tolerance in healthy predominantly AA individuals (Richardson et al., 2022), lower heat pain tolerance in AA compared to non-Hispanic White adults with chronic pain (Goodin et al., 2013), lower temporal summation of pain in Latinx compared to non-Hispanic White adults (Rassu et al., 2020), as well as enhanced temporal summation of the nociceptive flexion reflex and impaired conditioned pain modulation of nociceptive flexion reflex in Native American adults (Güereca et al., 2022). Although AA adults are more likely to experience different types of adversity over their lifetime than their non-Hispanic White counterparts (Brown et al., 2020; Slopen et al., 2016), the extent to which these exposures predict experimental pain responses in AA adults remains unclear. Identifying features of adversity that are associated with evoked pain responses among healthy AA adults - including types and timing - could improve understanding of pathways through which lived experiences contribute to racial disparities in pain.

The present study examined the extent to which early-life adversity (e.g., childhood abuse and neglect, parental incarceration, poverty), recent adversity (e.g., perceived stress levels, financial stressors, crime), and lifetime racial discrimination (e.g., made to feel like an outsider) were associated with experimental pain responses (i.e., pain tolerance, temporal summation of pain, pain habituation). These three experimental pain study indices capture distinct dimensions of pain processing (Greenspan et al., 2011). Pain habituation is defined as "a behavioral response decrement that results from repeated stimulation and that does not involve sensory adaptation/sensory fatigue or motor fatigue" (Rankin et al., 2009). Pain habituation is thought to reflect central anti-nociceptive activity (Bingel et al., 2007). Individuals with chronic pain exhibit weaker habituation to heat pain compared to healthy individuals (Smith et al., 2008). The present study sought to simultaneously evaluate linear increases in pain responses at the start of the protocol (temporal summation of pain) and rates of deceleration in pain responses across the task (pain habituation). We hypothesized that AA adults with higher levels of early-life adversity, recent adversity, and lifetime racial discrimination would exhibit enhanced pro-nociceptive features (as evident in lower pain tolerance and greater temporal summation of pain) and reduced anti-nociceptive features (as evident in slower pain habituation).

METHODS

Participants

This cross-sectional study included 160 healthy adults who self-identified as AA (98 women [61%]), were between the ages of 18 to 45 (inclusive), and were seen for a baseline assessment as part of a larger ongoing longitudinal study. Recruitment was conducted in a mid-size metropolitan area through online research participant registries, community and university webpages advertising research studies, flyers distributed at local Historically-Black Colleges and Universities, and flyers placed in waiting rooms of local clinics serving the AA community. Data included in the present analyses were derived exclusively from the baseline assessment of the larger study, which was focused on evaluating experimental pain responses and prolonged hypothalamic-pituitary-adrenal (HPA) activation as mechanisms linking adversity to daily pain complaints. Age range was restricted because age is known to influence pain sensitivity (Riley et al., 2014) and another key variable evaluated in the larger study – hair cortisol concentration (Staufenbiel et al., 2015). Further, this age range was selected to minimize potential confounds between age and cumulative exposure to adversity. Due to our particular interest in identifying early markers of risk for chronic pain among healthy individuals, participants were excluded if they had a current chronic pain condition (defined as pain 3 months in duration and determined by a modified version of the Persistent Pain Questionnaire (Bruehl et al., 2005)). Additional exclusion criteria included chronic medical conditions (e.g., sickle cell disease, Cushing's disease, hyperthyroidism, pregnancy), taking daily medications (e.g., opioid analgesics, corticosteroids) that could affect pain or stress (i.e., HPA axis) responses, or meeting criteria for a substance use disorder in the previous three months. This study was approved by the university institutional review board. Data that support the findings of this study are not publicly available because they contain information that could compromise the privacy of research participants.

Experimental pain protocol

The experimental pain protocol has been used by this group with a variety of populations to assess heat pain tolerance and temporal summation of pain (Morris et al., 2021a; Morris et al., 2015). Participants were instructed not to take any pain medications within four hours of their visit. Upon arrival, they completed orientation and training for pain testing procedures and stimuli. The experimental pain protocol was administered through a computerized Medoc TSA-II NeuroSensory Analyzer (Medoc US, Minneapolis, MN) using commercially available software (TPS-CoVAS version 3.19; Medoc Inc, Ramat Yishay, Israel). Temporal summation of pain was assessed with a standardized oscillating thermal stimulation protocol used previously by this group (Chung & Bruehl, 2008; Dengler-Crish et al., 2011; Morris et al., 2015) and others (Fillingim & Edwards, 2005). A sequence of 10 heat pulses with a 48°C target stimulus intensity was applied to the ventral forearm. Each pulse was 0.5 seconds in duration and started at a temperature of 40°C, with sequential pulses administered at a frequency of 0.4 Hz. During the temporal summation of pain protocol, participants rated the intensity of pain sensation shortly after the peak of each heat pulse using a 0 (*no pain*) to 100 (*worst pain possible*) scale. Within-person changes in pain ratings were used to evaluate the degree of temporal summation of pain as well as

pain habituation. Pain tolerance was determined using a thermode attached to the ventral forearm of each participant's nondominant arm. Participants were instructed to terminate the stimulus by clicking on a computer mouse "when you can't stand the heat pain any longer." Each of four trials started at an adaptation temperature of 40°C, followed by temperature increase at a ramp rate of 0.5°C per second until the maximum tolerance was reached. The thermode was moved upwards on the forearm to a new, nonoverlapping location during each 25-second interstimulus interval. The maximum temperature limit was 51°C. Pain tolerance was computed as the mean of the temperature tolerance for the last three trials.

Early-life Adversity

The Childhood Trauma Questionnaire (CTQ; Bernstein et al., 1994) is a 28-item, self-report measure used to assess the frequency of different types of abuse experienced as a child and teenager. CTQ item scores ranged from 1 (*never true*) to 5 (*very often true*), with total scores ranging from 28 to 140 (higher scores reflect more childhood trauma exposure). Current reliability was good for the CTQ (α=0.84). A brief 10-item version of the Family Adversity Questionnaire (FAQ) was used to assess the number of non-sexual, adverse early life experiences during childhood ("*when you were growing up*"), including parental incarceration, illness, disability, death and severe poverty (Kessler & Magee, 1993). Items were dichotomous (0 = *No*; 1 = *Yes*), with total scores ranging from 0 to 10 (higher scores reflect more adverse early life experiences). Current reliability was good for the FAQ (α=0.80). An early adversity composite was computed as the sum of standardized scores for the CTQ and FAQ.

Recent Adversity

The Chronic Burden Scale (CBS) is a 21-item scale used to measure the degree to which a variety of chronic stressors (e.g., economic, employment, crime, and legal problems) had been a problem for participants in the past 6 months (Gurung et al., 2004). CBS item scores ranged from 1 (*not a problem for me*) to 4 (*a major problem for me*), with total scores ranging from 15 to 84 (higher scores reflect greater burden from chronic stressors). Current reliability was good for the CBS (α=0.86). The Perceived Stress Scale-10 (PSS-10; Cohen et al., 1983) is a 10-item measure used to assess the degree to which individuals perceive their lives as stressful in the past month. PSS-10 item scores ranged from 0 (*never*) to 4 (*very often*), with total scores ranging from 0 to 40 (higher scores reflect higher levels of perceived stress). Current reliability was good for the PSS-10 (α=0.86). A recent adversity composite was computed as the sum of standardized scores for the CBS and PSS-10.

Discrimination

The 17-item Brief Perceived Ethnic Discrimination Questionnaire – Community Version (BPEDQ-CV; Brondolo et al., 2005) was used to assess lifetime experiences of discrimination because of one's race and ethnicity. Participants indicated the frequency of experiences with racial discrimination on a scale of 1 (*never*) to 5 (*very often*), with total scores ranging from 17 to 75 (higher scores reflect more experiences with racial discrimination). Current reliability was good for the BPDEQ-CV (α=0.88).

Covariates

A brief demographics form was used to determine participant age, gender, and education level (years completed).

Data analysis

Sample size was determined for the larger ongoing study based on estimates to achieve power of 0.80 for planned mediation hypotheses. Composite scores were computed for early-life adversity (sum of childhood trauma and family adversity z-scores) and recent adversity (sum of chronic stress burden and perceived stress z-scores). Composite stress exposure indices possess numerous conceptual and methodological advantages over individual measures, including increased predictive power, more accurate estimation across contexts, avoiding problems of highly-correlated individual predictors such as collinearity or suppression effects, and overcoming 'threshold effects' (Ettekal et al., 2019). These advantages are emphasized by theoretical models of stress exposure measurement (Rutter, 1981) and are particularly salient to the assessment of early-life and recent adversity, which involve individual adversity domains that are interconnected and unlikely to operate in isolation. Distinguishing the unique effects of early-life from recent adversity on mental and physical health outcomes is supported by our own recent work (Dickens et al., 2022) as well as that of others (Klaassens et al., 2012; Stern & Thayer, 2019; Tarullo & Gunnar, 2006).

Temporal summation of pain protocols typically administer a sequence of ten heat pulses using target intensities of 47°C or greater at frequencies ranging from 0.3–1.0 Hz (Anderson et al., 2013). Response patterns during these protocols vary across healthy individuals: ~30% exhibit temporal summation of pain; ~60% exhibit no significant changes in pain intensity; ~10% exhibit temporal decreases (i.e., habituation) in pain ratings (Anderson et al., 2013; Morris et al., 2015a). Quantifying temporal summation of pain responses using standard approaches (e.g., difference between 1st pain rating and either the 5th or maximum pain rating) or by examining linear slopes across all 10 ratings can be misleading in cases where changes are nonlinear (You, 2012). Animal studies reveal a biphasic curve with temporal summation of pain ("windup") occurring during the first 7 stimuli, followed by deceleration and subsequent decreases in pain responses (Herrero et al., 2000). The window for observing temporal summation of pain is slightly shorter in healthy humans, with increases in pain ratings typically occurring within the first 3 or 4 stimuli, followed by a plateau or decrease in pain ratings (Edwards & Fillingim, 2001; Herrero et al., 2000).

Multilevel models (MLMs) were conducted in HLM v.8 (Raudenbush et al., 2019) to evaluate relations between adversity/discrimination measures (level 2) and within-person changes in pain ratings across the 10 heat pulses (level 1). Preliminary analyses revealed that temporal summation of pain ratings exhibited a quadratic change ($b=-.15$, $SE=.02$, $t=6.55$, $p<.001$), as reflected in initial increases in pain ratings and deceleration in pain ratings across the task, with peak pain levels typically occurring at the fifth heat pulse (Figure 1). We conceptualized positive linear slopes as reflecting temporal summation of pain (i.e., instantaneous rate of change in pain ratings at the start of the task) and negative quadratic terms as reflecting pain habituation across all 10 heat pulses. Due to their known impact on pain processing (Fillingim, 2017), age, gender, and education were included a priori

as predictors of initial pain ratings (intercept), temporal summation of pain (linear slope), and pain habituation (quadratic term). Of primary interest were the cross-level interactions between adversity/discrimination measures and linear/quadratic change.

Multiple linear regressions were conducted in SPSS v.28 (IBM, Corp.) to evaluate relations between adversity/discrimination measures and pain tolerance, controlling for age, gender, and education (years completed). To account for multiple testing, we used the Benjamini-Hochberg false discovery rate correction to control for the rate of type I errors by adjusting the p-value based on the number of significant results in a family of tests (Benjamini & Hochberg, 1995). Significant interactions were probed and simple slopes were calculated using an online calculator (Preacher et al., 2006). Missing data for analyses of temporal summation of pain and pain habituation were handled using restricted maximum-likelihood estimation.

RESULTS

Preliminary Analyses

Descriptive statistics and correlations for demographic, adversity, discrimination, and experimental pain response measures are presented in Table 1. Scores on individual measures of early adversity, including the CTQ (mean=40.25, SD=14.74) and FAQ (mean=2.11, SD=2.38), revealed that, on average, the sample reported significant childhood trauma history (CTQ total score cutoff   36 recommended by Vahapoglu et al., 2018) and exposure to two adverse early life experiences. Scores on individual measures of recent adversity, including the CBS (mean=28.48, SD=7.82) and PSS (mean=15.14, SD=6.95), and lifetime racial discrimination (mean=31.45, SD=10.00), are comparable to community samples of primarily low-income, multiethnic adults reporting histories of either childhood sexual abuse or spousal abuse (Myers et al., 2015). Adversity composites and racial discrimination were all significantly and positively correlated (r's >.30). Older individuals reported higher levels of early-life adversity but age was not associated with recent adversity or racial discrimination. Education level was not associated with the adversity composites or racial discrimination. Four participants did not complete the full temporal summation of pain protocol due to pain ratings of 100 (a pre-determined stopping rule): three of these participants did not contribute temporal summation of pain data and were excluded from analyses; the remaining participant contributed 6 ratings and was included in analyses.

Pain Tolerance

Results of multiple linear regression models are presented in Table 2. Higher levels of lifetime racial discrimination were associated with higher heat pain tolerance, controlling for gender, age, and education. However, neither early-life adversity nor recent adversity were significantly associated with heat pain tolerance. Being female was associated with lower heat pain tolerance in all models (p's < .03).

Temporal Summation

Recent adversity significantly moderated both linear and quadratic changes in pain ratings, though it was not associated with initial pain ratings (Table 3). Simple slope analysis

revealed that temporal summation of pain was higher among adults with greater (+1 SD) levels of recent adversity (b=4.64, SE=1.41, t=3.29, p<.001) compared to adults with lower (−1 SD) levels of recent adversity (b=3.55, SE=1.40, t=2.53, p=.01). In addition, more rapid deceleration in pain ratings (i.e., faster habituation) was observed for adults with higher (+1 SD) compared to those with lower (−1 SD) levels of recent adversity (Figure 2).

Early-life adversity was neither associated with initial pain ratings nor with linear or quadratic changes in pain ratings (Table 4). Similarly, lifetime racial discrimination was neither associated with initial pain ratings nor with linear or quadratic changes in pain ratings (Table 5).

DISCUSSION

The present study evaluated how different types and timing of adversity exposure are associated with evoked pain responses in healthy AA adults. Improved understanding of these associations could elucidate pathways linking adverse exposures to the development of chronic pain and, ultimately, help to mitigate well-established racial disparities in pain severity, pain-related life interference, and pain sensitivity that disproportionately affect AA compared to non-Hispanic White adults (Anderson et al., 2009; Institute of Medicine, 2011). Consistent with our hypothesis, higher levels of recent adversity (i.e., chronic stress burden, perceived stress levels) were associated with increased temporal summation of pain - an indicator of central sensitization to painful stimuli and a risk factor for the development of chronic pain (Greenspan et al., 2013; Petersen et al., 2018). However, contrary to hypotheses, higher levels of recent adversity were also associated with more rapid pain habituation. The following sections explore several potential explanations for differential associations between adversity and evoked pain responses that could explain discrepancies in this study and in the extant literature.

The present findings suggest that among healthy AA adults, greater exposure to recent adversity was associated with elevated temporal summation of pain, which is considered a *pro-nociceptive* experimental pain response index. Results suggest that lifetime racial discrimination and early life adversity have less bearing on temporal summation of pain among AA adults as compared to more recent, ongoing stress levels. This finding contrasts with research showing that cumulative, lifespan approaches to measuring adversity are more fruitful for determining long-term physical and mental health risk compared to specific measures of childhood or adulthood adversity (Felitti et al., 1998; Kessler, 2000). Whereas indicators of lifetime or cumulative adversity have shown promise as predictors of relatively stable negative health conditions such as chronic pain, they may be less sensitive than acute stress indicators as predictors of relatively variable risk markers for chronic pain such as temporal summation of pain. The stability of temporal summation of pain, as evident in test-retest reliability, is considered strong for within-day and one-week intervals (Kong, Johnson, Balise & Mackey, 2013) but only poor-to-good over longer (i.e., two weeks to 4-months) intervals in healthy individuals (Alappattu et al., 2011; Marcuzzi et al., 2017). Evidence of temporal summation of pain variability over time suggests that this risk marker is more likely to be influenced by contextual than constitutional factors. Elevated temporal summation of pain in the context of short-term stress may represent

an intermediate point along theoretical pathways linking long-term stress to cumulative biopsychosocial vulnerabilities (Myers, 2009) and, ultimately, the development of chronic pain.

The Oklahoma Study of Native American Pain Risk (OK-SNAP; Rhudy et al., 2020) – another minoritized group disproportionately impacted by adversity (Beals et al., 2013; Manson et al., 2005; Turner & Lloyd, 2004) - showed that greater cumulative exposure to traumatic events was associated with enhanced temporal summation of nociceptive flexion reflex, which is also considered an indicator of (spinal) central sensitization to painful stimuli. Although lifetime trauma exposure was associated with higher overall pain (i.e., intercept) during the electrical temporal summation of pain protocol among healthy Native American adults, it was not associated with electrical temporal summation of pain (i.e., slope) (Sturycz et al., 2019). Comparisons between the present study and OK-SNAP are challenging due to differences in pain stimulus (heat versus electrical, respectively), temporal summation of pain rating method (10 ratings following each pulse at a frequency of 0.4 Hz versus ratings made after five trains of three stimuli, respectively), and measurement of adversity (early/recent adversity and lifetime discrimination versus lifetime trauma exposure). One possible interpretation of divergent findings is that initial pain ratings in multilevel models were higher in the OK-SNAP electrical temporal summation of pain (mean rating = 48.7 out of 100) as compared to the present study heat temporal summation of pain (mean rating = 41.5 out of 100), which suggests that the electrical stimulus was perceived as more painful than the heat stimulus and may have increased problems with ceiling effects. However, temporal summation of pain effects were detected in both studies despite differential associations with adversity measures; moreover, OK-SNAP participants who gave maximum pain ratings for all stimuli were excluded from analyses and covariance between intercept (initial pain) and slope of pain ratings (i.e., summation) was non-significant (Sturycz et al., 2019).

As alluded to above, the differential associations with temporal summation of pain between studies might be due to discrepancies in the measurement of adversity. The recent adversity composite used in the current study included the impact of chronic stress burden and perceived stress levels whereas in the aforementioned OK-SNAP study, the Life Events Checklist (LEC) captured lifetime trauma exposure. However, more recent OK-SNAP findings also revealed that psychological stress (a composite of PSS-10 and the Global Severity Index of the SCL90-R) contributed to enhanced temporal summation of pain via sleep problems in Native American adults (Kell et al., 2022). Whereas the LEC-based adversity measure linked to temporal summation of nociceptive flexion reflex in OK-SNAP more closely approximated the traumatic events captured by this study's early-life adversity measure, the psychological stress composite in OK-SNAP included the same measure (PSS-10) as this study's recent adversity composite. Thus, across both AA and Native American adults, greater temporal summation of pain was associated with higher ongoing stress levels.

Our prior work showed greater temporal summation of pain among chronic pain patients who reported early-life adversity (i.e., childhood physical or sexual assault or abuse) compared to chronic pain patients without early-life adversity or healthy controls (Sherman

et al., 2015). This finding suggests that enhanced temporal summation of pain could be one mechanism through which early-life adversity confers increased risk for development of chronic pain. Another study found enhanced heat temporal summation of pain (mean target of 48.5°C) in healthy young adults with higher compared to lower levels of early-life adversity (a measure that assessed incidents involving physical, sexual, and emotional abuse as well as general adversity) (You & Meagher, 2016). Although this finding appears to conflict with our own, it is possible given the mean age of that sample (18 years) that more proximal childhood adverse events (defined as occurring before age 18) could have also been capturing recent adversity. Future experimental pain studies should examine temporal windows that best capture recent adversity in healthy adult samples in order to distinguish stressor characteristics most likely to influence temporal summation of pain, including chronicity, timing of most recent event, levels of perceived stress, and whether or not the stressor could be considered ongoing.

Contrary to hypotheses, greater exposure to racial discrimination was associated with higher heat pain tolerance and greater exposure to recent adversity was associated with stronger pain habituation. Higher heat pain tolerance and stronger pain habituation are considered *anti-nociceptive* experimental pain response indices. These findings contrast with prior work showing that greater racial discrimination was associated with *lower* heat pain tolerance in older AA adults with chronic pain (symptomatic knee osteoarthritis) (Goodin et al., 2013). One interpretation of these discrepancies in the direction of relations between discrimination and pain tolerance is that they capture distinct phases along the transition from acute pain (discrimination associated with anti-nociceptive profile) to chronic pain (discrimination associated with pro-nociceptive profile). Goodin and colleagues highlight hypervigilance to threat and alterations in stress response systems as potential mechanisms linking racial discrimination and lower pain tolerance (Goodin et al., 2013). Meta-analytic reviews of chronic stress and hypothalamic-pituitary-adrenal (HPA) secretion suggest that positive associations between stressors and cortisol secretion (hyperactivity) during the acute phase eventually switch to negative associations (hypoactivity) as stressors become more chronic (Miller et al., 2007). Older AA adults are likely to have experienced more chronic racial discrimination during their lifetimes than younger AA adults due to the passage of time and changing sociocultural circumstances, and as a result are more likely to exhibit hypoactive (as opposed to hyperactive) stress response systems. Whereas younger AA adults may experience robust cortisol stress responses and stress-induced analgesic (SIA) effects, older AA adults may exhibit blunted cortisol stress responses and SIA effects due, in part, to downregulation of the HPA axis in the context of chronic discrimination experiences (Fries et al., 2005; Heim et al., 2000). Hence, SIA effects may account for differences between the current study - which consisted of young, healthy AA adults, for whom discrimination is likely associated with *anti*-nociceptive features – and previously described studies that consisted of primarily older AA adults with chronic pain, for whom discrimination is likely associated with *pro*-nociceptive features. Our prior work with healthy young adults suggests that a social-evaluative laboratory stressor elicits SIA effects, as evident in reduced initial pain ratings during a temporal summation of pain protocol, but was not associated with temporal summation slopes; these SIA effects on initial pain ratings were most pronounced among individuals who were high stress responders (Bruehl et al., 2022). Future studies are

needed to evaluate changes in SIA effects over time as a potential mechanism contributing to the transition from acute to chronic pain.

Chronic pain conditions are more prevalent among women than men (Tsang et al., 2008), with gender differences in experimental pain responses proposed as an important contributing factor (Fillingim, 2017). Consistent with this literature, women in the present study exhibited lower heat pain tolerance compared to males. A variety of mechanisms have been proposed to account for gender differences in pain experiences, including differences in pain-related fear, pain catastrophizing, and gender role expectations (Sorge & Strath, 2018). Future studies are needed to evaluate psychosocial and neuroimmune factors that may account for gender disparities in pain sensitivity and chronic pain prevalence (Gregus et al., 2021).

One important methodological contribution of the present study was the use of both linear and quadratic change components in a temporal summation of pain protocol to evaluate temporal summation of pain and pain habituation, respectively. This permitted identification of a unique pattern of stronger temporal summation of pain and pain habituation among AA adults who reported higher levels of recent adversity, suggesting that temporal summation of pain effects were present but relatively short-lived. Thermal experimental pain studies have previously reported patterns of increases in pain ratings with rapidly repeated stimuli within sessions (i.e., *sensitization*) and decreases in pain ratings across successive sessions (i.e., *habituation*) (Agostinho et al., 2009; Breimhorst et al., 2012; May et al., 2012). The present study demonstrated that both temporal summation of pain and within-session habituation are observed with a 48°C target among healthy, young AA adults. Prior work examining temporal summation of pain in both younger and older adults using a similar site (forearm) and thermal stimulus to the one administered in the present study showed temperature-dependent patterns reflecting temporal decreases in pain (47°C target), both temporal summation of pain and habituation (50°C target), and temporal summation of pain only (53°C target) (Edwards & Fillingim, 2001). Together with the present findings, this suggests that target temperatures between 48°C and 50°C may elicit a pattern of quadratic change capturing both temporal summation of pain and habituation.

LIMITATIONS

One important limitation of the present study is the absence of acute stress reactivity measures. Activation of stress response systems and associated SIA effects may reflect one potential mechanism linking discrimination and recent adversity to higher pain tolerance and more rapid pain habituation, respectively. Future studies including laboratory stress tasks are needed to examine associations among adversity/discrimination measures, acute stress reactivity, and potential SIA effects on experimental pain response indices. Second, participants in this study completed an average of 15 or more years of education, which is likely to be consistent with other experimental pain studies conducted in predominantly undergraduate samples (for a review see Kim et al., 2017), though comparisons are difficult due to infrequent reporting of SES. A relatively high average SES in the present sample may have been influenced by recruitment methods (e.g., participant registries on university webpages). Given the complex relations among race, SES, and pain experiences (Meghani

& Chittams, 2015), higher levels of education in this study should be considered whenever comparing to experimental pain studies conducted with minoritized individuals reporting lower SES (e.g., Riley et al., 2002). Finally, the present study recruited healthy AA adults and findings regarding relations between adversity and experimental pain response indices may not generalize to AA adults with chronic pain. Although healthy AA adults are more likely than their non-Hispanic White counterparts to experience adversity and to transition from acute to chronic pain (McLaughlin et al., 2016; McLean et al., 2005; McLean et al., 2014), it is likely that the present sample contains heterogeneity with regard to both risk and resilience factors for pain. Future studies should examine the role of cognitive factors (e.g., pain catastrophizing and pain resilience) as moderators of relations between adversity and experimental pain response indices.

CONCLUSIONS

The present study has several important conceptual and methodological implications. First, higher temporal summation of pain was associated with recent adversity but not with early-life adversity or lifetime racial discrimination, which suggests that current stress levels may be key determinants of this pro-nociceptive experimental pain response index. Future research is needed to identify physiologic stress-relevant mediators of temporal summation of pain (e.g., neuroendocrine, inflammation) and to determine whether stress management interventions have an impact on temporal summation of pain. Importantly, experimental pain response indices have previously been shown to predict clinical outcomes (i.e., pain-related interference with daily activities) over and above the effects of cognitive-behavioral treatment for chronic pain (Morris et al., 2021a). Elevated temporal summation of pain may complement psychosocial risk measures in determining personalized pain-risk profiles among healthy adults, which could help to identify individuals who may benefit from early interventions to prevent development of chronic pain. Second, temporal summation of pain protocols that include 10 ratings can be used to simultaneously capture temporal summation of pain and pain habituation (protocols with 5 or fewer ratings may be optimal for capturing temporal summation of pain only). These two dimensions of pain experiences may be analogous to acute psychosocial stress paradigms that capture stress reactivity and recovery: although these dimensions are correlated, exaggerated (or blunted) responses to stress and delayed return to baseline levels (i.e., prolonged activation) are differentially associated with physical and mental health outcomes (Brosschot et al., 2005; McEwen, 1998). Examining both dimensions simultaneously during temporal summation of pain protocols could improve understanding of differential pain risk phenotypes. Future studies could evaluate whether stronger pain habituation buffers healthy AA adults who exhibit higher temporal summation of pain against risk for developing persistent pain complaints. Alternately, individuals who exhibit both stronger temporal summation of pain ('pain reactivity') and weaker pain habituation ('prolonged pain activation') could be at greatest risk for developing chronic pain.

Availability of data and materials:

The datasets generated and analyzed for the current study are not publicly available due to concerns regarding the privacy of research participants. However, de-identified datasets are available from the corresponding author on reasonable request.

Acronyms:

AA	African-American
SES	socioeconomic
MLM	multilevel models

REFERENCES

Agostinho CMS, Scherens A, Richter H, Schaub C, Rolke R, Treede R-D, & Maier C (2009). Habituation and short-term repeatability of thermal testing in healthy human subjects and patients with chronic non-neuropathic pain. European journal of pain, 13(8), 779–785. [PubMed: 19019713]

Alappattu MJ, Bishop MD, Bialosky JE, George SZ, & Robinson ME (2011). Stability of behavioral estimates of activity-dependent modulation of pain. Journal of pain research, 151–157. [PubMed: 21811390]

Anderson KO, Green CR, & Payne R (2009). Racial and ethnic disparities in pain: causes and consequences of unequal care. J Pain, 10(12), 1187–1204. doi:10.1016/j.jpain.2009.10.002 [PubMed: 19944378]

Anderson RJ, Craggs JG, Bialosky JE, Bishop MD, George SZ, Staud R, & Robinson ME (2013). Temporal summation of second pain: variability in responses to a fixed protocol. Eur J Pain, 17(1), 67–74. doi:10.1002/j.1532-2149.2012.00190.x [PubMed: 22899549]

Arendt-Nielsen L, Simonsen O, Laursen MB, Roos EM, Rathleff MS, Rasmussen S, & Skou ST (2018). Pain and sensitization after total knee replacement or nonsurgical treatment in patients with knee osteoarthritis: Identifying potential predictors of outcome at 12 months. Eur J Pain, 22(6), 1088–1102. doi:10.1002/ejp.1193 [PubMed: 29369450]

Beals J, Belcourt-Dittloff A, Garroutte EM, Croy C, Jervis LL, Whitesell NR, … Team, A.-S. (2013). Trauma and conditional risk of posttraumatic stress disorder in two American Indian reservation communities. Social Psychiatry and Psychiatric Epidemiology, 48(6), 895–905. doi:10.1007/s00127-012-0615-5 [PubMed: 23135256]

Benjamini Y, & Hochberg Y (1995). Controlling the false discovery rate - A practical and powerful approach to multiple testing. Journal of the Royal Statistical Society Series B-Methodological, 57(1), 289–300. Retrieved from <Go to ISI>://WOS:A1995QE45300017

Bernstein DP, Fink L, Handelsman L, Foote J, Lovejoy M, Wenzel K, … Ruggiero J (1994). Initial reliability and validity of a new retrospective measure of child-abuse and neglect. American Journal of Psychiatry, 151(8), 1132–1136. Retrieved from <Go to ISI>://WOS:A1994NZ33400007 [PubMed: 8037246]

Bingel U, Schoell E, & Büchel C (2007). Imaging pain modulation in health and disease. Current opinion in neurology, 20(4), 424–431. [PubMed: 17620877]

Breimhorst M, Hondrich M, Rebhorn C, May A, & Birklein F (2012). Sensory and sympathetic correlates of heat pain sensitization and habituation in men and women. European journal of pain, 16(9), 1281–1292. [PubMed: 22407985]

Brondolo E, Kelly KP, Coakley V, Gordon T, Thompson S, Levy E, … Contrada RJ (2005). The perceived ethnic discrimination questionnaire: Development and preliminary validation of a community version. Journal of Applied Social Psychology, 35(2), 335–365. doi:10.1111/j.1559-1816.2005.tb02124.x

Brosschot JF, Pieper S, & Thayer JF (2005). Expanding stress theory: Prolonged activation and perseverative cognition. Psychoneuroendocrinology, 30(10), 1043–1049. [PubMed: 15939546]

Brown LL, Abrams LR, Mitchell UA, & Ailshire JA (2020). Measuring more than exposure: Does stress appraisal matter for black–white differences in anxiety and depressive symptoms among older adults? Innovation in Aging, 4(5), igaa040.

Bruehl S, France CR, France J, Harju A, & al'Absi M (2005). How accurate are parental chronic pain histories provided by offspring? Pain, 115(3), 390–397. doi:10.1016/j.pain.2005.03.017 [PubMed: 15911166]

Bruehl S, Morris MC, & Al'Absi M (2022). Stress-induced analgesia: an evaluation of effects on temporal summation of pain and the role of endogenous opioid mechanisms. Pain Reports, 7(2).

Burgess DJ, Grill J, Noorbaloochi S, Griffin JM, Ricards J, van Ryn M, & Partin MR (2009). The effect of perceived racial discrimination on bodily pain among older African American men. Pain Med, 10(8), 1341–1352. doi:10.1111/j.1526-4637.2009.00742.x [PubMed: 20021596]

Chung OY, & Bruehl S (2008). The impact of blood pressure and baroreflex sensitivity on wind-up. Anesthesia & Analgesia, 107(3), 1018–1025.

Cohen S, Kamarck T, & Mermelstein R (1983). A global measure of perceived stress. Journal of Health and Social Behavior, 24(4), 385–396. doi:10.2307/2136404 [PubMed: 6668417]

Dengler-Crish CM, Bruehl S, & Walker LS (2011). Increased wind-up to heat pain in women with a childhood history of functional abdominal pain. PAIN®, 152(4), 802–808. [PubMed: 21282006]

Dickens H, Bruehl S, Rao U, Myers H, Goodin B, Huber FA, … & Morris MC (2022). Cognitive-Affective-Behavioral Pathways Linking Adversity and Discrimination to Daily Pain in African-American Adults. Journal of Racial and Ethnic Health Disparities, 1–13.

Edwards RR (2008). The association of perceived discrimination with low back pain. J Behav Med, 31(5), 379–389. doi:10.1007/s10865-008-9160-9 [PubMed: 18581224]

Edwards RR, & Fillingim RB (2001). Effects of age on temporal summation and habituation of thermal pain: clinical relevance in healthy older and younger adults. J Pain, 2(6), 307–317. doi:10.1054/jpai.2001.25525 [PubMed: 14622810]

Ettekal I, Eiden RD, Nickerson AB, & Schuetze P (2019). Comparing alternative methods of measuring cumulative risk based on multiple risk indicators: Are there differential effects on children's externalizing problems?. PloS one, 14(7), e0219134. [PubMed: 31269048]

Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, … Marks JS (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults - The adverse childhood experiences (ACE) study. American journal of preventive medicine, 14(4), 245–258. doi:10.1016/s0749-3797(98)00017-8 [PubMed: 9635069]

Fillingim RB (2017). Individual differences in pain: understanding the mosaic that makes pain personal. Pain, 158(Suppl 1), S11. [PubMed: 27902569]

Fillingim RB, & Edwards RR (2005). Is self-reported childhood abuse history associated with pain perception among healthy young women and men? Clinical Journal of Pain, 21(5), 387–397. doi:10.1097/01.ajp.0000149801.46864.39 [PubMed: 16093744]

Fillingim RB, Maixner W, Kincaid S, & Silva S (1998). Sex differences in temporal summation but not sensory-discriminative processing of thermal pain. Pain, 75(1), 121–127. doi:10.1016/s0304-3959(97)00214-5 [PubMed: 9539681]

Fries E, Hesse J, Hellhammer J, & Hellhammer DH (2005). A new view on hypocortisolism. Psychoneuroendocrinology, 30(10), 1010–1016. [PubMed: 15950390]

Georgopoulos V, Akin-Akinyosoye K, Zhang W, McWilliams DF, Hendrick P, & Walsh DA (2019). Quantitative sensory testing and predicting outcomes for musculoskeletal pain, disability, and negative affect: a systematic review and meta-analysis. Pain, 160(9), 1920–1932. doi:10.1097/j.pain.0000000000001590 [PubMed: 31045746]

Geva N, & Defrin R (2013). Enhanced pain modulation among triathletes: a possible explanation for their exceptional capabilities. Pain®, 154(11), 2317–2323. [PubMed: 23806655]

Geva N, Pruessner J, & Defrin R (2014). Acute psychosocial stress reduces pain modulation capabilities in healthy men. Pain, 155(11), 2418–2425. doi:10.1016/j.pain.2014.09.023 [PubMed: 25250721]

Goodin BR, Pham QT, Glover TL, Sotolongo A, King CD, Sibille KT, … Staud R (2013). Perceived racial discrimination, but not mistrust of medical researchers, predicts the heat pain tolerance of African Americans with symptomatic knee osteoarthritis. Health Psychology, 32(11), 1117. [PubMed: 24219416]

Greenspan JD, Slade GD, Bair E, Dubner R, Fillingim RB, Ohrbach R, … Maixner W (2013). Pain sensitivity and autonomic factors associated with development of TMD: the OPPERA prospective cohort study. J Pain, 14(12 Suppl), T63–74 e61–66. doi:10.1016/j.jpain.2013.06.007 [PubMed: 24275224]

Greenspan JD, Slade GD, Bair E, Dubner R, Fillingim RB, Ohrbach R, … Maixner W (2011). Pain sensitivity risk factors for chronic TMD: descriptive data and empirically identified domains from the OPPERA case control study. The Journal of Pain, 12(11), T61–T74. [PubMed: 22074753]

Gregus AM, Levine IS, Eddinger KA, Yaksh TL, & Buczynski MW (2021). Sex differences in neuroimmune and glial mechanisms of pain. Pain, 160(8), 2186–2200.

Güereca YM, Kell PA, Kuhn BL, Hellman N, Sturycz CA, Toledo TA, … Palit S (2022). The Relationship Between Experienced Discrimination and Pronociceptive Processes in Native Americans: Results From the Oklahoma Study of Native American Pain Risk. The Journal of Pain.

Gurung RAR, Taylor SE, Kemeny M, & Myers H (2004). "HIV is not my biggest problem: The impact of HIV and chronic burden on depression in women at risk for AIDS. Journal of Social and Clinical Psychology, 23(4), 490–511. doi:10.1521/jscp.23.4.490.40305

Heim C, Ehlert U, & Hellhammer DH (2000). The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. Psychoneuroendocrinology, 25(1), 1–35. doi:10.1016/s0306-4530(99)00035-9 [PubMed: 10633533]

Herrero JF, Laird JM, & Lopez-Garcia JA (2000). Wind-up of spinal cord neurones and pain sensation: much ado about something? Progress in neurobiology, 61(2), 169–203. [PubMed: 10704997]

Institute of Medicine. (2011). Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research.

Kell PA, Huber FA, Street EN, Shadlow JO, & Rhudy JL (2022). Sleep Problems Mediate the Relationship Between Psychosocial Stress and Pain Facilitation in Native Americans: A Structural Equation Modeling Analysis from the Oklahoma Study of Native American Pain Risk. Annals of Behavioral Medicine.

Kessler RC (1979). Stress, social status, and psychological distress. Journal of health and social behavior, 259–272. [PubMed: 479536]

Kessler RC (2000). Posttraumatic stress disorder: The burden to the individual and to society. Journal of Clinical Psychiatry, 61, 4–14. Retrieved from <Go to ISI>://WOS:000086273100002

Kessler RC, & Magee WJ (1993). Childhood adversities and adult depression - basic patterns of association in a united-states national survey. Psychol Med, 23(3), 679–690. Retrieved from <Go to ISI>://WOS:A1993LX89700016 [PubMed: 8234575]

Kim HJ, Yang GS, Greenspan JD, Downton KD, Griffith KA, Renn CL, … Dorsey SG (2017). Racial and ethnic differences in experimental pain sensitivity: systematic review and meta-analysis. Pain, 158(2), 194–211. [PubMed: 27682208]

Klaassens ER, Giltay EJ, Cuijpers P, van Veen T, & Zitman FG (2012). Adulthood trauma and HPA-axis functioning in healthy subjects and PTSD patients: a meta-analysis. Psychoneuroendocrinology, 37(3), 317–331. [PubMed: 21802212]

Kong JT, Johnson KA, Balise RR, & Mackey S (2013). Test-retest reliability of thermal temporal summation using an individualized protocol. The Journal of Pain, 14(1), 79–88. [PubMed: 23273835]

Manson SM, Beals J, Klein SA, Croy CD, & Team A-S (2005). Social epidemiology of trauma among 2 American Indian reservation populations. American Journal of Public Health, 95(5), 851–859. doi:10.2105/ajph.2004.054171 [PubMed: 15855465]

Marcuzzi A, Wrigley PJ, Dean CM, Adams R, & Hush JM (2017). The long-term reliability of static and dynamic quantitative sensory testing in healthy individuals. Pain, 158(7), 1217–1223. [PubMed: 28328574]

May A, Rodriguez-Raecke R, Schulte A, Ihle K, Breimhorst M, Birklein F, & Jürgens T (2012). Within-session sensitization and between-session habituation: A robust physiological response

to repetitive painful heat stimulation. European journal of pain, 16(3), 401–409. [PubMed: 22337205]

McEwen BS (1998). Protective and damaging effects of stress mediators. New England journal of medicine, 338(3), 171–179. [PubMed: 9428819]

McLaughlin JM, Lambing A, Witkop ML, Anderson TL, Munn J, & Tortella B (2016). Racial Differences in Chronic Pain and Quality of Life among Adolescents and Young Adults with Moderate or Severe Hemophilia. J Racial Ethn Health Disparities, 3(1), 11–20. doi:10.1007/s40615-015-0107-x [PubMed: 26896101]

McLean SA, Clauw DJ, Abelson JL, & Liberzon I (2005). The development of persistent pain and psychological morbidity after motor vehicle collision: integrating the potential role of stress response systems into a biopsychosocial model. Psychosom Med, 67(5), 783–790. doi:10.1097/01.psy.0000181276.49204.bb [PubMed: 16204439]

McLean SA, Ulirsch JC, Slade GD, Soward AC, Swor RA, Peak DA, … Bair E (2014). Incidence and predictors of neck and widespread pain after motor vehicle collision among US litigants and nonlitigants. Pain, 155(2), 309–321. doi:10.1016/j.pain.2013.10.016 [PubMed: 24145211]

Meghani SH, & Chittams J (2015). Controlling for socioeconomic status in pain disparities research: all-else-equal analysis when "all else" is not equal. Pain Medicine, 16(12), 2222–2225. [PubMed: 26052869]

Miller GE, Chen E, & Zhou ES (2007). If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. Psychological Bulletin, 133(1), 25–45. doi:10.1037/0033-2909.133.1.25 [PubMed: 17201569]

Morris MC, Bruehl S, Stone AL, Garber J, Smith C, Palermo TM, & Walker LS (2021a). Does quantitative sensory testing improve prediction of chronic pain trajectories? A longitudinal study of youth with functional abdominal pain participating in a randomized controlled trial of cognitive behavioral treatment. The Clinical journal of pain, 37(9), 648. [PubMed: 34192714]

Morris MC, Bruehl S, Stone AL, Garber J, Smith C, Palermo TM, & Walker LS (2021b). Place and pain: Association between neighborhood disadvantage and quantitative sensory testing responses in youth with functional abdominal pain. Journal of pediatric psychology.

Morris MC, Walker L, Bruehl S, Hellman N, Sherman AL, & Rao U (2015). Race effects on temporal summation to heat pain in youth. Pain, 156(5), 917. [PubMed: 25734994]

Myers HF (2009). Ethnicity- and socio-economic status-related stresses in context: an integrative review and conceptual model. J Behav Med, 32(1), 9–19. doi:10.1007/s10865-008-9181-4 [PubMed: 18989769]

Myers HF, Wyatt GE, Ullman JB, Loeb TB, Chin D, Prause N, … & Liu H (2015). Cumulative burden of lifetime adversities: Trauma and mental health in low-SES African Americans and Latino/as. Psychological Trauma: Theory, Research, Practice, and Policy, 7(3), 243. [PubMed: 25961869]

O'Connor DB, Thayer JF, & Vedhara K (2021). Stress and health: A review of psychobiological processes. Annual review of psychology, 72, 663–688.

O'Leary H, Smart KM, Moloney NA, & Doody CM (2017). Nervous System Sensitization as a Predictor of Outcome in the Treatment of Peripheral Musculoskeletal Conditions: A Systematic Review. Pain Pract, 17(2), 249–266. doi:10.1111/papr.12484 [PubMed: 27538534]

Pascoe EA, & Richman LS (2009). Perceived Discrimination and Health: A Meta-Analytic Review. Psychological Bulletin, 135(4), 531–554. doi:10.1037/a0016059 [PubMed: 19586161]

Petersen KK, Simonsen O, Laursen MB, & Arendt-Nielsen L (2018). The Role of Preoperative Radiologic Severity, Sensory Testing, and Temporal Summation on Chronic Postoperative Pain Following Total Knee Arthroplasty. Clin J Pain, 34(3), 193–197. doi:10.1097/AJP.0000000000000528 [PubMed: 28654559]

Preacher KJ, Curran PJ, & Bauer DJ (2006). Computational tools for probing interactions in multiple linear regression, multilevel modeling, and latent curve analysis. Journal of Educational and Behavioral Statistics, 31(4), 437–448. doi:10.3102/10769986031004437

Price DD, Hu JW, Dubner R, & Gracely RH (1977). Peripheral suppression of 1st pain and central summation of 2nd pain evoked by noxious heat pulses. Pain, 3(1), 57–68. doi:10.1016/0304-3959(77)90035-5 [PubMed: 876667]

Rahim-Williams B, Riley JL, Williams AKK, & Fillingim RB (2012). A Quantitative Review of Ethnic Group Differences in Experimental Pain Response: Do Biology, Psychology, and Culture Matter? Pain medicine, 13(4), 522–540. doi:10.1111/j.1526-4637.2012.01336.x [PubMed: 22390201]

Rankin CH, Abrams T, Barry RJ, Bhatnagar S, Clayton DF, Colombo J, … Marsland S (2009). Habituation revisited: an updated and revised description of the behavioral characteristics of habituation. Neurobiology of learning and memory, 92(2), 135–138. [PubMed: 18854219]

Rassu FS, Luedke JC, Nanavaty N, Mathur VA, & Meagher MW (2020). Greater mechanical temporal summation of pain in Latinx-Americans and the role of adverse life experiences. Pain Reports, 5(5).

Raudenbush S, Bryk A, Cheong Y, Congdon R, & du Toit M (2019). HLM 8: Hierarchical linear and nonlinear modeling. Skokie, IL: Scientific Software International.

Rhudy JL, Lannon EW, Kuhn BL, Palit S, Payne MF, Sturycz CA, … Shadlow JO (2020). Assessing peripheral fibers, pain sensitivity, central sensitization, and descending inhibition in Native Americans: main findings from the Oklahoma Study of Native American Pain Risk. Pain, 161(2), 388–404. doi:10.1097/j.pain.0000000000001715 [PubMed: 31977838]

Richardson EJ, Trost Z, Payne M, & Wiggins A (2022). The Negative Effect of Social Discrimination on Pain Tolerance and the Moderating Role of Pain Catastrophizing. J Clin Psychol Med Settings. doi:10.1007/s10880-022-09860-1

Riley III JL, Cruz-Almeida Y, Glover TL, King CD, Goodin BR, Sibille KT, … & Fillingim RB (2014). Age and race effects on pain sensitivity and modulation among middle-aged and older adults. The Journal of Pain, 15(3), 272–282. [PubMed: 24239561]

Riley III JL, Wade JB, Myers CD, Sheffield D, Papas RK, & Price DD (2002). Racial/ethnic differences in the experience of chronic pain. Pain, 100(3), 291–298. [PubMed: 12468000]

Rutter M (1981). Stress, coping and development: Some issues and some questions. Journal of child psychology and psychiatry, 22(4), 323–356. [PubMed: 7287844]

Sherman AL, Morris MC, Bruehl S, Westbrook TD, & Walker LS (2015). Heightened Temporal Summation of Pain in Patients with Functional Gastrointestinal Disorders and History of Trauma. Annals of Behavioral Medicine, 49(6), 785–792. doi:10.1007/s12160-015-9712-5 [PubMed: 25967582]

Slopen N, Shonkoff JP, Albert MA, Yoshikawa H, Jacobs A, Stoltz R, & Williams DR (2016). Racial Disparities in Child Adversity in the U.S.: Interactions With Family Immigration History and Income. Am J Prev Med, 50(1), 47–56. doi:10.1016/j.amepre.2015.06.013 [PubMed: 26342634]

Smith BW, Tooley EM, Montague EQ, Robinson AE, Cosper CJ, & Mullins PG (2008). Habituation and sensitization to heat and cold pain in women with fibromyalgia and healthy controls. Pain, 140(3), 420–428. [PubMed: 18947923]

Sorge RE, & Strath LJ (2018). Sex differences in pain responses. Current opinion in physiology, 6, 75–81.

Staud R (2012). Abnormal endogenous pain modulation is a shared characteristic of many chronic pain conditions. Expert Review of Neurotherapeutics, 12(5), 577–585. doi:10.1586/ern.12.41 [PubMed: 22550986]

Staufenbiel SM, Penninx BW, de Rijke YB, van den Akker EL, & van Rossum EF (2015). Determinants of hair cortisol and hair cortisone concentrations in adults. Psychoneuroendocrinology, 60, 182–194. [PubMed: 26176863]

Stern KR, & Thayer ZM (2019). Adversity in childhood and young adulthood predicts young adult depression. International journal of public health, 64, 1069–1074. [PubMed: 31253994]

Sturycz CA, Hellman N, Payne MF, Kuhn BL, Hahn B, Lannon EW, … Rhudy JL (2019). Race/Ethnicity Does Not Moderate the Relationship Between Adverse Life Experiences and Temporal Summation of the Nociceptive Flexion Reflex and Pain: Results From the Oklahoma Study of Native American Pain Risk. J Pain, 20(8), 941–955. doi:10.1016/j.jpain.2019.02.006 [PubMed: 30776495]

Tarullo AR, & Gunnar MR (2006). Child maltreatment and the developing HPA axis. Hormones and behavior, 50(4), 632–639. [PubMed: 16876168]

Tesarz J, Eich W, Treede RD, & Gerhardt A (2016). Altered pressure pain thresholds and increased wind-up in adult patients with chronic back pain with a history of childhood

maltreatment: a quantitative sensory testing study. Pain, 157(8), 1799–1809. doi:10.1097/j.pain.0000000000000586 [PubMed: 27075429]

Tsang A, Von Korff M, Lee S, Alonso J, Karam E, Angermeyer MC, … De Graaf R (2008). Common chronic pain conditions in developed and developing countries: gender and age differences and comorbidity with depression-anxiety disorders. The Journal of Pain, 9(10), 883–891. [PubMed: 18602869]

Turner RJ, & Lloyd DA (2004). Stress burden and the lifetime incidence of psychiatric disorder in young adults - Racial and ethnic contrasts. Archives of general psychiatry, 61(5), 481–488. doi:10.1001/archpsyc.61.5.481 [PubMed: 15123493]

Vahapoglu A, Nacar SM, & Gungor Y (2018). Is childhood trauma a predictive factor for increased preoperative anxiety levels?. Medicine Science| International Medical Journal, 8(2), 1.

Walker JL, Harrison TC, Brown A, Thorpe RJ, & Szanton SL (2016). Factors associated with disability among middle-aged and older African American women with osteoarthritis. Disability and Health Journal, 9(3), 510–517. doi:10.1016/j.dhjo.2016.02.004 [PubMed: 27052590]

Weissman-Fogel I, Granovsky Y, Crispel Y, Ben-Nun A, Best LA, Yarnitsky D, & Granot M (2009). Enhanced presurgical pain temporal summation response predicts post-thoracotomy pain intensity during the acute postoperative phase. J Pain, 10(6), 628–636. doi:10.1016/j.jpain.2008.12.009 [PubMed: 19398382]

Williams DR, Lawrence JA, & Davis BA (2019). Racism and health: evidence and needed research. Annual review of public health, 40, 105–125.

Wylde V, Palmer S, Learmonth ID, & Dieppe P (2013). The association between pre-operative pain sensitisation and chronic pain after knee replacement: an exploratory study. Osteoarthritis Cartilage, 21(9), 1253–1256. doi:10.1016/j.joca.2013.05.008 [PubMed: 23973138]

Yarnitsky D, Crispel Y, Eisenberg E, Granovsky Y, Ben-Nun A, Sprecher E, … Granot M (2008). Prediction of chronic post-operative pain: pre-operative DNIC testing identifies patients at risk. Pain, 138(1), 22–28. [PubMed: 18079062]

You DS (2012). The Impact of Adverse Childhood Events on Temporal Summation of Second Pain. Texas A & M University,

You DS, & Meagher MW (2016). Childhood Adversity and Pain Sensitization. Psychosomatic medicine, 78(9), 1084–1093. doi:10.1097/psy.0000000000000399 [PubMed: 27755280]

You DS, & Meagher MW (2018). Childhood Adversity and Pain Facilitation. Psychosom Med, 80(9), 869–879. doi:10.1097/PSY.0000000000000638 [PubMed: 30211795]
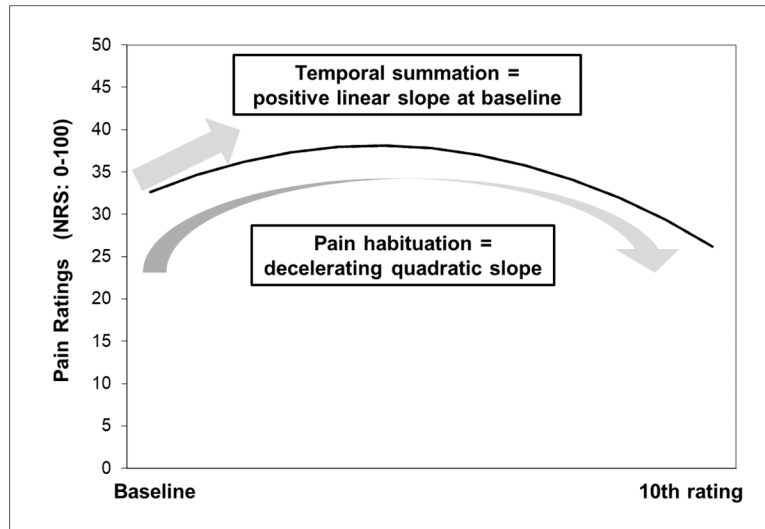
Figure 1.
Multilevel model testing linear and quadratic change in temporal summation pain ratings among healthy African-American adults. Note: NRS = numerical rating scale.
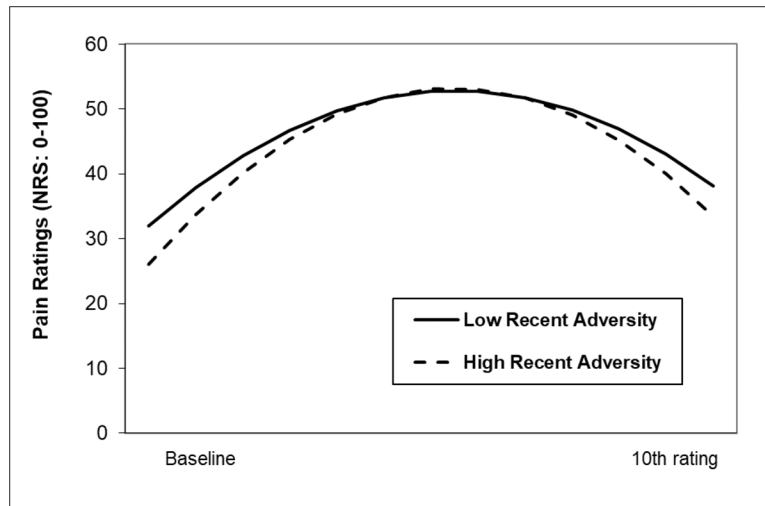
Figure 2.
Multilevel model testing recent adversity as a moderator of both temporal summation of pain and pain habituation among healthy African-American adults. Note: NRS = numerical rating scale.

Table 1.

Descriptive Statistics Summary for African-American Adults.

Variables	Mean	SD	Age	Education	Early-life Adversity	Recent Adversity	Discrimination
Age	25.89	6.39	-				
Education	15.71	3.61	.21[**]	-			
Early-life Adversity	0.00	1.82	.20[*]	−.04	-		
Recent Adversity	0.00	1.67	.07	−.07	.45[***]	-	
Discrimination	31.45	10.00	.15	−.02	.36[***]	.53[***]	-
Heat pain tolerance	47.13	2.02	−.01	.11	−.00	−.06	.20[*]

[***] *p*<.001;

[**] *p*<.01;

[*] *p*<.05.

Note. Early-life Adversity = composite of childhood trauma and family adversity z-scores; Recent Adversity = composite of chronic burden and perceived stress z-scores; Discrimination = lifetime racial discrimination.

Table 2.

Multiple Regression Models Predicting Pain Tolerance.

Predictor	Estimate	SE	t	p	F	R²	p
Model 1					2.13	.06	.08
Gender	−.72	.32	2.24	<.03			
Age	−.03	.02	1.18	.24			
Education	.07	.04	1.69	.09			
Recent adversity	−.05	.09	0.53	.60			
Model 2					2.08	.06	.09
Gender	−.72	.32	2.26	<.03			
Age	−.03	.03	1.26	.21			
Education	.08	.04	1.76	.08			
Early adversity	.03	.09	0.31	.76			
Model 3					4.03	.10	<.01
Gender	−.70	.31	2.24	<.03			
Age	−.04	.02	1.66	.10			
Education	.08	.04	1.91	.06			
Racial discrimination	.42	.15	2.73	<.01			

Note: Benjamini-Hochberg critical values: $p = .13$ (Model 1); $p = .06$ (Model 2); $p = .25$ (Model 3).

Table 3.

Multilevel Model: Recent Adversity Predicting Temporal Summation of Pain.

Predictor	Coefficient	SE	t	df	p
Intercept	41.50	13.04	3.18	139	<.01
Gender	2.05	4.23	.48	139	.63
Age	.13	.34	.40	139	.69
Education	−.83	.58	1.44	139	.15
Recent adversity	−.78	1.23	.63	139	.53
Linear change	4.10	1.39	2.94	1282	<.01
Gender	−.59	.45	1.30	1282	.19
Age	−.06	.04	1.56	1282	.12
Education	−.04	.06	.63	1282	.53
Recent adversity	.33	.13	2.48	1282	.01
Quadratic change	−.36	.15	2.44	1282	<.02
Gender	.03	.05	.61	1282	.54
Age	.00	.00	.79	1282	.43
Education	.01	.01	.83	1282	.40
Recent adversity	−.03	.01	2.13	1282	.03

Note: Benjamini-Hochberg critical values: $p = .13$ (linear change); $p = .06$ (quadratic change).

Table 4.

Multilevel Model: Early-Life Adversity Predicting Temporal Summation of Pain.

Predictor	Coefficient	SE	t	df	p
Intercept	41.60	13.07	3.18	139	<.01
Gender	2.00	4.23	.47	139	.64
Age	.12	.34	.35	139	.73
Education	−.81	.58	1.40	139	.16
Early-life adversity	−.12	1.19	.10	139	.92
Linear change	4.14	1.40	2.97	1282	<.01
Gender	−.58	.45	1.29	1282	.20
Age	−.05	.04	1.51	1282	.13
Education	−.04	.06	.72	1282	.47
Early-life adversity	.17	.13	1.31	1282	.19
Quadratic change	−.37	.15	2.46	1282	<.02
Gender	.03	.05	.60	1282	.55
Age	.00	.00	.73	1282	.47
Education	.01	.01	.92	1282	.36
Early-life adversity	−.01	.01	1.01	1282	.31

Note: Benjamini-Hochberg critical values: $p = .06$ (linear change); $p = .06$ (quadratic change).

Table 5.

Multilevel Model: Racial Discrimination Predicting Temporal Summation of Pain.

Predictor	Coefficient	SE	t	df	p
Intercept	40.41	12.99	3.11	139	<.01
Gender	1.89	4.20	.45	139	.65
Age	.18	.34	.55	139	.59
Education	−.83	.57	1.45	139	.15
Racial discrimination	−2.64	2.06	1.28	139	.20
Linear change	4.05	1.40	2.89	1282	<.01
Gender	−.56	.45	1.24	1282	.22
Age	−.05	.04	1.36	1282	.17
Education	−.05	.06	.81	1282	.42
Racial discrimination	.06	.22	.26	1282	.80
Quadratic change	−.36	.15	2.44	1282	<.02
Gender	.03	.05	.55	1282	.58
Age	.00	.00	.70	1282	.48
Education	.01	.01	.98	1282	.33
Racial discrimination	−.02	.02	.68	1282	.49

Note: Benjamini-Hochberg critical values: $p = .06$ (linear change); $p = .06$ (quadratic change).