Received: 17 August 2020 | Revised: 23 November 2020 | Accepted: 3 January 2021

DOI: 10.1002/jnr.24790

RESEARCH ARTICLE

Resilience, pain, and the brain: Relationships differ by sociodemographics

Jared J. Tanner[1] | Alisa J. Johnson[2,3] | Ellen L. Terry[2,4] | Josue Cardoso[2] | Cynthia Garvan[5] | Roland Staud[6] | Georg Deutsch[7] | Hrishikesh Deshpande[7,8] | Song Lai[9] | Adriana Addison[8,10] | David Redden[11] | Burel R. Goodin[8,10] | Catherine C. Price[1,5] | Roger B. Fillingim[2,3] | Kimberly T. Sibille[2,5,12]

[1]Department of Clinical and Health Psychology, College of Public Health and Health Professions, University of Florida, Gainesville, FL, USA

[2]Pain Research & Intervention Center of Excellence, University of Florida, Gainesville, FL, USA

[3]Department of Community Dentistry and Behavioral Science, University of Florida, Gainesville, FL, USA

[4]Department of Biobehavioral Nursing Science, College of Nursing, University of Florida, Gainesville, FL, USA

[5]Department of Anesthesiology, College of Medicine, University of Florida, Gainesville, FL, USA

[6]Department of Medicine, College of Medicine, University of Florida, Gainesville, FL, USA

[7]Department of Radiology, University of Alabama, Birmingham Medical Center, Birmingham, AL, USA

[8]Department of Anesthesiology, University of Alabama, Birmingham Medical Center, Birmingham, AL, USA

[9]Department of Radiation Oncology & CTSI Human Imaging Core, University of Florida, Gainesville, FL, USA

[10]Department of Psychology, University of Alabama at Birmingham, Birmingham, AL, USA

[11]Department of Biostatistics, University of Alabama at Birmingham, Birmingham, AL, USA

[12]Department of Aging and Geriatric Research, College of Medicine, UF Pain Research & Intervention Center of Excellence, University of Florida, Gainesville, FL, USA

Correspondance
Kimberly T. Sibille, Department of Anesthesiology, Division of Pain Medicine, Department of Aging and Geriatric Research, College of Medicine, UF Pain Research & Intervention Center of Excellence, University of Florida, PO Box 112610 Gainesville, FL 32610, USA.
Email: ksibille@ufl.edu

Funding information
Research funding and support provided by NIH/NIA Grants R01AG054370 (KTS); R37AG033906 (RBF) and UF CTSA Grant UL1TR001427 and UAB CTSA Grant UL1TR001417 from the NIH Center for Advancing Translational Sciences; 4K22NS102334-03 and 1P30AG059297 provided to the University of Florida and McKnight Brain Institute Career Development Award (ELT), minority supplement provided to the University of Florida (JSC). Data management was funded in part by NCATS grant UL1 TR000064. A portion of this work was performed in the McKnight Brain Institute at the National High Magnetic Field Laboratory's

Abstract

Chronic musculoskeletal (MSK) pain is disabling to individuals and burdensome to society. A relationship between telomere length and resilience was reported in individuals with consideration for chronic pain intensity. While chronic pain associates with brain changes, little is known regarding the neurobiological interface of resilience. In a group of individuals with chronic MSK pain, we examined the relationships between a previously investigated resilience index, clinical pain and functioning measures, and pain-related brain structures, with consideration for sex and ethnicity/race. A cross-sectional analysis of 166 non-Hispanic Black and non-Hispanic White adults, 45–85 years of age with pain ≥ 1 body site (s) over the past 3 months was completed. Measures of clinical pain and functioning, biobehavioral and psychosocial resilience, and structural MRI were completed. Our findings indicate higher levels of resilience associate with lower levels of clinical pain and functional limitations. Significant associations between resilience, ethnicity/race, and/or sex, and pain-related brain gray matter structure were demonstrated in the right amygdaloid complex, bilateral thalamus, and postcentral gyrus. Our findings provide compelling evidence that in order to decipher the neurobiological code of chronic pain and related protective factors, it

Edited by Bradley Kerr and Cristina Ghiani. Reviewed by Bruce Dick and Renato Leonardo de Freitas.

Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) Facility, which is supported by National Science Foundation Cooperative Agreement No. DMR-1157490 and DMR-1644779, and the State of Florida. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or other funding agencies

will be important to improve how chronic pain is phenotyped; to include an equal representation of females in studies including analyses stratifying by sex, and to consider other sociodemographic factors.

KEYWORDS

amygdaloid complex, chronic musculoskeletal pain, pain-related brain structure, resilience, sociodemographic factors

1 | INTRODUCTION

Chronic musculoskeletal (MSK) pain conditions affect a large proportion of the world population, represent a leading cause of functional decline and disability, and contribute toward significant societal burden (Briggs et al., 2016; Hoy et al., 2010; Vos et al., 2015). Research has predominantly focused on the role of risk factors in the development and exacerbation of chronic MSK pain (Blagojevic et al., 2010; Edwards et al., 2016; Mills et al., 2019; Silverwood et al., 2015). However, lower levels of clinical pain and greater functioning are predicted by protective factors (Haukka et al., 2017; Macfarlane et al., 2017; Thompson et al., 2018). Investigating factors associated with resilience may reveal new avenues to reduce pain severity and aid in therapeutic developments moving forward (Bartley et al., 2017; Johnson et al., 2019; Sturgeon & Zautra, 2010). Resilience is conceptualized as "the process by which people bounce back from adversity and reintegrate and ideally grow from the experience" (Resnick, 2014). Psychological resilience factors, such as positive affect, dispositional optimism, active coping, acceptance, and purpose in life, have been shown to be inversely related to the negative sequelae of chronic MSK pain (Ferreira & Sherman, 2007; Hassett & Finan, 2016; Karoly & Ruehlman, 2006; Newton-John et al., 2014; Ong et al., 2010; Strand et al., 2006). Behavioral and social resilience factors such as engaging in physical activity, being a non-smoker, consuming a nutritious diet, maintaining a healthy weight, and receiving positive social support, have been linked with better outcomes among individuals with chronic MSK pain, including lower morbidity and mortality (Geneen et al., 2017; Lambert et al., 1990; Lee et al., 2016; López-Martínez et al., 2008; Macfarlane et al., 2017; Messier et al., 2013; Sibille et al., 2016, 2018).

In addition to improving pain-related symptoms, resilience factors, as suggested by emerging evidence, may protect against the adverse biological consequences of chronic pain. Several studies have shown chronic pain severity and associated stress-related factors are inversely related to telomere length (Hassett et al., 2012; Sibille et al., 2017; Sibille, Langaee, et al., 2012), which is a measure of cellular aging and a downstream biomarker of stress system functioning (Epel et al., 2004; Sibille, Langaee, et al., 2012; Sibille, Witek-Janusek, et al., 2012). Thus, resilience factors might buffer the biological consequences of chronic pain and align with epidemiological studies indicating better health outcomes, that is, reduced risk of morbidity and mortality, in individuals with chronic MSK pain who report protective health behaviors (Macfarlane et al., 2017).

Significance

Chronic musculoskeletal pain is disabling to individuals and burdensome to society. In individuals with chronic musculoskeletal pain, we investigated relationships between resilience, pain, functioning, and pain-related brain structure with consideration for sociodemographic factors. Higher resilience associates with lower pain severity and functional limitations. Additionally, relationships between resilience and pain-related brain structure were indicated in the right amygdala, bilateral thalamus, and postcentral gyrus which differed by sex and ethnicity/race. Our research demonstrates a neurobiological correlate to resilience and the importance of considering sociodemographic factors in investigations.

Altered brain structure represents another biological consequence of chronic pain. A strong body of evidence confirms differences in brain morphology in individuals with varying chronic MSK pain conditions compared to pain-free controls (Baliki et al., 2011; Kuchinad et al., 2007). In general, a pattern of decreased gray matter volume across cortical and subcortical areas of the brain is indicated in chronic MSK pain (Coppieters et al., 2016; Davis et al., 2016; Hashmi et al., 2013). While brain changes might predate chronic MSK pain, evidence suggests pain influences brain structure. Indeed, studies show increased gray matter volume following surgical interventions for knee and hip osteoarthritis (Gwilym et al., 2010; Lewis et al., 2018; May, 2011; Rodriguez-Raecke et al., 2009, 2013). Although little is known regarding the relationship between resilience factors and the brain in individuals with chronic MSK pain, relationships have been reported between measures of resilience and brain function and structure associated with chronic pain (Bushnell et al., 2015; Hemington et al., 2018).

The research on the neurobiological interface of resilience specific to the stress responses and stress-related disorders (e.g., post-traumatic stress disorder and major depressive disorder) are well underway (Horn et al., 2016; Kautz et al., 2017; Osório et al., 2017). Resilience in response to stress is linked to a complex array of neurochemical responses and the structure and function of the hypothalamic–pituitary–adrenal axis, frontal and cingulate regions, and subcortical nuclei, among other larger brain networks

(Cathomas et al., 2019; Horn et al., 2016). The neurobiology of resilience involves numerous systems in the body which are influenced by predisposing factors such as genetics and temperament and exacerbated or buffered by environmental experiences and epigenetic changes (Cathomas et al., 2019; Ioannidis et al., 2020; Osório et al., 2017). Models of resilience in the brain frequently align with the concept of allostasis (McEwen, 2016). Differences in individual systems are considered to be the result of the cumulative array of biopsychosocial, behavioral, and environmental factors facilitating adaption or dysregulation, for example, symptom/disease onset (Casale et al., 2019; Ioannidis et al., 2020). Importantly, the multiple levels of functioning and complex array of factors provide numerous potential targets to better understand the neurobiology of resilience.

Evaluation of the relationship between pain and functioning, resilience, and pain-related areas of the brain will also require the consideration of sex and ethnicity/race. Compelling evidence demonstrates sex and ethnic/race group differences in severity of chronic MSK pain and pain-related disability. Specifically, women have a higher prevalence, incidence, and severity of chronic MSK pain conditions compared to men (Boyan et al., 2013; Srikanth et al., 2005). Underrepresented ethnic/race groups (e.g., non-Hispanic Blacks) experience greater clinical pain and functional limitations compared to their non-Hispanic White peers (Allen, 2010; Vaughn et al., 2019). Additionally, sex and ethnic/race group differences have also been observed in the relationship between risk and resilience factors and pain (Bartley, Hossain, et al., 2019; Booker et al., 2019) and in associations of pain catastrophizing with brain structure (Terry et al., 2020). Women are at greater risk for mood disorders and although not consistent, a number of studies indicate pain coping and social support differences by gender (Dowdy et al., 1996; El-Shormilisy et al., 2015; Li et al., 2014; Rovner et al., 2017). The evidence for differences in psychosocial measures by ethnic/race group are also not consistent, however, there is a pattern of findings showing that the relationships between psychosocial measures and clinical pain and neurobiological markers differ by ethnic/race group (Allen et al., 2006; Bartley, Hossain, et al., 2019; Booker et al., 2019; McIlvane, 2007; Terry et al., 2020).

The purpose of this study was to examine, in a group of individuals with chronic MSK pain, the relationships between a previously investigated biobehavioral/psychosocial resilience index (Johnson et al., 2019), clinical pain and functioning measures, and pain-related brain structure, with consideration for sociodemographic factors. Our objectives were to: (a) evaluate associations between the resilience index and clinical pain and functioning measures; (b) investigate associations between the resilience index and pain-related brain structures; and (c) explore sex and ethnic/race group differences in the resilience index and associations with pain-related brain structures. We hypothesized: (a) an inverse association between resilience and clinical pain, (b) that a relationship between resilience and pain-related areas of the brain would emerge, and (c) that the relationships between resilience and pain-related areas of the brain would differ by sex and ethnicity/race.

2 | MATERIALS AND METHODS

2.1 | Study overview

Data used in the current cross-sectional study were obtained from an ongoing prospective observational cohort study titled *Understanding Pain and Limitations in Osteoarthritic Disease-2* (*UPLOAD-2*). The study aims to investigate the mechanisms underlying ethnic/race group differences among adults with or at risk for knee osteoarthritis (OA). The UPLOAD-2 study is a multisite investigation conducted at the University of Florida (UF) and the University of Alabama at Birmingham (UAB). The participants described in the current analysis were recruited at both sites between August 2015 and May 2017. All procedures were reviewed and approved by the Institutional Review Boards at UF and UAB, and participants provided written and verbal informed consent. Participants were recruited through the community via multiple advertisement methods (e.g., posted fliers) and clinic-based methods.

2.2 | Participants

The UPLOAD-2 Study completed baseline data collection in 253 community-dwelling adults between 45 and 85 years of age who self-identified as non-Hispanic Black/African American (NHB) or non-Hispanic White/Caucasian/European (NHW). Forty participants did not complete neuroimaging due to contraindications (e.g., claustrophobia, safety concerns). Additional participants were excluded for poor image quality, neuropathology, or missing covariates ($n = 14$) or lack of pain at one or more body sites ($n = 33$). The final sample included 166 participants who reported experiencing pain at one or more body sites on more days than not, over the past 3 months, and who had completed the brain MRI. As the primary aim of the larger, ongoing parent study (UPLOAD-2) was to assess mechanisms underlying individual differences among those with/without knee pain, individuals were screened initially for the presence/absence of knee pain. Most participants reported pain at the knee ($n = 135$), but other pain sites were reported as well. To optimize the data available for the analysis of resilience, chronic pain, and the brain we included all people reporting chronic pain at any body site. Participants were excluded for systemic rheumatologic conditions including rheumatoid arthritis and fibromyalgia, knee replacement surgery, neurological diseases (e.g., Parkinson's disease, multiple sclerosis), chronic daily opioid use, uncontrolled hypertension, cardiovascular or peripheral arterial disease, psychiatric disorder requiring hospitalization within the past 12 months, and pregnancy or nursing. Participants were also excluded from the current study if they were unable to undergo

magnetic resonance imaging (MRI). The procedures described are limited to those relevant to the current investigation.

2.3 | Procedures

Initial eligibility was determined using a standardized telephone screening. Data acquired during screening included: sex, age, ethnic/race identity, and a brief health history to assess eligibility based on study exclusion criteria. After initial eligibility was determined, participants were invited to attend a health assessment session (HAS). Participants completed a health history questionnaire, which included sociodemographic information (e.g., education level) and behavioral habits (e.g., tobacco usage), followed by a pain history questionnaire, which inquired about pain location and intensity across multiple body sites. Anthropometric measurements were obtained, specifically waist and hip measurements (in centimeters), for calculating waist/hip ratio. Participants were invited to return within approximately 2 weeks following the HAS session to complete a brain imaging session. Participants completed questionnaires assessing measures of psychological resilience, social support, and clinical pain following the HAS session and before the brain imaging session.

2.4 | Measures

2.4.1 | Clinical pain and functioning

Revised short-form McGill pain questionnaire (Dworkin et al., 2009)

The revised short-form McGill pain questionnaire (SF-MPQ-2) consists of 22 descriptors assessing pain qualities on a 0 (none) to 10 (worst possible) numerical rating scale. The SF-MPQ-2 yields four subscales (Continuous pain, Intermittent pain, Neuropathic pain, and Affective descriptors), and a total pain score. The total score is the mean of all 22 items with scores ranging from 0 to 10. The four subscales are based on an average of subscale items with values also ranging from 0 to 10. Higher scores indicate more pain. Subscale and total scores have been demonstrated to be valid, reliable, and sensitive to change in clinical settings, and showed good internal consistency in the current sample (subscale α's = 0.88–0.93; total score α = 0.97). The SF-MPQ-2 has been shown to be a responsive measure assessing both neuropathic and non-neuropathic pain qualities across a wide array of chronic pain conditions (Dworkin et al., 2009). In the UPLOAD2 study, the SF-MPQ-2 was collected specific to knee pain.

Graded chronic pain scale (Von Korff et al., 1992)

The graded chronic pain scale (GCPS) is a self-report questionnaire assessing knee pain intensity and knee pain-related disability over the last 6 months (Von Korff et al., 1992). Participants were asked to rate their current, average, and worst knee pain on a 0–10 numeric rating scale (NRS). Ratings from the three items were averaged and multiplied by 10 to calculate a characteristic pain intensity score ranging from 0 to 100, with higher scores indicating more pain (Von Korff et al., 1992). Participants also reported the degree to which their knee pain interfered with daily activities during the past 6 months on the same scale. The responses were averaged and multiplied by 10 to generate a disability score (Von Korff et al., 1992). The GCPS has demonstrated good internal consistency in previous research (α = 0.74) (Von Korff et al., 1992), and in the current sample (α = 0.92). As the GCPS measure completed was specific to knee pain, analyses are limited to those who screened positive for knee pain in the study.

Western Ontario and McMaster universities osteoarthritis index (Bellamy et al., 1988)

The Western Ontario and McMaster universities osteoarthritis index (WOMAC) was administered to assess lower extremity (knee) pain and function in the past 48 hr (Bellamy et al., 1988). The WOMAC is a 24-item measure assessing pain, stiffness, and physical function rated on a 5-point Likert-type scale, with higher scores reflecting more clinical symptoms. Scores include a total score (0–96), a pain subscale (0–20), a stiffness subscale (0–8), and functional limitations (0–68). The WOMAC is a well-validated measure of clinical symptoms in persons with OA (Bellamy et al., 1988), and demonstrated good internal consistency in the current sample (subscale α's = 0.82–0.97; total score α = 0.97). As the WOMAC measure completed was specific to knee pain, analyses are limited to participants who screened positive for knee pain.

Total number of pain sites

Participants were asked to report where they experienced pain on more days than not over the past 3 months. Pain sites included hands, arms, shoulders, neck, head/face/jaw, chest, stomach, pelvic region, upper back, lower back, knees, legs, feet/ankles, and other. Either or both sides of the body could be endorsed for a total score ranging from 0 to 28.

PROMIS anxiety, depression, and sleep

The PROMIS Anxiety (7a) is comprised of seven items and measures symptoms of anxiety over the prior 7 days based on a 5-point Likert scale (1—never to 5—always). Higher scores indicate greater anxiety. The PROMIS Depression (Short Form 8b) is comprised of eight items and measures symptoms of depression over the prior 7 days based on a 5-point Likert scale (1—never to 5—always). Higher scores indicate greater depression. The PROMIS Sleep-Related Impairment (Short Form 8a) is comprised of eight items and assess sleep related impairment over the prior 7 days based on a 5-point Likert scale (1—never to 5—always). Higher scores indicate greater sleep disturbance. Based on scoring instructions, raw values are converted to T scores. The measures have been validated in chronic pain populations, including knee OA (Driban et al., 2015; Kroenke et al., 2014; Stone et al., 2016).

2.5 | Resilience index

As previously published, the biobehavioral/psychosocial resilience index consisted of a battery of validated biological behavioral,

psychological, and social measures (described below) that are recognized pain-related protective factors (Johnson et al., 2019): tobacco use, waist-to-hip ratio, optimism, positive and negative affect, active coping, perceived stress, and social support. Participant responses on each measure were coded as 0 (risk) or 1 (resilience) based on established clinical norms or referenced values. A total resilience index was computed based on a summation of the risk or resilience score from each measure (0–8) (Johnson et al., 2019).

2.5.1 | Biobehavioral components

Tobacco use

Participants responded to a question regarding smoking status: "Have you smoked at least 100 cigarettes in your entire life?"(CDC, 2017) "No" responses indicate resilience and were coded as 1. "Yes" responses were coded as 0 to indicate risk.

Waist-to-hip ratio

Participant's waist circumference and hip circumference were measured in centimeters using a standard measuring tape. Waist-to-hip ratio (WHR) was calculated by dividing waist circumference by hip circumference. The World Health Organization defines abdominal obesity as a WHR > 0.85 for women and >0.90 for men (World Health Organization, 2011). Consistent with prior research, WHR < 0.90 for both men and women was coded as 1, indicating resilience. WHRs ≥ 0.90 were coded as 0 indicating risk (Johnson et al., 2019).

2.5.2 | Psychological components

Optimism

Dispositional optimism was measured using the *Life Orientation Test-Revised (LOT-R)* (Scheier et al., 1994). The LOT-R is a 10-item self-report questionnaire that consists of three items assessing optimism (e.g., "In uncertain times, I usually expect the best"), three items assessing pessimism (e.g., "If something can go wrong for me, it will"), and four filler questions (e.g., "It's important for me to keep busy"). Responses are based on a 5-point Likert-type scale ranging from 0 (strongly disagree) to 4 (strongly agree) (Scheier et al., 1994). Scores range from 0 to 24, with higher scores indicating optimism. The measure has demonstrated good internal validity and test–retest reliability (0.79) (Scheier et al., 1994). Internal consistency for the sample was adequate (α = 0.79). Based on published normative data (Schou-Bredal et al., 2017), response totals ≥ 18 were coded as 1 (resilience); scores < 18 were coded as 0 (risk).

Positive and negative affect

The *Positive and Negative Affect Schedule (PANAS)* is a 20-item measure that consists of 10 positively valenced items (e.g., excited, proud) and 10 negatively valenced items (e.g., distressed, scared) (Watson et al., 1988). Items are self-rated on a 5-point Likert-type scale ranging from 1 (very slightly or not at all) to 5 (extremely) and summed to produce total subscale scores for positive and negative affect ranging from 10 to 50 with higher scores representing higher levels of each subscale (Crawford & Henry, 2004; Watson et al., 1988). The timeframe collected in this study was "to what extent you generally feel this way." The internal consistency for the current sample was good (positive affect subscale, α = 0.91; negative affect subscale, α = 0.91). High levels of trait positive affect and low levels of trait negative affect are considered resilience promoting (Hassett et al., 2008; Ong et al., 2020; Sibille, Kindler, et al., 2012; Strand et al., 2006; Zautra et al., 2005). Response totals for each subscale (i.e., positive affect ≥ 35 and negative affect ≤ 18.2), were coded as 1 to indicate resilience (Sibille, Kindler, et al., 2012; Watson et al., 1988).

Active coping

The *Coping Strategies Questionnaire-Revised (CSQ-R)* consists of 27 items designed to assess six coping responses to pain including: Distraction, Catastrophizing, Ignoring pain sensations, Distancing from pain, Coping self-statements, and Praying (Abbott, 2010; Riley & Robinson, 1997; Riley et al., 1999; Rosenstiel & Keefe, 1983). Participants are asked to rate the frequency of their use of each coping strategy on a 7-point Likert-type scale, from 0 (never do that) to 6 (always do that). Scores for each subscale are computed as the mean of responses to the corresponding items, with higher scores indicating greater use of that strategy.(Robinson et al., 1997) The mean scores of the Distraction, Ignoring pain sensations, Distancing from pain, and Coping self-statements subscales were averaged to signify total active coping (Robinson et al., 1997). The CSQ-R has demonstrated acceptable reliability (α's = 0.72–0.86) (Monticone et al., 2014; Riley & Robinson, 1997), and showed good internal consistency for each active coping subscale within our sample (α = 0.85–0.90). Consistent with previous study, response totals ≥ 2.87 indicated resilience and were coded as 1, while scores < 2.87 were coded as 0 to indicate risk (Johnson et al., 2019).

Perceived stress

The perceived stress scale (PSS) was used to assess participants' perceptions of stress (Cohen et al., 1983). The 10-item measure asks participants to rate statements about feelings and thoughts (e.g., "Felt that you were unable to control the important things in your life?"), during the last month on a 5-point Likert-type scale ranging from 0 (never) to 4 (very often). Positively worded items are reverse scored and a total score is computed by summing across all scale items (Cohen et al., 1994). The PSS is a reliable (α's = 0.84–0.86) and valid scale designed to measure the role of non-specific appraised stress (Cohen et al., 1983, 1994; Ezzati et al., 2014). Internal consistency was adequate in the current sample (α = 0.60). Resilience cut points were based on normative values, with PSS scores < 14 coded as 1 to delineate resilience and scores >= 14 coded as 0 to indicate risk (Cohen & Janicki-Deverts, 2012; Cohen et al., 1983, 1994).

2.5.3 | Social component

Social support

The *multidimensional scale of perceived social support (MSPSS)* is a 12-item self-report measure used to assess the extent to which an individual perceives social support from family (FA; items 3, 4, 8, and 11), friends (FR; items 6, 7, 9, and 12), and significant others (SO; items 1, 2, 5, and 10) (Zimet et al., 1988). Each item is rated on a 7-point Likert-type scale, ranging from 1 (very strongly disagree) to 7 (very strongly agree). A total scale score was computed by summing across all items, ranging from 12 to 84, with higher scores indicating higher levels of perceived support. The MSPSS has been previously demonstrated to be a reliable measure (α's = 0.81–0.98) (Osman et al., 2014; Zimet et al., 1990). Each subscale demonstrated high internal consistency in the current sample (FA: $\alpha = 0.95$; FR: $\alpha = 0.95$; SO: $\alpha = 0.96$). Based on published values, scores ≥ 49 were coded as 1 to indicate resilience; total scores < 49 were coded as 0 to indicate risk (Zimet et al., 1988).

2.6 | Brain imaging

MRI data were acquired using a 3.0 Tesla Philips Achieva whole body scanner with a 32-channel head coil at the University of Florida and an 8-channel head coil at the University of Alabama – Birmingham). Anatomical images were acquired using a high resolution three-dimensional (3D) T1-weighted MP-RAGE sequence and used for analyses (TR/TE/α = 7.0 ms/3.2 ms/8°, 1 mm^3 isotropic voxels, FOV: 240 × 240 × 176.).

2.6.1 | MRI processing

MP-RAGE files were processed (by trained professional [JJT]) using FreeSurfer 6.0 (Fischl, 2012). FreeSurfer is a set of software tools for the study of cortical and subcortical anatomy (Fischl et al., 2002, 2004; Fischl & Dale, 2000). Segmentation of subcortical and related structures (including amygdaloid complex [referred to as the amygdala throughout for simplicity] and thalamus) was performed. The cerebral cortex was parcellated into units with respect to gyral and sulcal structure (Fischl et al., 2004b; Klein & Tourville, 2012; Salat et al., 2004). FreeSurfer's morphometric procedures show good test–retest reliability across scanner manufacturers and across field strengths (Han et al., 2006; Reuter et al., 2012).

2.6.2 | Brain structure

Recognized cortical and subcortical areas of the brain associated with chronic MSK pain based on a systematic review were included in the analyses (Coppieters et al., 2016). Mean thickness values in mm for each cortical region (DKT parcellation) and subcortical volumes in mm^3 were exported for analyses. Specifically, mean thickness for postcentral gyrus (somatosensory), insula, medial orbitofrontal (medial prefrontal), rostral and caudal anterior cingulate (ACC), and rostral middle frontal gyrus (dorsolateral prefrontal cortex [DLPFC]) were exported bilaterally and averaged by region across hemispheres. Amygdala and thalamus volumes were also exported and adjusted for estimated total intracranial volume (Buckner et al., 2004). Based on established evidence (Baeken et al., 2014; Davidson, 2002) of subcortical laterality effects, we evaluated the left and right amygdala and thalamus separately.

2.7 | Data analyses

Data analyses were conducted in SPSS v. 26 (IBM). Data were checked for normality, outliers, missing data, and multicollinearity. All testing was two sided using a 0.05 level of significance. Chi-square and Student's *t* test were used to examine ethnic/race and sex group differences in sociodemographic characteristics, pain outcomes, the resilience index, and individual resilience factors. Where applicable, covariates in the models included: age, site, education, sex, ethnicity/race, and total number of body pain sites. Due to the cognitive and affective components of pain self-report and the high positive correlations with resilience, total number of pain sites was entered as a covariate in the models to adjust for chronic pain severity, which is a well-supported approach (Bergman et al., 2019; McBeth et al., 2008; Viniol et al., 2013). Additionally, as the pattern of the relationship with resilience was not known (possibly non-linear), high and low resilience groups were also compared and are also presented (Bushnell et al., 2015; Maleki et al., 2013).

For Objective 1, regression analyses were conducted to determine the associations between the resilience index and clinical pain and functioning measures. Unadjusted and adjusted models are reported for resilience and clinical pain and functioning. As the SF-MPQ-2, GCPS and WOMAC were assessed specific to knee pain, analyses involving those measures are limited to participants screened positive for knee pain ($n = 135$). All clinical pain and functioning measures were entered as continuous variables in the analyses. Covariates included age, site, education, sex, ethnicity/race, and total number of body pain sites. Further analyses as noted above, Objective 1—part 2, were completed with participants categorized as being "high" or "low" on the resilience index based on a group median split (*Mdn* = 5; 0–4 = low resilience; 5–8 = high resilience). Multivariate analyses of covariance (MANCOVAs) were used to compare differences in clinical pain and functioning measures between participants classified as "high" or "low" resilience, controlling for age, site, education, sex, ethnicity/race, and number of body pain sites.

For Objective 2, to investigate the relationship between the resilience index and pain-related brain structures, multivariate multiple regressions were conducted. Covariates included age, site, education, sex, ethnicity/race, and total number of pain sites. For Objective 2—part 2, MANCOVAs were used to compare differences in pain-related brain structures between participants classified as "high" or "low" resilience, controlling for age, site, education, sex, ethnicity/race, and number of body pain sites.

For Objective 3, to explore potential differences in associates between resilience and brain structure based on sex and ethnic/race groups, we conducted two multivariate multiple regressions (cortical regions of interest and subcortical regions of interest) controlling for age, site, education, sex, ethnicity/race, and total number of pain sites to investigate relationships between resilience and brain structure with added resilience*ethnicity/race, resilience*sex, and resilience*ethnicity/race*sex interaction terms. Post hoc analyses calculating and using a ratio of right to left amygdala volume was performed. Using this ratio variable, a Pearson correlation was run to assess correlations with handedness and then an ANCOVA was conducted to assess amygdala volume asymmetry controlling for the covariates listed previously. Additionally, summary brain structure results (see Table 8) were adjusted for multiple comparisons using a false discovery rate (FDR) (Benjamini & Hochberg, 1995).

For Objective 3—part 2, we used MANCOVAs to compare differences between individuals with high/low resilience comparing (e.g., low resilience males vs. low resilience females) and then stratifying by sex (e.g., low resilience males vs. high resilience males) and ethnic/race group in pain-related brain structures, controlling for age, site, education, total pain sites, and sex or ethnicity/race when applicable.

3 | RESULTS

3.1 | Descriptive

Sociodemographic and clinical characteristics of the sample are shown in Table 1. Non-Hispanic Blacks (NHBs) were younger than non-Hispanic Whites (NHWs), $p < 0.001$. Most participants were female (66.3%). The representation of males and females was equivalent across ethnic/race groups. Education differed by ethnic/race group ($p = 0.019$), but not by sex.

A majority (53.4%) of participants reported pain at five or more sites on most days over the past 3 months. The most frequently reported pain sites were knees (78.3%), low back (53.6%), hands (42.8%), shoulders (40.4%), neck (33.7%), and feet/ankles (36.1%). The pain experienced was reported as bilateral (80.7%), right side only (13.9%), and left side only (5.4%).

In individuals who screened positive for knee pain ($n = 135$), total number of pain sites was significantly correlated with the Revised Short-Form McGill Pain Questionnaire (SF-MPQ-2) total score ($r = 0.24$, $p = 0.006$), the Graded Chronic Pain Scale (GCPS) characteristic pain intensity ($r = 0.27$, $p = 0.002$), the GCPS disability score ($r = 0.20$, $p = 0.024$), and WOMAC total score ($r = 0.31$, $p < 0.001$).

Means and standard deviations for pain and functional measures are reported in Table 1. Violin plots distributions of GCPS characteristic pain intensity and GCPS disability scores in individuals with knee pain are presented in Figure 1. Total number of pain sites reported did not differ significantly by ethnic/race group or sex. There were no significant sex differences on the clinical pain or functional measures. There were significant ethnic/race group differences on all clinical pain measures, with NHBs reporting significantly greater pain than NHWs, $p's < 0.001$.

3.2 | Associations between the resilience index and clinical pain and functioning

An inverse association emerged between the resilience index and clinical knee pain as measured by the SF-MPQ-2 total score (unadjusted model: $b = -0.35$, $p < 0.001$). This relationship remained statistically significant after controlling for age, site, education, sex, ethnicity/race, and total number of pain sites (adjusted model: $b = -0.26$, $p = 0.002$). Partial correlations between the resilience index and each subscale of the SF-MPQ-2 were significant after controlling for all covariates (continuous: $r = -0.21$, $p = 0.017$; intermittent: $r = -0.22$, $p = 0.013$; neuropathic: $r = -0.26$, $p = 0.003$; affective: $r = -0.32$, $p < 0.001$), Table 2.

The resilience index was associated with GCPS characteristic knee pain intensity (unadjusted model: $b = -0.28$, $p = 0.001$) such that higher levels of resilience were associated with lower characteristic knee pain intensity. After controlling for age, site, education, sex, ethnicity/race, and total number of pain sites, the association did not remain statistically significant (adjusted model: $b = -0.14$, $p = 0.068$). Resilience was inversely related to GCPS knee disability score (unadjusted model: $b = -0.32$, $p < 0.001$), and remained significantly associated after controlling for all covariates (adjusted model: $b = -0.26$, $p = 0.002$), Table 2.

The resilience index was also inversely related to the WOMAC total score in the unadjusted ($b = -0.26$, $p = 0.002$) and adjusted models ($b = -0.17$, $p = 0.037$), Table 2. Partial correlations, controlling for all covariates, demonstrated significant inverse relationships between resilience and WOMAC stiffness subscale, ($r = -0.20$, $p = 0.028$) and WOMAC physical function subscale, ($r = -0.20$, $p = 0.028$).

In all study participants ($n = 166$), the resilience index was also inversely related to the PROMIS Anxiety, Depression, and Sleep-Related Impairment measures in unadjusted, (Anxiety: $b = -0.48$, $p < 0.0001$; Depression: $b = -0.48$, $p < 0.0001$; Sleep-Related Impairment: $b = -0.36$, $p < 0.0001$) and adjusted models (Anxiety: $b = -0.50$, $p < 0.0001$; Depression: $b = -0.47$, $p < 0.0001$; Sleep-Related Impairment: $b = -0.34$, $p < 0.0001$). As anticipated, higher resilience is associated with lower levels of recent symptoms of anxiety, depression, and sleep related impairment.

TABLE 1 Sociodemographic and clinical characteristics of participants across sociodemographic groups

Variable	Overall *N* = 166	Female *N* = 110	Male *N* = 56	NHB *N* = 76	NHW *N* = 90
Age in years, *M(SD)*[*]	57.97(8.2)	57.57(8.3)	58.75(7.9)	56.26(6.5)	59.41(9.2)
Sex, *N(%)*					
Female	110(66.3)	…	…	47(61.8)	63(70)
Male	56(33.7)	…	…	29(38.2)	27(30)
Ethnicity/Race, *N(%)*					
NHB	76(45.8)	47(42.7)	29(51.8)	…	…
NHW	90(54.2)	63(57.3)	27(48.2)	…	…
Education, *N(%)*					
Some high school	12(7.2)	6(5.5)	6(10.7)	8(10.5)	4(4.4)
High school degree[*]	61(36.7)	43(39.1)	18(32.1)	36(47.4)	25(27.8)
Associate degree	30(18.1)	23(20.9)	7(12.5)	13(17.1)	17(18.9)
Bachelor's degree[*]	35(21.1)	18(16.4)	17(30.4)	9(11.8)	26(28.9)
Master's degree	21(12.7)	16(14.5)	5(8.9)	8(10.5)	13(14.4)
Doctoral degree	7(4.2)	4(3.6)	3(5.4)	2(2.6)	5(5.6)
Site, *N(%)*					
UF	103(62)	69(67)	34(33)	44(42.7)	59(57.3)
UAB	63(38)	41(65.1)	22(34.9)	32(50.8)	31(49.2)
No. pain sites, *M(SD)*					
Range: 0–21	5.38(3.5)	5.66(3.8)	4.82(2.9)	5.78(3.7)	5.04(3.4)
PROMIS, *M(SD)*					
Anxiety					
Range:36.3–82.7	49.9(9.6)	49.8(9.1)	50.1(10.5)	49.7(10.0)	50.1(9.2)
Depression					
Range:37.1–81.1	47.1(8.9)	46.7(8.5)	47.7(9.6)	47.8(9.4)	46.5(8.5)
Sleep					
Range:30–76.9	49.9(10.6)	50.3(10.7)	49.1(10.5)	50.5(9.9)	49.4(11.2)
GCPS, *M(SD)*					
Pain intensity[*]					
Range: 10–100	53.8(23.5)	51.8(23.6)	57.5(23.0)	65.8(21.7)	42.7(19.2)
Disability[*]					
Range: 0–100	44.5(31.1)	43.0(33.5)	47.0(26.3)	57.3(29.9)	32.5(27.3)
SF-MPQ–2, *M(SD)*					
Total scale[*]					
Range: 0–8.27	2.4(2.1)	2.3(2.2)	2.5(2.1)	3.4(2.2)	1.5(1.6)
Affective[*]					
Range: 0–10	2.1(2.6)	2.0(2.7)	2.1(2.5)	3.0(2.8)	1.2(2.1)
Neuropathic[*]					
Range: 0–7.67	1.5(1.8)	1.4(1.8)	1.7(1.8)	2.3(2.1)	0.8(1.1)
Intermittent[*]					
Range: 0–10	2.7(2.5)	2.4(2.3)	3.2(2.9)	3.8(2.7)	1.7(1.9)
Continuous[*]					
Range: 0–10	3.3(2.6)	3.2(2.7)	3.4(2.5)	4.5(2.5)	2.2(2.2)
WOMAC, *M(SD)*					
Total scale[*]					

(Continues)

TABLE 1 (Continued)

Variable	Overall *N* = 166	Female *N* = 110	Male *N* = 56	NHB *N* = 76	NHW *N* = 90
Range: 0–87	34.3(19.8)	33.9(20.0)	35.0(20.0)	41.9(18.8)	27.1(18.1)
Pain*					
Range: 0–20	7.4(4.4)	7.3(4.4)	7.6(4.4)	8.9(4.1)	6.0(4.1)
Stiffness*					
Range: 0–8	3.1(1.9)	3.1(1.9)	3.2(2.0)	3.8(1.8)	2.6(1.8)
Physical function*					
Range: 0–62.69	23.8(14.4)	23.4(14.5)	24.6(14.4)	29.6(13.8)	18.5(12.9)

Note: Pain questionnaires are limited to participants who screened positive for knee pain (*N* = 135; 87W/48M; 65NHB/70NHW).

Abbreviations: GCPS, Graded Chronic Pain Scale; NHB, non-Hispanic Black; NHW, non-Hispanic White; SF-MPQ-2, Revised Short-Form McGill Pain Questionnaire; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

*$p < 0.05$ NHB versus NHW.

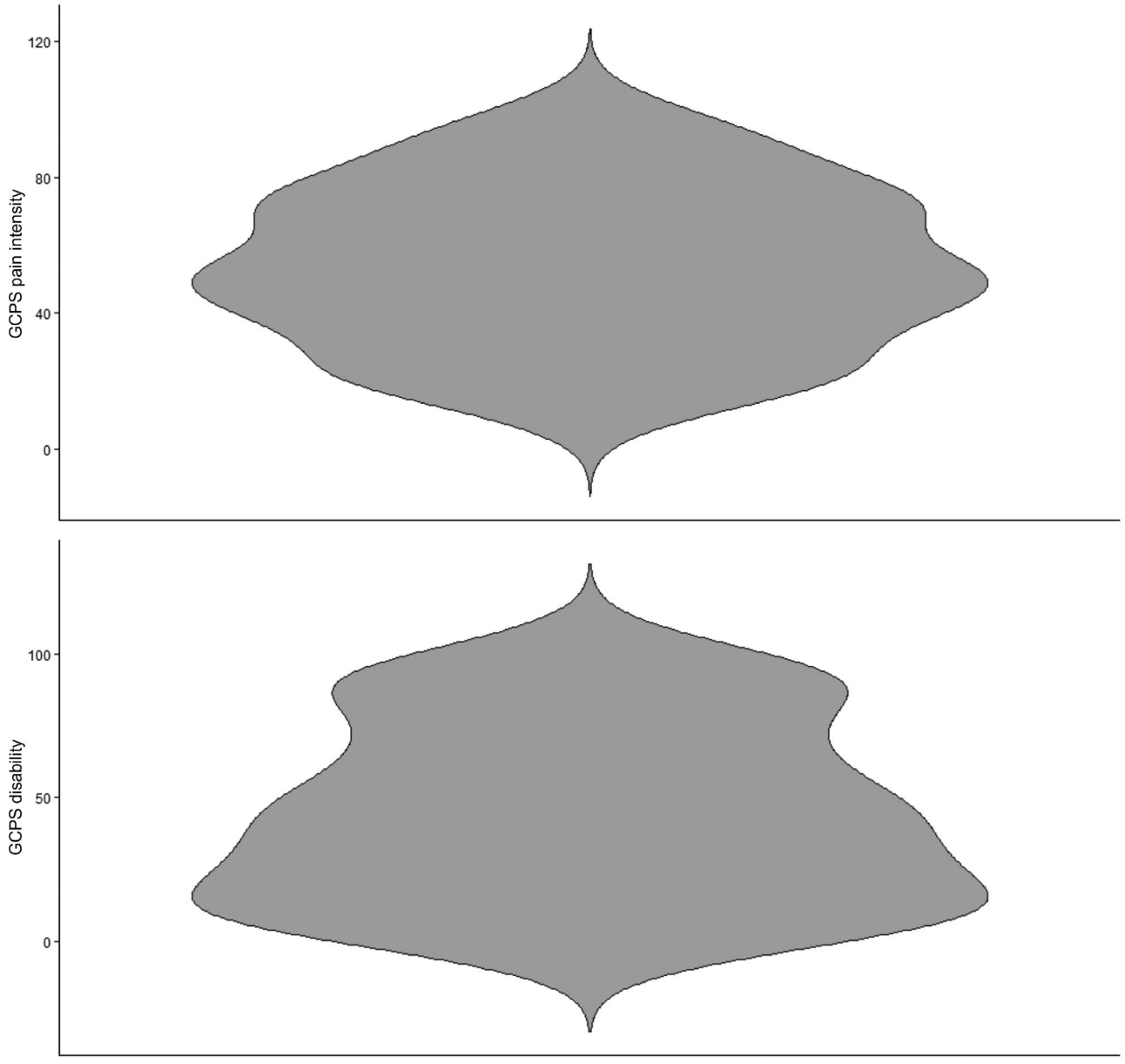

FIGURE 1 Violin plots distributions of GCPS characteristic pain intensity and GCPS disability scores in individuals with knee pain. The distribution indicates data from individuals who screened positive for knee pain, *n* = 135

TABLE 2 Linear regression models examining resilience index and clinical pain

	GCPS Pain intensity		GCPS Disability score		SF-MPQ–2 Total scale		WOMAC Total scale	
Variable	***b*(*SE*)**	***t***	***b*(*SE*)**	***t***	***b*(*SE*)**	***t***	***b*(*SE*)**	***t***
Age	−0.22(0.2)	−3.0**	−0.20(0.3)	−2.4*	−0.14(0.0)	−1.77	−0.15(0.2)	−1.9
Site	0.01(3.4)	0.17	−0.03(4.9)	−0.4	0.06(0.3)	0.84	0.08(3.1)	1.0
Education	−0.11(1.3)	−1.5	−0.02(1.9)	−0.18	−1.0(0.1)	−1.21	−0.08(1.2)	−1.0
Sex	−0.06(3.7)	−0.74	0.04(5.3)	0.5	0.04(0.4)	0.44	0.03(3.4)	0.3
Ethnicity/race	−0.38(3.4)	−5.3**	−0.33(4.9)	−4.1**	−0.35(0.3)	−4.5**	−0.28(3.1)	−3.6**
No. pain sites	0.18(0.5)	2.4*	0.10(0.7)	1.3	0.14(0.0)	1.78	0.23(0.5)	2.8**
Resilience	−0.14(1.0)	−1.8	−0.26(1.4)	−3.2**	−0.26(0.1)	−3.2**	−0.17(0.9)	−2.1*

Note: Adjusted model; reference category for sex = male; reference category for ethnicity/race = non-Hispanic Black. Data are limited to participants who screened positive for knee pain ($n = 135$).

Abbreviations: *b*, standardized coefficient; GCPS, graded chronic pain scale; SE, standard error; SF-MPQ-2, Revised Short-Form McGill Pain Questionnaire; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

*$p < 0.05$; **$p < 0.01$.

TABLE 3 Measures of the resilience index by clinical criteria presented by sociodemographic groups

Variable	Overall M or *N* (*SD* or %)	Male M or *N* (*SD* or %)	Female M or *N* (*SD* or %)	NHB M or *N* (*SD* or %)	NHW M or *N* (*SD* or %)	Resilience value
LOT-R	18.2(5.1)	17.4(5.3)	18.7(5.0)	18.0(4.8)	18.4(5.4)	≥18
PANAS-PA	35.4(8.0)	34.2(8.8)	36.1(7.6)	36.0(8.1)	35.0(8.0)	≥35
PANAS-NA	15.7(6.3)	16.3(7.0)	15.3(6.0)	16.3(7.0)	15.2(5.7)	<18.2
CSQ-R-Active coping*	2.5(1.2)	2.5(1.1)	2.6(1.2)	2.8(1.2)	2.3(1.1)	≥2.87
PSS	13.4(6.5)	13.5(5.9)	13.4(6.8)	13.8(6.4)	13.0(6.6)	<14
MPSS	64.8(18.7)	62.2(17.5)	66.2(19.2)	65.3(19.9)	64.5(17.7)	≥49
Tobacco use‡	84(51%)	16(29%)	68(62%)	38(50%)	46(51%)	<100 cigarettes/lifetime
WHR‡	0.90(0.10)	0.97(0.08)	0.87(0.09)	0.90(0.10)	0.90(0.09)	<0.90
Resilience Index‡	4.6(1.8)	3.8(1.8)	5.0(1.7)	4.5(1.8)	4.7(1.9)	

Note: $N = 166$; M-Mean and *SD*-Standard Deviation or *N*-Number by %.

Abbreviations: CSQ-R, Coping Strategies Questionnaire – Revised; LOT-R, Life Orientation Test-Revised; MPSS, Multidimensional Scale of Perceived Social Support; PANAS-NA, Positive and Negative Affect Schedule–Negative Affect; PANAS-PA, Positive and Negative Affect Schedule–Positive Affect; PSS, Perceived Stress Scale; WHR, waist/hip ratio in centimeters.

*$p < 0.05$ NHB versus NHW;

‡$p < 0.05$ male versus female difference.

3.2.1 | High and low resilience and clinical pain and functioning measures

High and low resilience groups differed on self-reported clinical pain and functioning measures, Table 4. Clinical knee pain measures were significantly different between high/low resilience groups in the unadjusted analysis (p values = 0.012 to <0.001). After controlling for age, site, education, sex, ethnicity/race, and total number of pain sites, there remained significant differences between "high" and "low" resilience on GCPS disability, $F(1,127) = 8.08$, $p = 0.005$, and SF-MPQ total and subscales (Total: $F(1,122) = 6.4$, $p = 0.012$; Neuropathic: $F(1,123) = 8.5$, $p = 0.004$; Affective: $F(1,124) = 9.29$, $p = 0.003$), and WOMAC stiffness, $F(1,126) = 8.21$, $p = 0.005$, and physical function, $F(1,127) = 4.27$, $p = 0.041$, subscales.

Regarding functioning, the PROMIS Anxiety, Depression, and Sleep-Related Impairment measures were significantly different between high/low resilience groups in the unadjusted analyses ($p < 0.0001$). After controlling for age, site, education, sex, ethnicity/race, and total number of pain sites, there remained significant differences between "high" and "low" resilience on PROMIS Anxiety, $F(1,157) = 32.8$, $p < 0.0001$; Depression: $F(1,158) = 32.2$, $p < 0.0001$; and Sleep-Related Impairment: $F(1, 152) = 18.8$, $p < 0.0001$. All differences were in the expected direction with participants characterized as "high" resilience reporting less clinical pain, anxiety, depression, and sleep-related impairment than those characterized as "low" resilience.

3.2.2 | Resilience index and sociodemographic group differences

Components of the resilience index are shown in Table 3 with Table 4 showing component scores separated by median split resilience

TABLE 4 Adjusted group comparison of high and low resilience on pain and functioning measures

	High resilience	Low resilience	
	M (*SD*)	*M* (*SD*)	*p* value
Functioning	(*N* = 90)	(*N* = 76)	
PROMIS Anxiety	46.2 (7.6)	54.4 (9.8)	<0.0001
PROMIS Depression	43.4 (6.6)	51.4 (9.4)	<0.0001
PROMIS Sleep	46.6 (10.0)	54.0 (9.8)	<0.0001
Pain	(*N* = 70)	(*N* = 65)	
GCPS Pain Intensity	48.6 (22.5)	59.4 (23.3)	0.376
GCPS Disability	34.9 (29.8)	54.7 (29.3)	0.005
SF-MPQ-2 Total	1.7 (1.7)	3.1 (2.4)	0.012
Continuous	2.7 (2.3)	4.0 (2.8)	0.088
Intermittent	2.0 (2.0)	3.5 (2.8)	0.068
Neuropathic	0.9 (14)	2.2 (2.0)	0.004
Affective	1.2 (1.8)	3.0 (3.1)	0.003
WOMAC Total	29.3 (17.3)	39.4 (21.0)	0.060
Pain	6.5 (3.8)	8.4 (4.7)	0.237
Stiffness	2.6 (1.7)	3.7 (1.9)	0.005
Physical Function	20.1 (12.8)	27.8 (15.1)	0.041

Note: Covariates in the model: site, age, gender, education, ethnicity/race group, and total number of pain sites. Pain data are limited to participants who screened positive for knee pain (*n* = 135).

Abbreviations: GCPS, Graded Chronic Pain Scale; SF-MPQ-2, Revised Short-Form McGill Pain Questionnaire; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

groups. Given patterns of findings presented below and in Figures 3 and 4, we completed additional descriptive statistics including sample size, resilience index ranges, and clinical pain measures for NHB females, NHW females, NHB males, and NHW males for an improved appreciation of findings (see Table 5).

3.3 | Associations between the resilience index and pain-related brain structures

3.3.1 | Resilience and pain-related cortex

In the omnibus model, prior to inclusion of the interaction terms, there was no relationship between resilience and the cortical regions of interest ($F(5,154) = 0.10$, $p = 0.993$; partial $\eta^2 = 0.003$; univariate p values > 0.675), controlling for study site, age, site, education, sex, ethnicity/race, and total number of pain sites.

With the inclusion of resilience interaction terms, the omnibus model demonstrated significant two-way interactions: resilience*ethnicity/race ($F(5,151) = 2.68$, $p = 0.024$) and resilience*sex ($F(5,151) = 2.38$, $p = 0.044$). The three-way interaction (resilience*ethnicity/race*sex) was not significant ($p = 0.149$). From a univariate standpoint, the postcentral gyrus demonstrated two-way (resilience*ethnicity/race) and three-way interactions. Specifically, for the three-way interaction, the relationship between resilience and postcentral gyrus differed within males by ethnicity/race (NHB and NHW) and within ethnicity/race by sex (NHB males and NHB females) (see Table 6 and Figure 2). The other cortical ROIs did not have

TABLE 5 Low/high resilience index by stratified sociodemographic groups and clinical knee pain measures

	Low (0–4)	High (5–8)	
	N	*N*	
NHB male	22	6	
NHW male	11	9	
NHB female	15	22	
NHW female	17	33	
		Low resilience (0–4)	High resilience (5–8)
		M (*SD*)	*M* (*SD*)
NHB male	SF-MPQ-2 total	3.99 (2.1)	2.33 (1.8)
	WOMAC total	44.04 (21.0)	32.67 (14.6)
	GCPS pain intensity	67.73 (19.9)	72.78 (14.1)
	GCPS disability	59.02 (26.9)	49.44 (22.4)
NHW male	SF-MPQ-2 total	1.56 (1.5)	0.84 (0.6)
	WOMAC total	27.64 (17.9)	23.11 (14.2)
	GCPS pain intensity	44.85 (20.7)	37.78 (17.3)
	GCPS disability	45.45 (16.1)	18.15 (13.4)
NHB female	SF-MPQ-2 total	4.28 (2.5)	2.47 (2.0)
	WOMAC total	49.33 (18.4)	37.05 (16.3)
	GCPS pain intensity	73.78 (19.1)	56.67 (24.4)
	GCPS disability	71.56 (26.6)	48.03 (34.0)
NHW female	SF-MPQ-2 total	2.01 (2.3)	1.40 (1.5)
	WOMAC total	32.35 (20.7)	25.34 (17.8)
	GCPS pain intensity	45.49 (20.7)	41.82 (19.0)
	GCPS disability	40.39 (33.7)	28.13 (27.3)

Note: Data are limited to participants who screened positive for knee pain (*n* = 135).

Abbreviations: GCPS, Graded Chronic Pain Scale; SF-MPQ-2, Revised Short-Form McGill Pain Questionnaire; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

TABLE 6 Multivariate multiple linear regression model examining biobehavioral/psychosocial resilience in relation to cortical regions of interest

Variable	Omnibus Model	ACC		DLPFC		Insula		Medial Orbitofrontal		Postcentral Gyrus	
	F	b(SE)	t	b(SE)	t	b(SE)	t	b(SE)	t	b(SE)	t
Age	7.14**	−0.36(0.08)	−4.70**	−0.23(0.08)	−2.79**	−0.30(0.08)	−3.82**	−0.23(0.08)	−2.71**	−0.36(0.07)	−4.68**
Site	5.02**	0.12(0.07)	1.639	0.14(0.08)	1.84	0.15(0.07)	1.98*	0.09(0.08)	1.13	−0.16(0.07)	−2.37*
Education	1.29	−0.07(0.08)	−1.07	−0.06(0.08)	0.76	0.08(0.08)	1.07	0.01(0.08)	0.09	−0.00(0.07)	−0.04
Sex	2.66*	0.24(0.08)	3.106**	0.10(0.09)	1.13	0.14(0.08)	1.72	0.03(0.09)	0.34	0.13(0.07)	1.82
Ethnicity/Race	15.30**	0.03(0.08)	0.40	0.05(0.08)	0.62	0.24(0.08)	3.00**	0.12(0.09)	1.45	0.51(0.07)	7.11**
No. pain sites	1.74	−0.12(0.07)	−1.67	−0.05(0.08)	−0.64	−0.08(0.08)	−1.01	−0.15(0.08)	−1.86	−0.14(0.07)	−2.09*
Resilience	0.13	−0.00(0.08)	−0.03	0.02(0.09)	0.22	0.02(0.08)	0.19	−0.04(0.09)	−0.45	0.04(0.7)	0.49
Resilience*Ethnicity/Race	2.68*	0.06(0.07)	0.75	0.16(0.08)	1.94	−0.04(0.08)	−0.57	0.09(0.08)	1.17	0.18(0.07)	2.69**
Resilience*Sex	2.35*	−0.14(0.07)	−1.91	−0.11(0.08)	−1.39	−0.08(0.07)	−1.05	−0.07(0.08)	−0.86	0.09(0.07)	1.38
Resilience*Ethnicity/Race*Sex	1.66	−0.01(0.07)	−0.10	−0.03(0.08)	−0.33	−0.03(0.08)	−0.34	0.02(0.08)	0.22	−0.17(0.07)	−2.47*

Note: Adjusted model; reference category for sex = male; reference category for ethnicity/race = non-Hispanic Black. See Figure 2.

Abbreviations: ACC, anterior cingulate cortex; *b*, standardized coefficient; DLPFC, Dorsolateral Prefrontal Cortex; SE, standard error.

*$p < 0.05$; **$p < 0.01$.

evidence of significant relationships with resilience or the interaction terms. Additionally, the postcentral gyrus thickness was lower in NHBs compared to NHWs ($p < 0.001$) and was inversely associated with the number of pain sites ($p = 0.038$). ACC was thicker in females than males irrespective of ethnicity/race ($p = 0.002$).

3.3.2 | Resilience and pain-related subcortical structures: Amygdala and thalamus

In the omnibus model prior to inclusion of interaction terms, the resilience index was associated with subcortical volume (multivariate $F(4,155) = 3.19$, $p = 0.015$; partial $\eta^2 = 0.076$). Adjusting for covariates, univariate results were significant for right amygdala ($F(1,158) = 3.83$, $p = 0.018$; partial $\eta^2 = 0.035$; FDR $p = 0.072$) but not left amygdala or bilateral thalamus (p values ≥ 0.186).

With the inclusion of interaction terms, the omnibus model demonstrated significant relationships between resilience*ethnicity/race ($F(4,152) = 3.91$, $p = 0.005$, partial $\eta^2 = 0.093$), and the three-way interaction, resilience*ethnicity/race*sex ($F(4,152) = 3.13$, $p = 0.017$, partial $\eta^2 = 0.076$). Resilience*sex was not significant ($p = 0.398$; Table 7). In the univariate models, all ROIs demonstrated two-way (resilience*ethnicity/race) interactions and three-way interactions were demonstrated for all ROIs except the left amygdala (see Table 7 and Figure 3). Specifically, for the three-way interaction, the relationship between resilience and subcortical structure differed within females by ethnicity/race (NHB and NHW) and within ethnicity/race by sex (NHB males and NHB females). Of note, among NHB females, resilience was positively associated with subcortical volumes, while the other groups exhibited weaker or inverse relationships between resilience and subcortical volumes (Figure 3). Subcortical ROIs also had significant ethnicity/race and sex effects (see Table 8 and Figure 4). Figure 5 provides a visual summary of resilience and brain two-way group analyses.

Post hoc analyses were completed to investigate the pattern of larger right compared to left amygdala and, in a subsample of participants with reported dominant hand data ($n = 111$), possible associations with handedness (Zald, 2003). The overall group mean for the right amygdala was larger than the left amygdala by 11%. Greater right/left amygdala volume asymmetry, however, was positively associated with resilience ($F(1,156) = 5.25$, $p = 0.023$, partial $\eta^2 = 0.032$), see Figure 6. The difference observed was not significantly associated with handedness ($p = 0.691$) in the subsample. To assist with interpretation, we provide median split resilience group comparisons below.

3.4 | Sociodemographic group differences in high/low resilience and pain-related brain structures

3.4.1 | Between sex group differences

Pain-related cortical areas

Sex differences were indicated for pain-related cortical areas in the overall model. With further investigation specific to resilience,

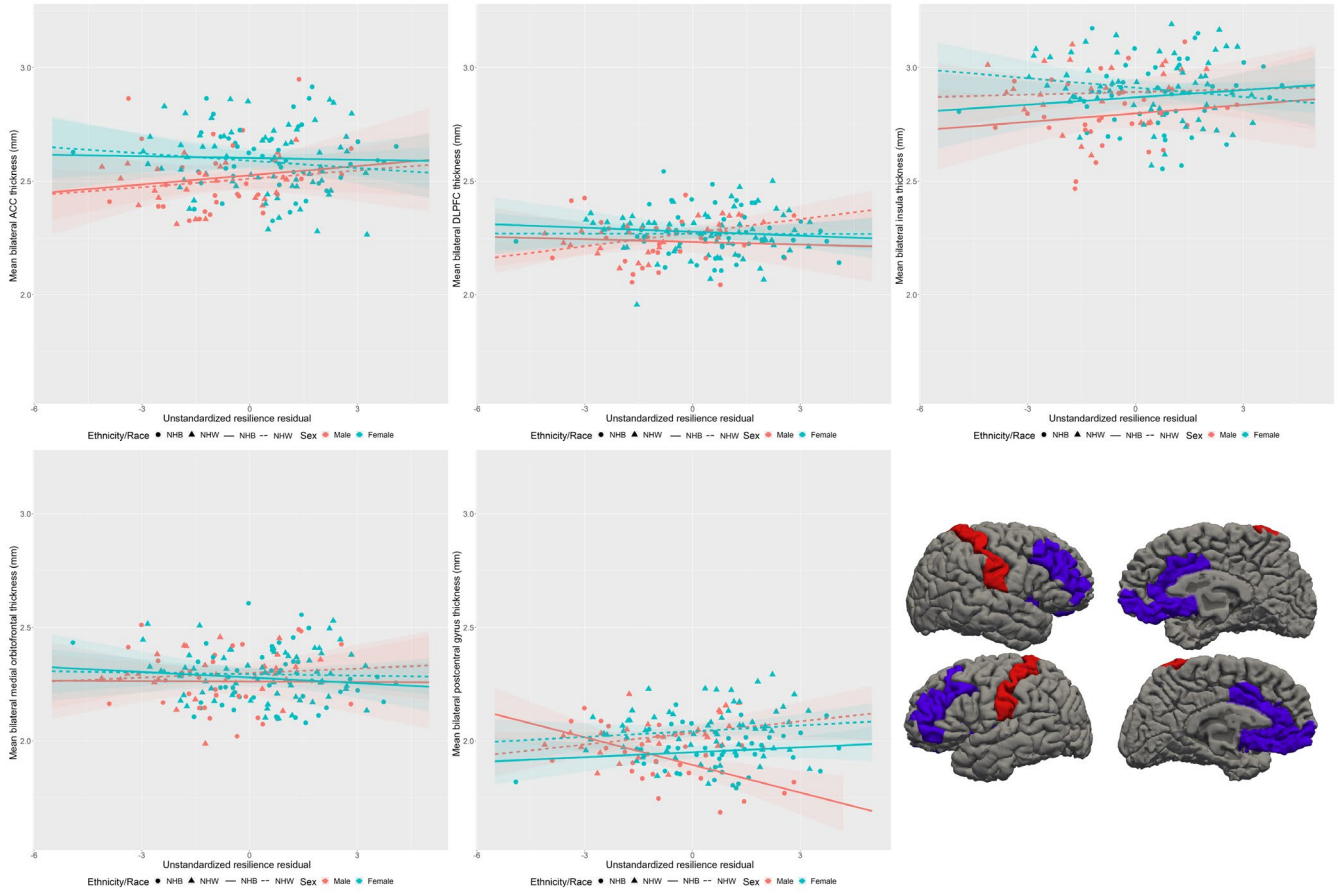

FIGURE 2 Sociodemographic group relationships between resilience and cortical thickness. X axes are unstandardized residuals of resilience with age, site, education, and pain sites regressed out. Y axes are scaled the same to allow for direct thickness comparisons between regions. Circles and solid lines are NHB, triangles and dashed lines are NHW. Postcentral gyrus (in red) has significant Resilience*Ethnicity/Race and Resilience*Ethnicity/Race*Sex interactions (p values < 0.05). The other regions (in blue) did not show significant associations with resilience or resilience interactions (see Table 6) [Color figure can be viewed at wileyonlinelibrary.com]

low resilience men ($n = 37$) and women ($n = 39$) differed in cortical thickness across the investigated regions of interest ($F(5,65) = 4.10$, $p = 0.003$, partial $\eta^2 = 0.240$). There were univariate differences (women > men) in ACC ($F(1,69) = 17.76$, $p < 0.001$), DLPFC ($F(1,69) = 7.26$, $p = 0.009$), and insula ($F(1,69) = 7.13$, $p = 0.034$) with the other areas not significantly different (p values ≥ 0.132).

High resilience men ($n = 19$) and women ($n = 71$) did not differ in cortical thickness across the investigated regions of interest ($F(5,79) = 0.92$, $p = 0.472$, partial $\eta^2 = 0.055$). Significant univariate differences were not found (p values ≥ 0.182).

Pain-related subcortical areas

Sex differences were indicated for pain-related subcortical areas in the overall model. With further investigation specific to resilience, low resilience men ($n = 37$) and women ($n = 39$) differed in subcortical volume across all investigated regions of interest ($F(4,66) = 7.22$, $p < 0.001$, partial $\eta^2 = 0.305$). There were univariate differences (women > men) in all areas (left and right amygdala and thalamus; p values ≤ 0.006). High resilience men ($n = 19$) and women ($n = 71$) differed in subcortical volume across all investigated regions of interest ($F(4,80) = 4.80$, $p = 0.002$, partial $\eta^2 = 0.193$). There were univariate differences (women > men) in all areas (amygdala and thalamus; p values ≤ 0.003).

3.4.2 | Within sex group differences

Men

Pain-related cortical areas. There was no indication of differences between men with high ($n = 19$) versus low ($n = 37$) resilience ($F(5,45) = 1.50$, $p = 0.208$, partial $\eta^2 = 0.143$). All univariate regions of interest were not significant (p values > 0.121).

Pain-related subcortical areas. There was no indication of difference between men with high versus low resilience ($F(4,46) = 0.69$, $p = 0.605$, partial $\eta^2 = 0.056$).

Women

Pain-related cortical areas. There was no indication of differences among women with high ($n = 71$) versus low ($n = 39$) resilience ($F(5,99) = 0.92$, $p = 0.475$, partial $\eta^2 = 0.044$). No areas were significant using univariate statistics (p values > 0.174).

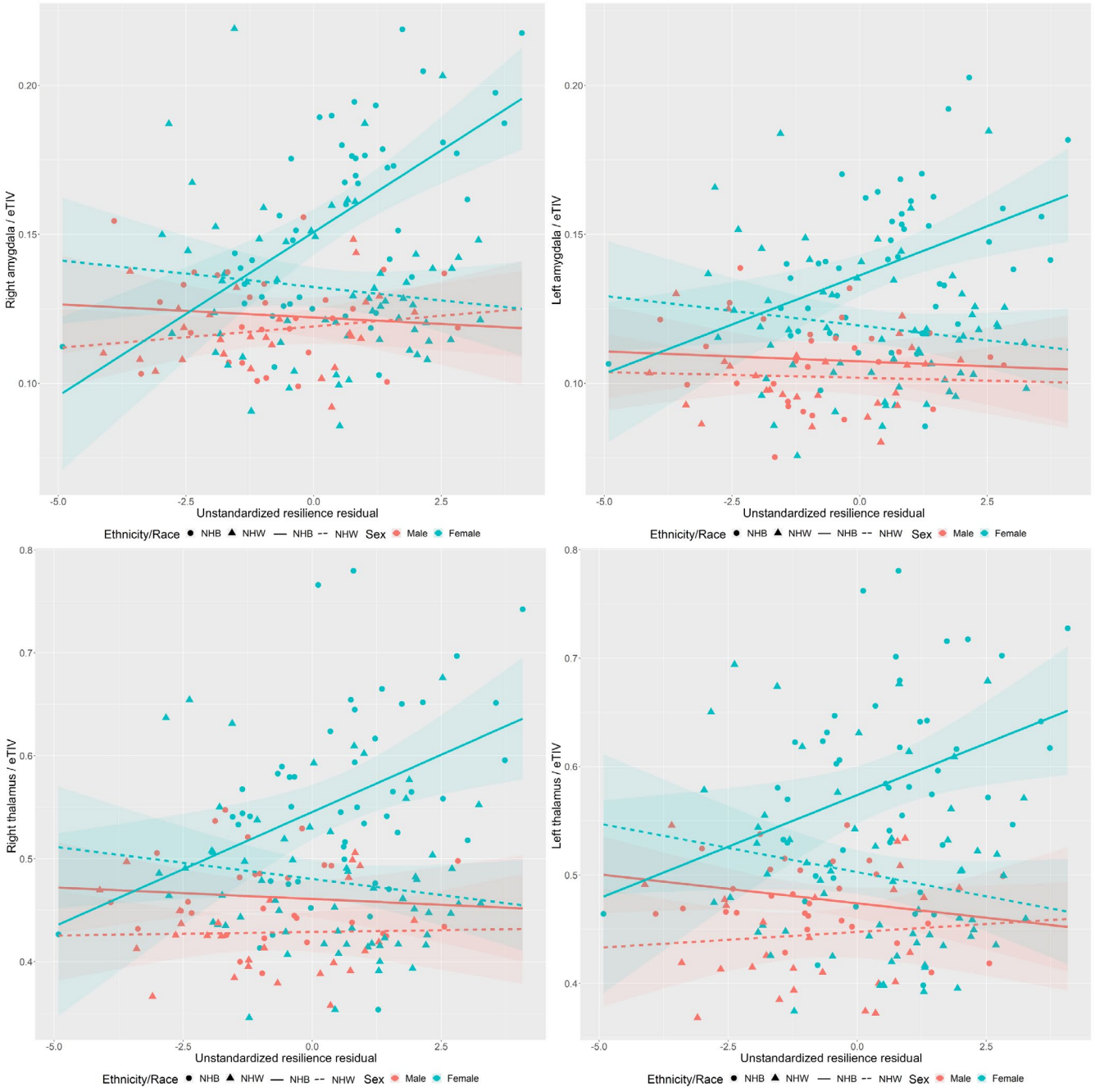

FIGURE 3 Sociodemographic group relationships between resilience and subcortical volume. X axes are unstandardized residuals of resilience with age, site, education, and pain sites. Circles and solid lines are NHB, triangles and dashed lines are NHW. Refer to Table 5 for a summary of which interactions are significant. Also refer to Figure 4 for two-way interaction graphs [Color figure can be viewed at wileyonlinelibrary.com]

Pain-related subcortical areas. In a multivariate model there were differences for subcortical areas (amygdala and thalamus) between high and low resilience women (high > low; $F(4,100) = 3.67$, $p = 0.008$; partial $\eta^2 = 0.128$). From a univariate standpoint, right amygdala volumes differed between groups ($F(1,103) = 8.41$, $p = 0.018$, partial $\eta^2 = 0.075$). There was insufficient evidence of differences in left amygdala or bilateral thalamus volumes (p values > 0.068).

Between ethnic/race group differences

Pain-related cortical areas. Ethnic/race group differences were indicated for pain-related cortical areas in the overall model. Low resilience NHB ($n = 38$) and NHW ($n = 38$) participants differed in cortical thickness across the investigated regions of interest ($F(5,65) = 4.73$, $p = 0.001$, partial $\eta^2 = 0.267$). There were univariate differences in cortical thickness in the insula (NHB < NHW, $p = 0.026$) with no evidence of differences in the other regions (p values ≥ 0.074).

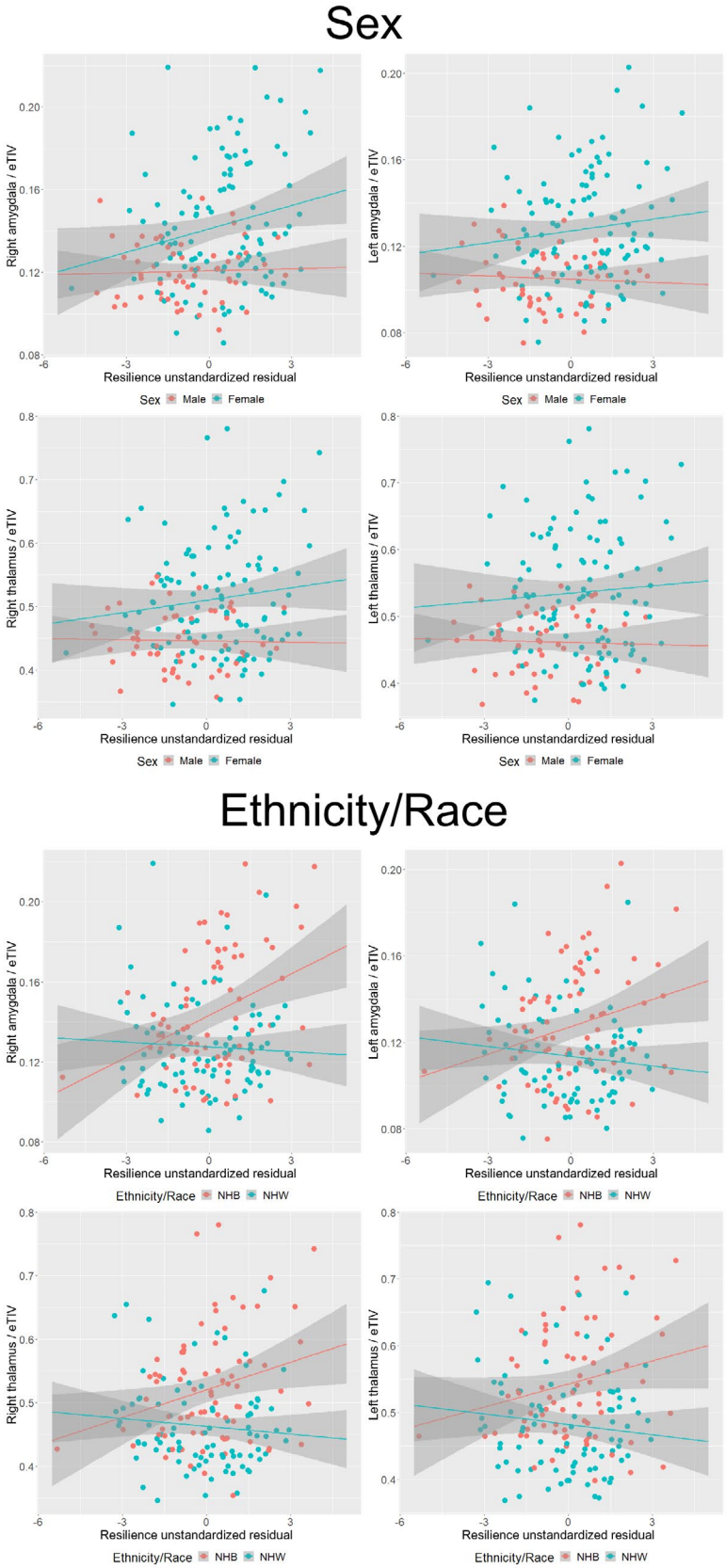

FIGURE 4 Relationships between resilience and stratified sociodemographic variables. X axes are unstandardized residuals of resilience with age, site, education, and pain sites with ethnicity/race and sex as appropriate. Y axes are subcortical volumes adjusted for total intracranial head size [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 7 Multivariate multiple linear regression models examining biobehavioral/psychosocial resilience in relation to subcortical regions of interest

	Omnibus Model	Left Thalamus		Right Thalamus		Left Amygdala		Right Amygdala	
Variable	F	*b*(*SE*)	*t*	*b*(*SE*)	*t*	*b*(*SE*)	*t*	*b*(*SE*)	*t*
Age	9.48**	−0.38(0.06)	−6.06**	−0.33(0.07)	−5.16**	−0.24(0.07)	−3.71**	−0.26(0.07)	−3.94**
Site	1.84	−0.07(0.06)	−1.15	−0.04(0.06)	−0.70	0.06(0.06)	0.92	0.04(0.06)	0.69
Education	0.16	0.00(0.06)	0.07	0.01(0.07)	−0.13	−0.02(0.07)	−0.27	−0.03(0.07)	−0.43
Sex	11.67**	0.38(0.06)	5.88**	0.35(0.07)	5.32**	0.42(0.07)	6.28**	0.33(0.07)	4.96**
Ethnicity/race	4.64**	−0.27(0.06)	−4.15**	−0.28(0.07)	−4.17**	−0.23(0.07)	−3.39**	−0.20(0.07)	−3.04**
No. pain sites	0.30	0.02(0.06)	0.37	0.01(0.06)	0.18	−0.02(0.06)	−0.36	0.01(0.06)	0.11
Resilience	4.18**	0.07(0.06)	1.05	0.11(0.07)	1.69	0.10(0.07)	1.43	0.20(0.07)	3.00**
Resilience*Ethnicity/Race	3.91**	−0.15(0.06)	−2.46*	−0.17(0.06)	−2.76**	−0.20(0.06)	−3.17**	−0.25(0.06)	−3.89**
Resilience*Sex	1.02	0.02(0.06)	0.24	0.05(0.06)	0.78	0.07(0.06)	1.08	0.08(0.06)	1.19
Resilience*Ethnicity/Race*Sex	3.13*	−0.15(0.06)	−2.42*	−0.14(0.06)	−2.22*	−0.13(0.07)	−1.92	−0.21(0.06)	−3.19**

Note: Adjusted model; thalamus and amygdala volumes are adjusted for estimated total intracranial volume; *b*, standardized coefficient; SE, standard error; reference category for sex = male; reference category for Ethnicity/Race = non-Hispanic Black.

See Figure 3.

*$p < 0.05$; **$p < 0.01$.

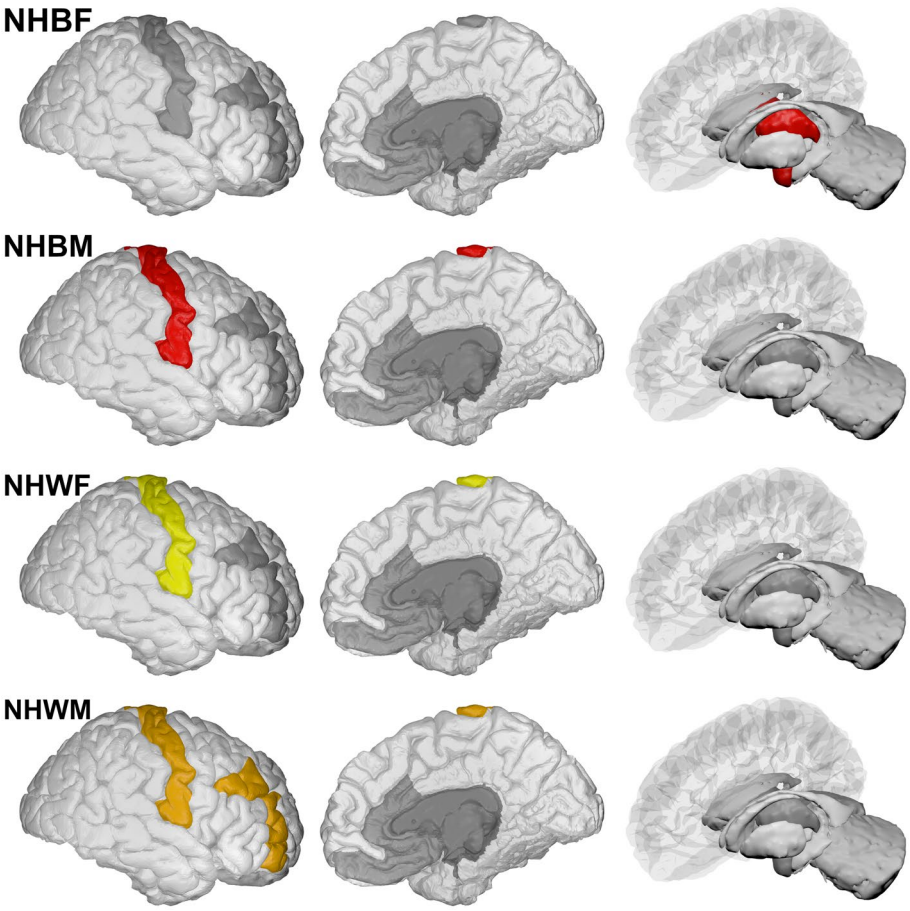

FIGURE 5 Resilience and brain patterns by sociodemographic groups. NHBF, non-Hispanic Black female; NHBM, non-Hispanic Black male; NHWF, non-Hispanic White female; NHWM, non-Hispanic White male. Five cortical and two subcortical areas were investigated: ACC, DLPFC, insula, medial orbitofrontal, postcentral gyrus, amygdala, and thalamus. Areas in dark gray have correlation *p* values > 0.20, yellow indicates $0.10 > p > 0.05$, orange $p < 0.05$, red $p < 0.01$. Figure generated using BrainPainter (Marinescu et al., 2019) [Color figure can be viewed at wileyonlinelibrary.com]

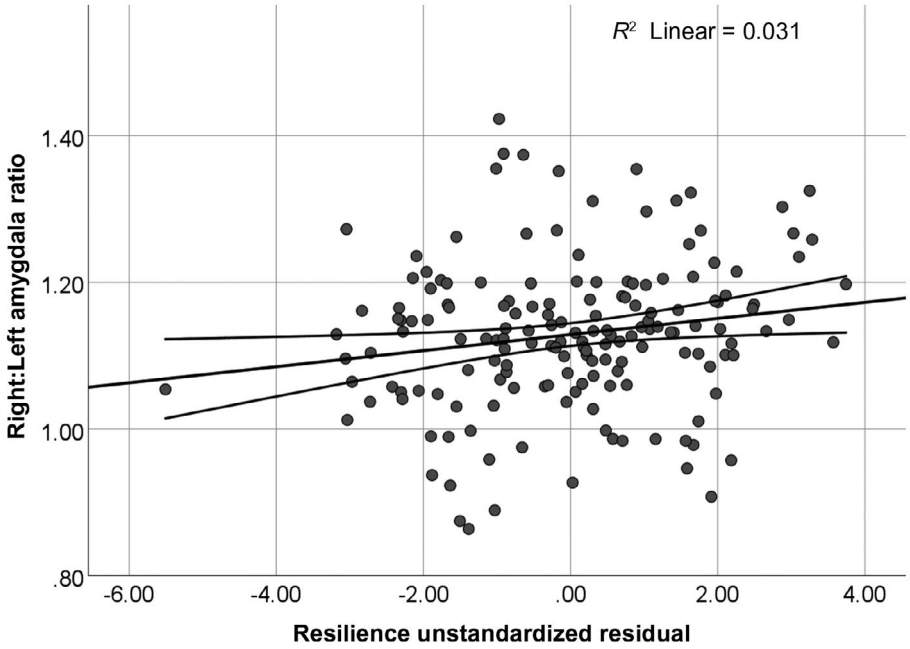

FIGURE 6 Relationship between resilience index and a ratio measure between the right and left amygdala. The resilience residual on the X axis controls for age, study site, sex, pain sites, education, and ethnicity/race. The Y axis is the ratio of right:left amygdala volume. This relationship is significant ($p = 0.023$). The lines represent a linear least squares fit with 95% confidence intervals

TABLE 8 Summary of resilience-related brain findings

	Mean (*SD*)	Resilience	Resilience*Ethnicity/Race	Resilience*Sex	Resilience*Ethnicity/Race*Sex
ACC	2.56 (0.14)	$p = 0.976$	$p = 0.456$	$p = 0.058$	$p = 0.920$
DLPFC	2.26 (0.10)	$p = 0.830$	$p = 0.054$	$p = 0.166$	$p = 0.741$
Insula	2.87 (0.14)	$p = 0.851$	$p = 0.571$	$p = 0.295$	$p = 0.735$
Medial orbitofrontal	2.28 (0.12)	$p = 0.654$	$p = 0.246$	$p = 0.390$	$p = 0.820$
Postcentral gyrus	2.00 (0.11)	$p = 0.627$	**$p = 0.003$***	$p = 0.171$	$p = 0.015$ *
Left Thalamus/TICV	0.51 (0.09)	$p = 0.295$	**$p = 0.015$***	$p = 0.808$	$p = 0.017$ *
Right thalamus/TICV	0.49 (0.08)	$p = 0.094$	**$p = 0.006$***	$p = 0.439$	$p = 0.028$ *
Left amygdala/TICV	0.12 (0.02)	$p = 0.155$	**$p = 0.002$***	$p = 0.282$	$p = 0.056$
Right amygdala/TICV	0.14 (0.03)	**$p = 0.003$***	**$p < 0.001$***	$p = 0.200$	**$p = 0.002$***

Note: **Bolding indicates $p < 0.05$ with FDR set at 0.05**. The omnibus cortical model had significant Resilience*Ethnicity/Race ($p = 0.024$) and Resilience*Sex ($p = 0.044$) interactions. Neither resilience ($p = 0.984$) nor the three-way interaction were significant ($p = 0.149$). All values are unadjusted mean (standard deviation). The omnibus subcortical model had significant Resilience ($p = 0.003$) and Resilience*Ethnicity/Race ($p = 0.005$) and Resilience*Ethnicity/Race*Sex ($p = 0.017$) interactions. Resilience*Sex was not significant ($p = 0.398$). Cortical means are thickness values in mm. Subcortical values are the ratio between the region of interest volume and estimate total intracranial volume (TICV).

Abbreviations: ACC, anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex; *SD*, standard deviation.

*Unadjusted $p < 0.05$.

High resilience NHB ($n = 38$) and NHW ($n = 52$) participants differed in cortical thickness across the investigated regions of interest ($F(5,79) = 11.40$, $p < 0.001$, partial $\eta^2 = 0.419$). Postcentral gyrus differed between ethnic/race groups (NHB < NHW; $p < 0.001$) with a trend for DLPFC (NHB < NHW; $p = 0.059$). The other regions of interest did not have evidence of difference (p values > 0.110).

Pain-related subcortical areas. Ethnic/race group differences were indicated in the pain-related subcortical areas in the overall model. Low resilience NHB ($n = 38$) and NHW ($n = 38$) showed no evidence of difference in subcortical volume across all investigated regions of interest ($F(4,66) = 0.80$, $p = 0.533$, partial $\eta^2 = 0.046$). Univariate p values ≥ 0.132.

High resilience NHB ($n = 38$) and NHW ($n = 52$) participants differed in subcortical volume across all investigated regions of interest ($F(4,80) = 7.75$, $p < 0.001$, partial $\eta^2 = 0.279$). There were univariate differences (NHB > NHW) in all areas (left and right amygdala and thalamus; p values < 0.001).

3.4.3 | Within ethnic/race group differences

Non-Hispanic Black

Pain-related cortical areas. There were no multivariate differences between NHB participants with high ($n = 38$) versus low ($n = 38$) resilience ($F(5,65) = 1.45$, $p = 0.218$, partial $\eta^2 = 0.10$). There was a univariate difference (high > low) in postcentral gyrus cortex ($p = 0.011$) and a trend for DLPFC (high > low; $p = 0.077$). There was no evidence of differences in other regions (p values ≥ 0.777).

Pain-related subcortical areas. Multivariate differences were found between NHB participants with high versus low resilience (high > low; $F(4,66) = 5.31$, $p = 0.001$, partial $\eta^2 = 0.243$). From a univariate standpoint, all volumes were different between groups (high > low): left thalamus ($p = 0.009$, partial $\eta^2 = 0.095$); right thalamus ($p = 0.003$, partial $\eta^2 = 0.120$); left amygdala ($p = 0.004$, partial $\eta^2 = 0.137$); right amygdala ($p < 0.001$, partial $\eta^2 = 0.221$).

Non-Hispanic White

Pain-related cortical areas. There were no differences between NHW participants with high ($n = 52$) versus low ($n = 38$) resilience ($F(5,79) = 1.48$, $p = 0.207$, partial $\eta^2 = 0.085$; univariate p values ≥ 0.118).

Pain-related subcortical areas. There were no differences between NHW participants with high ($n = 52$) versus low ($n = 38$) resilience ($F(4,80) = 0.46$, $p = 0.763$, partial $\eta^2 = 0.023$; univariate p values > 0.677).

4 | DISCUSSION

The current study aimed to determine the association of a previously investigated biobehavioral and psychosocial resilience index (Johnson et al., 2019) with clinical pain measures and pain-related brain structure, and whether associations differ by sex and ethnicity/race. First, as hypothesized, higher levels of resilience were associated with lower levels of clinical pain and functional limitations. Second, a relationship between resilience and pain-related brain structure emerged, higher resilience was associated with larger right and more right-lateralized amygdala volumes. Third, further investigations with consideration for sex and ethnicity/race showed: (a) males had a lower resilience index and smaller subcortical volumes than females after adjusting for intracranial volume; (b) ethnic/race groups did not differ on the resilience index; and (c) significant interactions between sex, ethnicity/race, and resilience were indicated, particularly in subcortical volumes for pain-related areas of the brain. Our findings align with a strong foundation of animal and human research demonstrating complex relationships between sociodemographic factors, chronic pain, resilience, and brain structure.

4.1 | Associations between the resilience index and clinical pain and functioning measures

Resilience factors have been consistently associated with less clinical pain and greater functioning (Ferreira & Sherman, 2007; Hassett & Finan, 2016; Karoly & Ruehlman, 2006; Newton-John et al., 2014; Ong et al., 2010; Strand et al., 2006). Studies have previously investigated either protective psychosocial or behavioral/lifestyle factors (Brown et al., 2003; Eisenberger et al., 2007; Geneen et al., 2017; Lambert et al., 1990; Lee et al., 2016; López-Martínez et al., 2008; Macfarlane et al., 2017; Master et al., 2009; Messier et al., 2013; Sibille et al., 2016, 2018). From a clinical perspective, investigations that consider the additive benefit of multiple protective factors are needed. Macfarlane and colleagues demonstrated an additive benefit with combined protective factors reducing excess mortality risk in individuals with chronic widespread pain (Macfarlane et al., 2017). Additionally, we reported an additive benefit between the same biobehavioral and psychosocial resilience index implemented in the present study and telomere length in individuals with or at risk for knee OA (Johnson et al., 2019). Importantly, the current study extends previous findings by demonstrating a linear relationship between greater resilience and lower clinical pain, functional limitations, and disability.

A comprehensive approach to investigating resilience has clinical relevance (Bartley, Palit, et al., 2019; Liu et al., 2017; Puterman & Epel, 2012). Risk factor indexes are well recognized and frequently utilized for assessing risk for various health conditions. An important component of a risk factor index is the inclusion of established clinical values that are additive in nature (Dufouil et al., 2017; Lindstrom & Tuomilehto, 2003; Nickson et al., 2018; Zhang et al.,). The development of a "chronic pain resilience index" could be similarly constructed, that is, a measure predicting improved health outcomes based on clinically validated values. The current formulation of the resilience index is based on validated and recognized measures that have been associated with lower levels of clinical pain (Table 2). Current findings suggest there is an additive benefit of resilience factors with lower levels of clinical pain. Frequently, resilience research in chronic pain is focused on relative values limited by study sample representation, reducing the ability to evaluate clinically relevant phenotypes and associated physiological correlates. Values derived from validated measures indicate population-based norms and clinically relevant ranges. Identifying and compiling a validated and normed chronic pain resilience index that is predictive of improved pain-related outcomes would have significant clinical utility.

4.2 | Associations between the resilience index and pain-related brain structures

In cortical areas of the brain previously related with chronic pain (Coppieters et al., 2016), we showed associations with resilience that differed based on sociodemographic variables (ethnicity/race and sex). This implies that these cortical areas are important for resilience, but such relationships might be unclear without assessing the influence of sociodemographic variables. Of note, the postcentral gyrus (primary somatosensory cortex) demonstrated two-way (resilience*ethnicity/race) and three-way (resilience*ethnicity/

race*sex) interactions. The relationship between resilience and cortical thickness in the postcentral gyrus differed among NHB males compared to the other three groups. In this group, higher resilience was associated with thinner somatosensory cortex. Previous research in other populations has revealed relationships between resilience and ACC, insula, and orbitofrontal regions in adults (Kong et al., 2015, 2018; Son et al., 2019). Beyond resilience, findings show sex differences in ACC thickness (Male < Female, $p < 0.01$; see Table 4) and ethnicity/race differences in insula and postcentral gyrus thickness (NHB < NHW, p values < 0.01). These same areas of the brain have also been indicated in experiences of social pain which share similar areas of activation with physical pain (Eisenberger, 2012; Macdonald & Leary, 2005). Our results suggest that relationships between volumes of pain-related brain regions and resilience vary by sociodemographic variables; such variables should be considered in future analyses.

In the subcortical areas of the brain, the right amygdala and bilateral thalamus showed direct relationships with resilience or resilience/sociodemographic interactions. The cortico-limbic areas of the brain are well recognized as primary structures associated with chronic pain, particularly the medial prefrontal cortex, amygdala, and thalamus (Apkarian, 2011; Davis et al., 2016; Hashmi et al., 2013). Previous research demonstrates relationships between chronic pain and thalamus volume (Apkarian et al., 2004). Stroke within the thalamus, particularly the pulvinar nucleus, can lead to a severe central pain syndrome (Vartiainen et al., 2016). In addition to pain, previous research has implicated the dorsomedial nucleus of the thalamus in resilience to mood disorders (Russo et al., 2012). Our results add to existing research by indicating the importance of the thalamus in relationship to resilience in chronic MSK pain.

The right amygdala stood out as the primary resilience-related structure across all analyses. The amygdala serves a vital role in the integration of sensory, emotional/affective, and cognitive responses including nociceptive input (Gandhi et al., 2020; Simons et al., 2014; Thompson & Neugebauer, 2017). Intricately connected with numerous cortical and subcortical brain areas, the amygdala links internal and external stimuli with areas of the brain regulating cognition, affect, and physiological and behavioral responses (Abivardi & Bach, 2017; Bickart et al., 2012; Rizzo et al., 2018; Saygin et al., 2011). Within both the right and left side, nuclei within the amygdala have been classified into to sub-regions. Of these sub-regions, the central nucleus of the amygdala has been identified as a key component in pain processing (Allen et al., 2020; Simons et al., 2014). Recent findings from rodents indicate the central nucleus serves a dual or bidirectional role with cells mediating inhibitory functions and others serving a facilitating function (Hua et al., 2020; Neugebauer et al., 2020; Wilson et al., 2019).

Hemispheric asymmetries in structure and function between the left and right amygdala are well recognized (Baas et al., 2004; Baeken et al., 2014; Brierley et al., 2002; Davidson, 2002; Gotink et al., 2018; Zald, 2003). Structurally, we found the overall group mean for the right amygdala was larger than the left amygdala, which matches laterality findings of some but not all previous research(Brierley et al., 2002; Gotink et al., 2018). While we did not assess function, a meta-analysis completed by Wager and colleagues indicated hemispheric laterality such that the left amygdala has a role in negative emotion processing (Baeken et al., 2014; Wager et al., 2003). A strong body of animal and human research shows that lateralization and specialized functioning also applies to pain (Allen et al., 2020; Thompson & Neugebauer, 2017). Investigations regarding hemispheric lateralization of amygdala function specific to pain in humans are in early stages and complicated by factors such as acute versus chronic, pain side (unilateral/bilateral), type of pain, affective aspects of pain, and sex differences (Allen et al., 2020). In a meta-analysis of human pain-related studies, a pattern of greater left amygdala activation was indicated in chronic pain studies while more frequent activation of the right amygdala was shown in experimental pain studies (Simons et al., 2014). Three limiting factors of the meta-analysis were the small sample sizes across studies, criteria for chronic pain phenotyping, and the greater representation of males in the experimental studies and females in the clinical studies (more about pain phenotyping and sex differences addressed further below) (Simons et al., 2014).

The right amygdala has been associated with resilience in healthy participants. The relationship between self-reported resilience and brain structures associated with cortico-limbic inhibition was investigated in 48 healthy young adults (33 females and 15 males) (Gupta et al., 2017). Trait resilience scores were associated with morphology in the parietal/posterior cingulate region and the amygdala. A subscale measuring resilience persistence was *positively* associated with gray matter volume in the right amygdala. In contrast, *reduced* right amygdala gray matter density was shown following an 8-week mindful meditation intervention study of 27 participants (41% males, average age 32.5 years) reporting high perceived stress at baseline (Hölzel et al., 2010). Greater reductions in the perceived stress scale were associated with greater decreases in right amygdala gray matter density. Notably, the perceived stress scale is a measure included in the resilience index investigated in the current study.

The right amygdala has also been related to persistent pain. In a prospective study of individuals with subacute low back pain, a smaller right amygdala at baseline was predictive of those who would transition to chronic pain, suggesting that trait-related or prolonged negative mood and negative affect are predisposing risk factors (Vachon-Presseau et al., 2016). Moreover, the persisting chronic pain group showed changes in amygdala shape and volume differences compared to healthy controls indicating amygdala atrophy over time, but those who recovered from subacute pain had stable volumes. Hence, in two prospective studies, *opposing patterns* were indicated. Namely, both the reduction of perceived stress and the persistence of chronic back pain associated with reduced right amygdaloid gray matter (Hölzel et al., 2010; Vachon-Presseau et al., 2016).

Most studies in rodents have been completed in the context of acute injury and indicate a pronociceptive role for the right amygdala and an anti-nociceptive role for the left amygdala. The persistence of chronic pain may influence right versus left amygdala

functioning patterns seen in human studies (Simons et al., 2014; Vachon-Presseau et al., 2016). Additionally, the amygdaloid pattern differences described above align with the theoretical model of allostatic load which is represented by the hormesis, inverted "U" pattern (Epel, 2020; Osório et al., 2017). Specifically, the young healthy adults were likely on the adaptive "stress load" side of the dose curve while those individuals with persisting chronic pain due to predisposing factors (e.g., mood-related) were on the "stress overload" side of the curve contributing to their increased risk for persisting chronic pain (Hölzel et al., 2010; Vachon-Presseau et al., 2016). Our findings reveal complex but highly relevant relationships among resilience, chronic pain, sociodemographic characteristics, and the right amygdala, bilateral thalamus, and postcentral gyrus.

A few factors warrant acknowledgment in advance of considering the above differing findings and further evaluation of our results. First, samples sizes in cited studies were limited and most were not sufficient to consider sex independently. Well-documented sex differences in cortico-limbic functioning require consideration (Allen et al., 2020; Andreano et al., 2013; Cahill et al., 2001; Linnman et al., 2012a; McEwen, 2017). Second, the amygdala is highly responsive to and shaped by a combination of factors (Allen et al., 2020; Davidson & McEwen, 2012; Eisenberger, 2012; Gandhi et al., 2020; McEwen, 2017; Neugebauer et al., 2020; Sambuco et al., 2020). Third, few studies have considered the influence of sociodemographic, cultural, and ethnicity/race factors in the relationships between chronic pain and brain structure. Fourth, the amygdala is activated both in the inhibition and amplification of pain experiences; an improved understanding of this dual role is necessary in the evaluation of structural changes in individuals with chronic pain. Fifth, there is a substantial body of evidence showing inconsistencies in research findings. Applying principles of neuroplasticity and careful pain phenotyping may improve interpretability of findings (Bushnell et al., 2015; Coppieters et al., 2016; Maleki et al., 2013). Finally, prospective studies will be essential to determine relationships between pain-related resilience factors and brain structure differences. To effectively decipher the code of chronic pain in brain structure, consideration of sociodemographic factors and the neurobiological effects of stress and pain will be necessary and are explored further below.

4.3 | Sex differences in the resilience index and pain-related brain structures

Men had a lower resilience index than women in the current study. There has been a general understanding to suggest that men experience greater psychological resilience than women (Boardman et al., 2008). However, in the previously described study by Gupta and colleagues, the trait resilience measure did not differ by sex, and a recent meta-analysis on positive affect and chronic pain showed that the effects of positive affect on chronic pain were moderated by gender, such that effect sizes were larger in studies with a greater proportion of women (Gupta et al., 2017; Ong et al., 2020). One factor distinguishing our study from prior investigations is that our resilience index includes biobehavioral factors (tobacco use and waist/hip ratio) both of which differed by sex in our sample.

Sex differences were observed in our cortical and subcortical analyses. There is strong and consistent evidence of sex differences in neurobiological functioning with indications of specific differences in cortico-limbic areas and cognitive and emotional processes (Andreano et al., 2013; Cahill et al., 2001; Gruene et al., 2015; Hamann, 2005; Kogler et al., 2016; McEwen & Milner, 2017; Wellman et al., 2018). Wager and colleagues in a meta-analysis reported sex differences across cortical and sub-cortical regions related to emotional processing (Baeken et al., 2014; Wager et al., 2003). Between and within sex differences in pain processing are also evident in preclinical and clinical pain studies (Allen et al., 2020; Da Silva et al., 2020; Linnman et al., 2012a, 2012b). Our findings also suggest within-sex-group differences (e.g., NHB males compared to NHW males in the postcentral gyrus and NHB females compared to NHW females in the subcortical regions) and warrant further investigation.

Additionally, in the comparison of resilience and pain-related brain structure by sex, males had lower subcortical volume compared to females. One factor warranting caution with interpretability of our findings is the lower number of males compared to females in the analyses, particularly males reporting high resilience across both ethnic/race groups. However, our findings add to a strong body of evidence of the importance of including females in animal and human pain research and that additional analyses specific to evaluating sex differences is necessary.

4.4 | Ethnic/race differences in the resilience index and pain-related brain structures

Although NHB participants reported greater clinical pain compared to their NHW peers, the resilience index did not differ by ethnic/race group. We have previously reported ethnic/race group differences in the relationship between risk and resilience factors and pain such that higher perceived stress and higher psychological resilience were associated with greater and lesser movement evoked pain (respectively) in NHB participants but not NHW participants (Bartley, Hossain, et al., 2019; Booker et al., 2019). Additionally, a recent finding shows the relationship between pain catastrophizing and brain structure also differs by ethnic/race group such that among NHB participants with knee pain, a trend for higher pain catastrophizing was associated with slightly thinner insula while catastrophizing was significantly related to thinner bilateral somatosensory cortex among NHWs (Terry et al., 2020).

Participants in our ethnic/race groups differed in age and education. Socioeconomic and environmental factors are strong contributors influencing neuroplasticity and shaping the brain (Davidson & McEwen, 2012). Investigations regarding the neurobiological interface of environment, culture, ethnicity/race, and sociodemographic factors are contributing to an improved understanding of individual differences in biobehavioral research (Chattarji et al., 2015; Han, 2015). Our

findings indicate that ethnicity/race contributed to the two- and three-way interactions in the cortical and subcortical models. In our study, the pattern of higher resilience being related to greater right amygdala volume among NHB females aligns with the previously described resilience persistence findings (Gupta et al., 2017). However, the pattern of the other three groups is more similar to the findings described by Hölzel and colleagues (2010). Table 4 shows a pattern for lower clinical pain when comparing those with high and low resilience. Clinically relevant differences are most apparent for the NHB women (Table 5). Our findings contribute to a growing body of evidence, which will help further inform interpretations of ethnic/race group differences in clinical and experimental pain and identify potential targets to reduce health disparities and improve chronic pain prevention strategies (Campbell & Edwards, 2012; Kim et al., 2019; Letzen et al., 2020; Losin et al., 2020).

4.5 | Additional considerations: Stress and pain

The brain is the relay center for life experiences, perceiving and evaluating stress, and orchestrating all behavioral responses (McEwen, 2016, 2017). Adaptive in nature, stress serves as a stimulus promoting neurobiological change and growth through alterations in function and structure. In general, based on the principles of neuroplasticity, increases in activation are often associated with increases in brain structure. However, persisting stress with inadequate recovery results in functional dysregulation and eventual structural degradation (Lupien et al., 2009; McEwen, 2003, 2017, 2019). The timing of stress experiences also influences neuroplastic changes and functional alterations (Edmiston et al., 2011; Lupien et al., 2009; Romeo, 2017). Early life stressful experiences significantly influence brain development and function (Davidson & McEwen, 2012; Lupien et al., 2009; Tottenham et al., 2010). A general pattern of lower prefrontal volume, smaller hippocampal structure, and larger amygdala is associated with early life stress and low socioeconomic status (Davidson & McEwen, 2012; Tottenham et al., 2010). However, opposing patterns have also been described (e.g., smaller amygdala volume) (Edmiston et al., 2011; Gupta et al., 2017; Luby et al., 2013).

Several factors have been identified that likely contribute to the stress-related structural and functional incongruences reported (Lupien et al., 2009; Pagliaccio et al., 2015). Neurobiological alterations in response to life stress are greatly influenced by the age at which the experiences occur, genetic and personality trait predispositions, sex, the type, number, intensity, duration, frequency, and persistence of stressful experiences, and the environmental buffers available (Luby et al., 2013; Lupien et al., 2009; McEwen, 2010, 2016, 2017; Pagliaccio et al., 2015; Tottenham et al., 2010). Similar to the discordant findings with stress and brain structure, chronic pain and brain research are also hampered by inconsistencies (Bushnell et al., 2015; Coppieters et al., 2016). Simple classification of chronic pain is common in brain imaging research; however, such categorizations may not be sufficient. There is a strong body of evidence showing that a combination of pain frequency, intensity, duration, and extent of painful body sites influences brain structure and function (Bushnell et al., 2015; Maleki et al., 2013; Vachon-Presseau et al., 2016). To account for the overall burden of pain, we controlled for number of pain sites, which is associated with chronic pain severity (Kutch et al., 2017). However, improved pain phenotyping capturing "stages" of chronic pain severity may further inform interpretation of findings (Sibille et al., 2016, 2017; Vachon-Presseau et al., 2016).

Our study was comprised of community-dwelling adults reporting mild to moderate chronic musculoskeletal pain at one or more sites for 3 months or greater at varying intensities, frequencies, and durations. Thus, the influence of differing pain signals contrasted to possible resilience/inhibitory signals may contribute to the variability of patterns indicated in our sample. Additionally, persistent stress associated with chronic pain can also lead to a feed-forward cycle where engagement of limbic areas, such as the amygdala, can contribute to worsening of pain through the same or interconnected descending pain structure (e.g., periaqueductal gray) (Johnson & Greenwood-Van Meerveld, 2014). Resilience may play a role in short-circuiting the feed-forward loop. Additionally, our NHB and NHW participants differed by neurobiologically relevant sociodemographic variables. Environmental and socioeconomic factors are significant predictors of health disparities (Bagby et al., 2019; Palmer et al., 2019). There is a body of evidence to suggest that environmental stress contributes to a greater allostatic load contributing toward eventual "overload" resulting in greater disease burden and worse health outcomes in underrepresented ethnic/race groups (Epel, 2020; Mickle et al., 2020; Myers, 2009). Finally, given the amygdala's intricate role in emotion, cognition, sensory processing including bidirectional activation with nociception, and the morphological influences of stress and sex; all these factors contribute to the amygdala's structural alterations. Interpreting directionality will require consideration of several factors moving forward.

5 | STRENGTHS, LIMITATIONS, AND FUTURE DIRECTIONS

There are several strengths in the study. First, findings are bolstered by a large sample size with comparable representation of males/females and NHB/NHW participants. Second, a comprehensive array of data, questionnaires, and imaging were collected for each participant within approximately a 2-week timeframe to address study questions. Third, the resilience index is replicated from a previous study demonstrating a positive, additive relationship between resilience and telomere length (Johnson et al., 2019) and is comprised of validated measures, applying referenced norms. Fourth, imaging findings are based on identical protocols at both study sites with minor scanner differences (i.e., same make and model but different head coils), data processing was completed on one system at one site with well-validated processing methods, and study site was included as a covariate in the statistical models.

Several limitations are also important to note. First, while we tried to address the considerable disparities between our ethic/race groups

by including specific covariates in the analyses, we recognize such statistical modeling incompletely accounts for differences. Ethnic/race group differences are affected by and reflect cultural, environmental, health, psychological, and social factors. As such, we interpret our findings as based on sociodemographic factors. While these disparities exist in our sample, they are somewhat reflective of societal disparities. This gives our study a measure of ecological validity. Second, our study is cross-sectional; prospective longitudinal analyses are an important next step to better understand the relationship between resilience and brain structure in individuals with chronic musculoskeletal pain. Importantly, we will have the opportunity to complete prospective analyses on the current sample. Third, all participants in the study met criteria for chronic pain at a minimum of one body site, the majority of whom endorsed knee pain. The three clinical pain measures analyzed in the study were specific to knee pain, and thus did not represent the pain experienced by the entire sample. It will be important to explore replication of findings in individuals grouped by specific chronic pain conditions. Additionally, although number of pain sites was included in the model to account for chronic pain severity, improved consideration for stage of pain severity will be an important consideration moving forward. Fourth, measures of mood (i.e., anxiety and depression), are important considerations in chronic pain. Inclusion of more comprehensive psychological measures will further inform understanding specific to how mood is related in the resilience and pain-related brain structure interface. Fifth, inclusion of amygdala nuclei should improve comparisons between studies (Simons et al., 2014). Sixth, other areas of the brain may be relevant to consider in relation to resilience but were beyond the focus of our study aims. Seventh, based on our replication of findings with the resilience index, further development is warranted. If the current index is applied in future studies, the Coping Strategies Questionnaire-Revised (CSQ-R) active coping score should be excluded as there are no clear published norms available and the resilience value incorporated in the study was higher than the group mean. Additionally, the Waist–Hip Ratio (WHR) resilience value applied was specific to men, incorporation of the World Health Organization recommended range for women in future studies could improve the resilience formulation. Also, tobacco use categorization might benefit from further evaluation to optimize classification (former smoker vs. less than 100 cigarettes in a lifetime) (CDC, 2017). Lastly, although our study benefited from a large sample size, our findings in combination with a strong body of evidence regarding sex differences in brain function and structure warrant ample representation of males and females and the consideration of relevant sociodemographic factors in future studies.

6 | CONCLUSIONS

In individuals with chronic MSK pain, resilience is associated with lower levels of clinical pain and functional limitations, and with pain-related brain structure (right amygdala, bilateral thalamus, and postcentral gyrus). Findings demonstrate a neurobiological correlate to resilience in individuals with musculoskeletal chronic pain and extend our previous work showing a positive and additive relationship between resilience and telomere length (Johnson et al., 2019). Further and importantly, we show that the relationship between resilience and pain-related brain structure differs by sociodemographic factors. If efforts to decipher the code of chronic pain and associated protective factors in the brain are to be successful, results provide additional compelling evidence regarding the necessity to: (a) improve chronic pain phenotyping, (b) include an equal representation of females in studies and incorporate analyses stratifying by sex, and (c) incorporate neurobiologically relevant sociodemographic factors into investigations.

DECLARATION OF TRANSPARENCY

The authors, reviewers and editors affirm that in accordance to the policies set by the *Journal of Neuroscience Research*, this manuscript presents an accurate and transparent account of the study being reported and that all critical details describing the methods and results are present.

ACKNOWLEDGMENTS

The authors thank Dr. Larry Bradley for his invaluable contributions to developing and implementing the UPLOAD Projects; Angela Mickle, MS, CCRP for her thoughtful and extensive efforts; and Shivani Hanchate, BS for her literature search assistance. We are also appreciative for the expertise and feedback provided by Drs. Benedict J. Kolber, PhD and Nicola Sambuco, PhD. Finally, we express our heartfelt sadness regarding the passing of Dr. Bruce McEwen. We are grateful for the guidance, support, and mentoring that he provided to us over the years toward our efforts investing the biological interface of chronic pain and resilience.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

All authors have full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Conceptualization*, K.T.S., J.J.T., A.J.J., E.L.T., and C.G.; *Methodology*, K.T.S., J.J.T., A.J.J., E.L.T., and C.G.; *Investigation*, E.L.T., J.C., R.S., G.D., H.D., S.L., and A.A.; *Formal analysis*, J.T.T. and A.J.J.; *Visualization*, J.T.T. and A.J.J.; *Data Curation*, J.J.T., J.C., R.B.F., D.R., G.D., H.D., S.L., and C.G.; *Writing – Original Draft*, K.T.S., J.J.T., A.J.J., and E.L.T.; *Writing – Review & Editing*, J.J.T., A.J.J., E.L.T., J.C., C.G., R.S., G.D., H.D., S.L., A.A., D.R., B.R.G., C.C.P., R.B.F., and K.T.S.; *Supervision*, K.T.S.; *Project Administration*, R.B.F., K.T.S., B.R.G., R.S., S.L., D.R., G.D., and C.C.P.; *Funding Acquisition*, R.B.F. and K.T.S.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1002/jnr.24790.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Jared J. Tanner https://orcid.org/0000-0001-6821-0029

REFERENCES

Abbott, A. (2010). The coping strategy questionnaire. *Journal of Physiotherapy*, *56*, 63. https://doi.org/10.1016/S1836-9553(10)70061-8

Abivardi, A., & Bach, D. R. (2017). Deconstructing white matter connectivity of human amygdala nuclei with thalamus and cortex subdivisions in vivo. *Human Brain Mapping*, *38*, 3927–3940. https://doi.org/10.1002/hbm.23639

Allen, H. N., Bobnar, H. J., & Kolber, B. J. (2020). Left and right hemispheric lateralization of the amygdala in pain. *Progress in Neurobiology*, *196*, 101891. https://doi.org/10.1016/j.pneurobio.2020.101891

Allen, K. (2010). Racial and ethnic disparities in osteoarthritis phenotypes. *Current Opinion in Rheumatology*, *22*, 528–532. https://doi.org/10.1097/BOR.0b013e32833b1b6f

Allen, K. D., Golightly, Y. M., & Olsen, M. K. (2006). Pilot study of pain and coping among patients with osteoarthritis: A daily diary analysis. *Journal of Clinical Rheumatology*, *12*, 118–123. https://doi.org/10.1097/01.rhu.0000221801.63880.3f

Andreano, J. M., Dickerson, B. C., & Barrett, L. F. (2013). Sex differences in the persistence of the amygdala response to negative material. *Social Cognitive and Affective Neuroscience*, *9*, 1388–1394. https://doi.org/10.1093/scan/nst127

Apkarian, A. V., Sosa, Y., Sonty, S., Levy, R. M., Harden, R. N., Parrish, T. B., & Gitelman, D. R. (2004). Chronic Back Pain Is Associated with Decreased Prefrontal and Thalamic Gray Matter Density. *Journal of Neuroscience*, *24*(46), 10410–10415. http://dx.doi.org/10.1523/jneurosci.2541-04.2004

Apkarian, A. V. (2011). The brain in chronic pain: Clinical implications. *Pain Management*, *1*, 577–586. https://doi.org/10.2217/pmt.11.53

Baas, D., Aleman, A., & Kahn, R. S. (2004). Lateralization of amygdala activation: A systematic review of functional neuroimaging studies. *Brain Research Reviews*, *45*, 96–103. https://doi.org/10.1016/j.brainresrev.2004.02.004

Baeken, C., Marinazzo, D., Van Schuerbeek, P., Wu, G.-R., De Mey, J., Luypaert, R., & De Raedt, R.. (2014). Left and right amygdala—Mediofrontal cortical functional connectivity is differentially modulated by harm avoidance. *PLoS ONE*, *9*, e95740. https://doi.org/10.1371/journal.pone.0095740

Bagby, S. P., Martin, D., Chung, S. T., & Rajapakse, N. (2019). From the outside. In: Biological mechanisms linking social and environmental exposures to chronic disease and to health disparities. *American Journal of Public Health*, *109*, S56–S63. https://doi.org/10.2105/ajph.2018.304864

Baliki, M. N., Schnitzer, T. J., Bauer, W. R., & Apkarian, A. V. (2011). Brain morphological signatures for chronic pain. *PLoS ONE*, *6*, e26010. https://doi.org/10.1371/journal.pone.0026010

Bartley, E. J., Hossain, N. I., Gravlee, C. C., Sibille, K. T., Terry, E. L., Vaughn, I. A., Cardoso, J. S., Booker, S. Q., Glover, T. L., Goodin, B. R., Sotolongo, A., Thompson, K. A., Bulls, H. W., Staud, R., Edberg, J. C., Bradley, L. A., & Fillingim, R. B. (2019). Race/ethnicity moderates the association between psychosocial resilience and movement-evoked pain in knee osteoarthritis. *ACR Open Rheumatology*, *1*, 16–25. https://doi.org/10.1002/acr2.1002

Bartley, E. J., Palit, S., Fillingim, R. B., & Robinson, M. E. (2019). Multisystem resiliency as a predictor of physical and psychological functioning in older adults With chronic low back pain. *Frontiers in Psychology*, *10*, 1932. http://dx.doi.org/10.3389/fpsyg.2019.01932

Bartley, E. J., Palit, S., & Staud, R. (2017). Predictors of osteoarthritis pain: The importance of resilience. *Current Rheumatology Reports*, *19*(9), 57. https://doi.org/10.1007/s11926-017-0683-3

Bellamy, N., Buchanan, W. W., Goldsmith, C. H., Campbell, J., & Stitt, L. W. (1988). Validation study of WOMAC: A health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *Journal of Rheumatology*, *15*, 1833–1840.

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*, 289–300.

Bergman, S., Thorstensson, C., & Andersson, M. L. E. (2019). Chronic widespread pain and its associations with quality of life and function at a 20-year follow-up of individuals with chronic knee pain at inclusion. *BMC Musculoskeletal Disorders*, *20*, 592. https://doi.org/10.1186/s12891-019-2976-3

Bickart, K. C., Hollenbeck, M. C., Barrett, L. F., & Dickerson, B. C. (2012). Intrinsic amygdala-cortical functional connectivity predicts social network size in humans. *Journal of Neuroscience*, *32*, 14729–14741. https://doi.org/10.1523/jneurosci.1599-12.2012

Blagojevic, M., Jinks, C., Jeffery, A., & Jordan, K. (2010). Risk factors for onset of osteoarthritis of the knee in older adults: A systematic review and meta-analysis. *Osteoarthritis and Cartilage*, *18*, 24–33. https://doi.org/10.1016/j.joca.2009.08.010

Boardman, J. D., Blalock, C. L., & Button, T. M. M. (2008). Sex differences in the heritability of resilience. *Twin Research and Human Genetics*, *11*, 12–27. https://doi.org/10.1375/twin.11.1.12

Booker, S., Cardoso, J., Cruz-Almeida, Y., Sibille, K. T., Terry, E. L., Powell-Roach, K. L., Riley, J. L., Goodin, B. R., Bartley, E. J., Addison, A. S., Staud, R., Redden, D., Bradley, L., & Fillingim, R. B. (2019). Movement-evoked pain, physical function, and perceived stress: An observational study of ethnic/racial differences in aging non-Hispanic Blacks and non-Hispanic Whites with knee osteoarthritis. *Experimental Gerontology*, *124*, 110622. https://doi.org/10.1016/j.exger.2019.05.011

Boyan, B. D., Tosi, L. L., Coutts, R. D., Enoka, R. M., Hart, D. A., Nicolella, D. P., Berkley, K. J., Sluka, K. A., Kwoh, C. K., O'Connor, M. I., Kohrt, W. M., & Resnick, E. (2013). Addressing the gaps: Sex differences in osteoarthritis of the knee. *Biology of Sex Differences*, *4*, 4. https://doi.org/10.1186/2042-6410-4-4

Brierley, B., Shaw, P., & David, A. S. (2002). The human amygdala: A systematic review and meta-analysis of volumetric magnetic resonance imaging. *Brain Research Reviews*, *39*, 84–105. https://doi.org/10.1016/s0165-0173(02)00160-1

Briggs, A. M., Cross, M. J., Hoy, D. G., Sànchez-Riera, L., Blyth, F. M., Woolf, A. D., & March, L. (2016). Musculoskeletal health conditions represent a global threat to healthy aging: A report for the 2015 World Health Organization World Report on Ageing and Health. *The Gerontologist*, *56*(Suppl. 2), S243–S255. https://doi.org/10.1093/geront/gnw002

Brown, J. L., Sheffield, D., Leary, M. R., & Robinson, M. E. (2003). Social support and experimental pain. *Psychosomatic Medicine*, *65*, 276–283. https://doi.org/10.1097/01.psy.0000030388.62434.46

Buckner, R. L., Head, D., Parker, J., Fotenos, A. F., Marcus, D., Morris, J. C., & Snyder, A. Z. (2004). A unified approach for morphometric and functional data analysis in young, old, and demented adults using automated atlas-based head size normalization: Reliability and validation against manual measurement of total intracranial volume. *NeuroImage*, *23*, 724–738. https://doi.org/10.1016/j.neuroimage.2004.06.018

Bushnell, M. C., Case, L. K., Ceko, M., Cotton, V. A., Gracely, J. L., Low, L. A., Pitcher, M. H., & Villemure, C. (2015). Effect of environment on the long-term consequences of chronic pain. *Pain*, *156*(Suppl 1), S42–S49. https://doi.org/10.1097/01.j.pain.0000460347.77341.bd

Cahill, L., Haier, R. J., White, N. S., Fallon, J., Kilpatrick, L., Lawrence, C., Potkin, S. G., & Alkire, M. T. (2001). Sex-related difference in amygdala activity during emotionally influenced memory storage. *Neurobiology of Learning and Memory*, *75*, 1–9. https://doi.org/10.1006/nlme.2000.3999

Campbell, C. M., & Edwards, R. R. (2012). Ethnic differences in pain and pain management. *Pain Management*, *2*, 219–230. https://doi.org/10.2217/pmt.12.7

Casale, R., Sarzi-Puttini, P., Botto, R., Alciati, A., Batticciotto, A., Marotto, D., & Torta, R. (2019). Fibromyalgia and the concept of resilience. *Clinical and Experimental Rheumatology*, *37*, 105–113.

Cathomas, F., Murrough, J. W., Nestler, E. J., Han, M.-H., & Russo, S. J. (2019). Neurobiology of resilience: Interface between mind and body. *Biological Psychiatry*, *86*, 410–420. https://doi.org/10.1016/j.biopsych.2019.04.011

CDC. (2017). *National Health Interview Survey: Adult Tobacco Use Information*. https://www.cdc.gov/nchs/nhis/tobacco/tobacco_glossary.htm

Chattarji, S., Tomar, A., Suvrathan, A., Ghosh, S., & Rahman, M. M. (2015). Neighborhood matters: Divergent patterns of stress-induced plasticity across the brain. *Nature Neuroscience*, *18*, 1364–1375. https://doi.org/10.1038/nn.4115

Cohen, S., & Janicki-Deverts, D. (2012). Who's stressed? Distributions of psychological stress in the united states in probability samples from 1983, 2006, and 2009 1. *Journal of Applied Social Psychology*, *42*, 1320–1334.

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

Cohen, S., Kamarck, T., & Mermelstein, R. (1994). Perceived stress scale. In S. Cohen, R. C. Kessler, & L. U. Gordon (Eds.), *Measuring stress: A guide for health and social scientists* (pp. 235–283). Oxford University Press.

Coppieters, I., Meeus, M., Kregel, J., Caeyenberghs, K., De Pauw, R., Goubert, D., & Cagnie, B. (2016). Relations between brain alterations and clinical pain measures in chronic musculoskeletal pain: A systematic review. *The Journal of Pain*, *17*, 949–962. https://doi.org/10.1016/j.jpain.2016.04.005

Crawford, J. R., & Henry, J. D. (2004). The positive and negative affect schedule (PANAS): Construct validity, measurement properties and normative data in a large non-clinical sample. *The British Journal of Clinical Psychology*, *43*, 245–265. https://doi.org/10.1348/0144665031752934

Da Silva, J. T., Tricou, C., Zhang, Y., Seminowicz, D. A., & Ro, J. Y. (2020). Brain networks and endogenous pain inhibition are modulated by age and sex in healthy rats. *Pain*, *161*, 1371–1380. https://doi.org/10.1097/j.pain.0000000000001810

Davidson, R. J. (2002). Anxiety and affective style: Role of prefrontal cortex and amygdala. *Biological Psychiatry*, *51*, 68–80. https://doi.org/10.1016/s0006-3223(01)01328-2

Davidson, R. J., & McEwen, B. S. (2012). Social influences on neuroplasticity: Stress and interventions to promote well-being. *Nature Neuroscience*, *15*, 689–695. https://doi.org/10.1038/nn.3093

Davis, D. A., Ghantous, M. E., Farmer, M. A., Baria, A. T., & Apkarian, A. V. (2016). Identifying brain nociceptive information transmission in patients with chronic somatic pain. *PAIN Reports*, *1*, e575. https://doi.org/10.1097/pr9.0000000000000575

Dowdy, S. W., Dwyer, K. A., Smith, C. A., & Wallston, K. A. (1996). Gender and psychological well-being of persons with rheumatoid arthritis. *Arthritis Care & Research*, *9*, 449–456. https://doi.org/10.1002/art.1790090606

Driban, J. B., Morgan, N., Price, L. L., Cook, K. F., & Wang, C. (2015). Patient-Reported Outcomes Measurement Information System (PROMIS) instruments among individuals with symptomatic knee osteoarthritis: A cross-sectional study of floor/ceiling effects and construct validity. *BMC Musculoskeletal Disorders*, *16*, 253. https://doi.org/10.1186/s12891-015-0715-y

Dufouil, C., Beiser, A., McLure, L. A., Wolf, P. A., Tzourio, C., Howard, V. J., Westwood, A. J., Himali, J. J., Sullivan, L., Aparicio, H. J., Kelly-Hayes, M., Ritchie, K., Kase, C. S., Pikula, A., Romero, J. R., D'Agostino, R. B., Samieri, C., Vasan, R. S., Chêne, G.., … Seshadri, S. (2017). Revised framingham stroke risk profile to reflect temporal trends. *Circulation*, *135*, 1145–1159. https://doi.org/10.1161/circulationaha.115.021275

Dworkin, R. H., Turk, D. C., Revicki, D. A., Harding, G., Coyne, K. S., Peirce-Sandner, S., Bhagwat, D., Everton, D., Burke, L. B., Cowan, P., Farrar, J. T., Hertz, S., Max, M. B., Rappaport, B. A., & Melzack, R.. (2009). Development and initial validation of an expanded and revised version of the Short-form McGill Pain Questionnaire (SF-MPQ-2). *Pain*, *144*, 35–42. https://doi.org/10.1016/j.pain.2009.02.007

Edmiston, E. E., Wang, F., Mazure, C. M., Guiney, J., Sinha, R., Mayes, L. C., & Blumberg, H. P. (2011). Corticostriatal-limbic gray matter morphology in adolescents with self-reported exposure to childhood maltreatment. *Archives of Pediatrics & Adolescent Medicine*, *165*(12), 1069–1077. http://dx.doi.org/10.1001/archpediatrics.2011.565

Edwards, R. R., Dworkin, R. H., Sullivan, M. D., Turk, D. C., & Wasan, A. D. (2016). The role of psychosocial processes in the development and maintenance of chronic pain. *Journal of Pain*, *17*, T70–T92. https://doi.org/10.1016/j.jpain.2016.01.001

Eisenberger, N. I. (2012). The pain of social disconnection: Examining the shared neural underpinnings of physical and social pain. *Nature Reviews Neuroscience*, *13*, 421–434. https://doi.org/10.1038/nrn3231

Eisenberger, N. I., Taylor, S. E., Gable, S. L., Hilmert, C. J., & Lieberman, M. D. (2007). Neural pathways link social support to attenuated neuroendocrine stress responses. *NeuroImage*, *35*, 1601–1612. https://doi.org/10.1016/j.neuroimage.2007.01.038

El-Shormilisy, N., Strong, J., & Meredith, P. J. (2015). Associations between gender, coping patterns and functioning for individuals with chronic pain: A systematic review. *Pain Research and Management*, *20*, 48–55. https://doi.org/10.1155/2015/490610

Epel, E. S. (2020). The geroscience agenda: Toxic stress, hormetic stress, and the rate of aging. *Ageing Research Reviews*, *63*, 101167. https://doi.org/10.1016/j.arr.2020.101167

Epel, E. S., Blackburn, E. H., Lin, J., Dhabhar, F. S., Adler, N. E., Morrow, J. D., & Cawthon, R. M.. (2004). Accelerated telomere shortening in response to life stress. *Proceedings of the National Academy of Sciences of the United States of America*, *101*, 17312–17315. https://doi.org/10.1073/pnas.0407162101

Ezzati, A., Jiang, J., Katz, M. J., Sliwinski, M. J., Zimmerman, M. E., & Lipton, R. B. (2014). Validation of the Perceived Stress Scale in a community sample of older adults. *International Journal of Geriatric Psychiatry*, *29*, 645–652. https://doi.org/10.1002/gps.4049

Ferreira, V. M., & Sherman, A. M. (2007). The relationship of optimism, pain and social support to well-being in older adults with osteoarthritis. *Aging & Mental Health*, *11*, 89–98. https://doi.org/10.1080/13607860600736166

Fischl, B., Salat, D. H., Busa, E., Albert, M., Dieterich, M., Haselgrove, C., van der Kouwe, A., Killiany, R., Kennedy, D., Klaveness, S., Montillo, A., Makris, N., Rosen, B., & Dale, A. M. (2002). Whole brain segmentation. *Neuron*, *33*(3), 341–355. http://dx.doi.org/10.1016/s0896-6273(02)00569-x

Fischl, B., van der Kouwe, A., Destrieux, C., Halgren, E., Segonne, F., Salat, D. H., Busa, E., Seidman, L. J., Goldstein, J., Kennedy, D., Caviness, V., Makris, N., Rosen, B., & Dale, A. M. (2004). Automatically parcellating the human cerebral cortex. *Cerebral Cortex*, *14*(1), 11–22. http://dx.doi.org/10.1093/cercor/bhg087

Fischl, B. (2012). FreeSurfer. *NeuroImage*, *62*, 774–781. https://doi.org/10.1016/j.neuroimage.2012.01.021

Fischl, B., & Dale, A. M. (2000). Measuring the thickness of the human cerebral cortex from magnetic resonance images. *Proceedings of the National Academy of Sciences of the United States of America*, *97*, 11050–11055. https://doi.org/10.1073/pnas.200033797

Fischl, B., Salat, D. H., van der Kouwe, A. J. W., Makris, N., Ségonne, F., Quinn, B. T., & Dale, A. M. (2004). Sequence-independent segmentation of magnetic resonance images. *NeuroImage*, *23*, S69–S84. https://doi.org/10.1016/j.neuroimage.2004.07.016

Gandhi, W., Rosenek, N. R., Harrison, R., & Salomons, T. V. (2020). Functional connectivity of the amygdala is linked to individual differences in emotional pain facilitation. *Pain*, *161*, 300–307. https://doi.org/10.1097/j.pain.0000000000001714

Geneen, L. J., Moore, R. A., Clarke, C., Martin, D., Colvin, L. A., & Smith, B. H.. (2017). Physical activity and exercise for chronic pain in adults: An overview of Cochrane Reviews. *Cochrane Database Systematic Review*, *4*, CD011279. https://doi.org/10.1002/14651858.CD011279.pub3

Gotink, R. A., Vernooij, M. W., Ikram, M. A., Niessen, W. J., Krestin, G. P., Hofman, A., Tiemeier, H., & Hunink, M. G. M.. (2018). Meditation and yoga practice are associated with smaller right amygdala volume: The Rotterdam study. *Brain Imaging and Behavior*, *12*, 1631–1639. https://doi.org/10.1007/s11682-018-9826-z

Gruene, T. M., Roberts, E., Thomas, V., Ronzio, A., & Shansky, R. M. (2015). Sex-specific neuroanatomical correlates of fear expression in prefrontal-amygdala circuits. *Biological Psychiatry*, *78*, 186–193. https://doi.org/10.1016/j.biopsych.2014.11.014

Gupta, A., Love, A., Kilpatrick, L. A., Labus, J. S., Bhatt, R., Chang, L., Tillisch, K., Naliboff, B., & Mayer, E. A.. (2017). Morphological brain measures of cortico-limbic inhibition related to resilience. *Journal of Neuroscience Research*, *95*, 1760–1775. https://doi.org/10.1002/jnr.24007

Gwilym, S. E., Filippini, N., Douaud, G., Carr, A. J., & Tracey, I. (2010). Thalamic atrophy associated with painful osteoarthritis of the hip is reversible after arthroplasty: A longitudinal voxel-based morphometric study. *Arthritis and Rheumatism*, *62*, 2930–2940. https://doi.org/10.1002/art.27585

Hamann, S. (2005). Sex differences in the responses of the human amygdala. *Neuroscientist*, *11*, 288–293. https://doi.org/10.1177/1073858404271981

Han, S. (2015). Understanding cultural differences in human behavior: A cultural neuroscience approach. *Current Opinion in Behavioral Sciences*, *3*, 68–72. https://doi.org/10.1016/j.cobeha.2015.01.013

Han, X., Jovicich, J., Salat, D., van der Kouwe, A., Quinn, B., Czanner, S., Busa, E., Pacheco, J., Albert, M., Killiany, R., Maguire, P., Rosas, D., Makris, N., Dale, A., Dickerson, B., & Fischl, B.. (2006). Reliability of MRI-derived measurements of human cerebral cortical thickness: The effects of field strength, scanner upgrade and manufacturer. *NeuroImage*, *32*, 180–194. https://doi.org/10.1016/j.neuroimage.2006.02.051

Hashmi, J. A., Baliki, M. N., Huang, L., Baria, A. T., Torbey, S., Hermann, K. M., Schnitzer, T. J., & Apkarian, A. V.. (2013). Shape shifting pain: Chronification of back pain shifts brain representation from nociceptive to emotional circuits. *Brain*, *136*, 2751–2768. https://doi.org/10.1093/brain/awt211

Hassett, A. L., Epel, E., Clauw, D. J., Harris, R. E., Harte, S. E., Kairys, A., Buyske, S., & Williams, D. A.. (2012). Pain is associated with short leukocyte telomere length in women with fibromyalgia. *Journal of Pain*, *13*, 959–969. https://doi.org/10.1016/j.jpain.2012.07.003

Hassett, A. L., & Finan, P. H. (2016). The role of resilience in the clinical management of chronic pain. *Current Pain and Headache Reports*, *20*, 39. https://doi.org/10.1007/s11916-016-0567-7

Hassett, A. L., Simonelli, L. E., Radvanski, D. C., Buyske, S., Savage, S. V., & Sigal, L. H. (2008). The relationship between affect balance style and clinical outcomes in fibromyalgia. *Arthritis and Rheumatism*, *59*, 833–840. https://doi.org/10.1002/art.23708

Haukka, E., Ojajärvi, A., Kaila-Kangas, L., & Leino-Arjas, P. (2017). Protective determinants of sickness absence among employees with multisite pain—A 7-year follow-up. *Pain*, *158*, 220–229. https://doi.org/10.1097/j.pain.0000000000000741

Hemington, K. S., Rogachov, A., Cheng, J. C., Bosma, R. L., Kim, J. A., Osborne, N. R., Inman, R. D., & Davis, K. D. (2018). Patients with chronic pain exhibit a complex relationship triad between pain, resilience, and within- and cross-network functional connectivity of the default mode network. *Pain*, *159*, 1621–1630. https://doi.org/10.1097/j.pain.0000000000001252

Hölzel, B. K., Carmody, J., Evans, K. C., Hoge, E. A., Dusek, J. A., Morgan, L., Pitman, R. K., & Lazar, S. W. (2010). Stress reduction correlates with structural changes in the amygdala. *Social Cognitive and Affective Neuroscience*, *5*, 11–17. https://doi.org/10.1093/scan/nsp034

Horn, S. R., Charney, D. S., & Feder, A. (2016). Understanding resilience: New approaches for preventing and treating PTSD. *Experimental Neurology*, *284*, 119–132. https://doi.org/10.1016/j.expneurol.2016.07.002

Hoy, D. T., March, L., Brooks, P., Blyth, F., Woolf, A., Bain, C., Williams, G., Smith, E., Vos, T., Barendregt, J., Murray, C., Burstein, R., & Buchbinder, R.. (2014). The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. *Annals of the Rheumatic Diseases*, *73*(6), 968–974. https://doi.org/10.1136/annrheumdis-2013-204428

Hua, T., Chen, B., Lu, D., Sakurai, K., Zhao, S., Han, B.-X., Kim, J., Yin, L., Chen, Y., Lu, J., & Wang, F.. (2020). General anesthetics activate a potent central pain-suppression circuit in the amygdala. *Nature Neuroscience*, *23*(7), 854–868. https://doi.org/10.1038/s41593-020-0632-8

Ioannidis, K., Askelund, A. D., Kievit, R. A., & Van Harmelen, A.-L. (2020). The complex neurobiology of resilient functioning after childhood maltreatment. *BMC Medicine*, *18*, 32https://doi.org/10.1186/s12916-020-1490-7

Johnson, A. C., & Greenwood-Van Meerveld, B. (2014). Stress-induced pain: A target for the development of novel therapeutics. *Journal of Pharmacology and Experimental Therapeutics*, *351*, 327–335. https://doi.org/10.1124/jpet.114.218065

Johnson, A. J., Terry, E., Bartley, E. J., Garvan, C., Cruz-Almeida, Y., Goodin, B., Glover, T. L., Staud, R., Bradley, L. A., Fillingim, R. B., & Sibille, K. T. (2019). Resilience factors may buffer cellular aging in individuals with and without chronic knee pain. *Molecular Pain*, *15*, 1744806919842962. https://doi.org/10.1177/1744806919842962

Karoly, P., & Ruehlman, L. S. (2006). Psychological, "resilience" and its correlates in chronic pain: Findings from a national community sample. *Pain*, *123*, 90–97. https://doi.org/10.1016/j.pain.2006.02.014

Kautz, M., Charney, D. S., & Murrough, J. W. (2017). Neuropeptide Y, resilience, and PTSD therapeutics. *Neuroscience Letters*, *649*, 164–169. https://doi.org/10.1016/j.neulet.2016.11.061

Kim, H. J., Greenspan, J. D., Ohrbach, R., Fillingim, R. B., Maixner, W., Renn, C. L., Johantgen, M., Zhu, S., & Dorsey, S. G.. (2019). Racial/ethnic differences in experimental pain sensitivity and associated factors—Cardiovascular responsiveness and psychological status. *PLoS ONE*, *14*, e0215534. https://doi.org/10.1371/journal.pone.0215534

Klein, A., & Tourville, J. (2012). 101 labeled brain images and a consistent human cortical labeling protocol. *Frontiers in Neuroscience*, *6*, 171. https://doi.org/10.3389/fnins.2012.00171

Kogler, L., Müller, V. I., Seidel, E.-M., Boubela, R., Kalcher, K., Moser, E., Habel, U., Gur, R. C., Eickhoff, S. B., & Derntl, B.. (2016). Sex differences in the functional connectivity of the amygdalae in association with cortisol. *NeuroImage*, *134*, 410–423. https://doi.org/10.1016/j.neuroimage.2016.03.064

Kong, F., Ma, X., You, X., & Xiang, Y. (2018). The resilient brain: Psychological resilience mediates the effect of amplitude of

low-frequency fluctuations in orbitofrontal cortex on subjective well-being in young healthy adults. *Social Cognitive and Affective Neuroscience*, *13*, 755–763. https://doi.org/10.1093/scan/nsy045

Kong, F., Wang, X., Hu, S., & Liu, J. (2015). Neural correlates of psychological resilience and their relation to life satisfaction in a sample of healthy young adults. *NeuroImage*, *123*, 165–172. https://doi.org/10.1016/j.neuroimage.2015.08.020

Kroenke, K., Yu, Z., Wu, J., Kean, J., & Monahan, P. O. (2014). Operating characteristics of PROMIS four-item depression and anxiety scales in primary care patients with chronic pain. *Pain Medicine*, *15*, 1892–1901. https://doi.org/10.1111/pme.12537

Kuchinad, A., Schweinhardt, P., Seminowicz, D. A., Wood, P. B., Chizh, B. A., & Bushnell, M. C.. (2007). Accelerated brain gray matter loss in fibromyalgia patients: Premature aging of the brain? *Journal of Neuroscience*, *27*, 4004–4007. https://doi.org/10.1523/jneurosci.0098-07.2007

Kutch, J. J., Ichesco, E., Hampson, J. P., Labus, J. S., Farmer, M. A., Martucci, K. T., Ness, T. J., Deutsch, G., Apkarian, A. V., Mackey, S. C., Klumpp, D. J., Schaeffer, A. J., Rodriguez, L. V., Kreder, K. J., Buchwald, D., Andriole, G. L., Lai, H. H., Mullins, C., Kusek, J. W., … Harris, R. E.. (2017). Brain signature and functional impact of centralized pain: A multidisciplinary approach to the study of chronic pelvic pain (MAPP) network study. *Pain*, *158*, 1979–1991. https://doi.org/10.1097/j.pain.0000000000001001

Lambert, V. A., Lambert, C. E., Klipple, G. L., & Mewshaw, E. A. (1990). Relationships among hardiness, social support, severity of illness, and psychological well-being in women with rheumatoid arthritis. *Health Care for Women International*, *11*, 159–173. https://doi.org/10.1080/07399339009515886

Lee, J. E., Kahana, B., & Kahana, E. (2016). Social support and cognitive functioning as resources for elderly persons with chronic arthritis pain. *Aging & Mental Health*, *20*, 370–379. https://doi.org/10.1080/13607863.2015.1013920

Letzen, J. E., Mun, C. J., Kuwabara, H., Burton, E. F., Boring, B. L., Walls, T., Speed, T. J., Wong, D. F., & Campbell, C. M.. (2020). Ethnic disparities in pain processing among healthy adults: μ-opioid receptor binding potential as a putative mechanism. *Pain*, *161*, 810–820. https://doi.org/10.1097/j.pain.0000000000001759

Lewis, G. N., Parker, R. S., Sharma, S., Rice, D. A., & McNair, P. J. (2018). Structural brain alterations before and after total knee arthroplasty: A longitudinal assessment. *Pain Medicine*, *19*, 2166–2176. https://doi.org/10.1093/pm/pny108

Li, H.-J., Sun, J.-Z., Zhang, Q.-L., Wei, D.-T., Li, W.-F., Jackson, T., Hitchman, G., & Qiu, J.. (2014). Neuroanatomical differences between men and women in help-seeking coping strategy. *Scientific Reports*, *4*, 5700. https://doi.org/10.1038/srep05700

Lindstrom, J., & Tuomilehto, J. (2003). The Diabetes Risk Score: A practical tool to predict type 2 diabetes risk. *Diabetes Care*, *26*, 725–731. https://doi.org/10.2337/diacare.26.3.725

Linnman, C., Beucke, J. C., Jensen, K. B., Gollub, R. L., & Kong, J. (2012). Sex similarities and differences in pain-related periaqueductal gray connectivity. *Pain*, *153*, 444–454. https://doi.org/10.1016/j.pain.2011.11.006

Liu, J. J. W., Reed, M., & Girard, T. A. (2017). Advancing resilience: An integrative, multi-system model of resilience. *Personality and Individual Differences*, *111*, 111–118. https://doi.org/10.1016/j.paid.2017.02.007

López-Martínez, A. E., Esteve-Zarazaga, R., & Ramírez-Maestre, C. (2008). Perceived social support and coping responses are independent variables explaining pain adjustment among chronic pain patients. *Journal of Pain*, *9*, 373–379. https://doi.org/10.1016/j.jpain.2007.12.002

Losin, E. A. R., Woo, C.-W., Medina, N. A., Andrews-Hanna, J. R., Eisenbarth, H., & Wager, T. D. (2020). Neural and sociocultural mediators of ethnic differences in pain. *Nature Human Behaviour*, *4*, 517–530. https://doi.org/10.1038/s41562-020-0819-8

Luby, J., Belden, A., Botteron, K., Marrus, N., Harms, M. P., Babb, C., Nishino, T., & Barch, D.. (2013). The effects of poverty on childhood brain development: The mediating effect of caregiving and stressful life events. *JAMA Pediatrics*, *167*, 1135–1142. https://doi.org/10.1001/jamapediatrics.2013.3139

Lupien, S. J., McEwen, B. S., Gunnar, M. R., & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nature Reviews Neuroscience*, *10*, 434–445. https://doi.org/10.1038/nrn2639

Macdonald, G., & Leary, M. R. (2005). Why does social exclusion hurt? The relationship between social and physical pain. *Psychological Bulletin*, *131*, 202–223. https://doi.org/10.1037/0033-2909.131.2.202

Macfarlane, G. J., Barnish, M. S., & Jones, G. T. (2017). Persons with chronic widespread pain experience excess mortality: Longitudinal results from UK Biobank and meta-analysis. *Annals of the Rheumatic Diseases*, *76*, 1815–1822. https://doi.org/10.1136/annrheumdis-2017-211476

Maleki, N., Becerra, L., Brawn, J., McEwen, B., Burstein, R., & Borsook, D.. (2013). Common hippocampal structural and functional changes in migraine. *Brain Structure and Function*, *218*, 903–912. https://doi.org/10.1007/s00429-012-0437-y

Marinescu, R. V., Eshaghi, A., Alexander, D. C., & Golland, P. (2019). BrainPainter: A software for the visualisation of brain structures, biomarkers and associated pathological processes. In D. Zhu, J. Yan, H. Huang, L. Shen, P. M. Thompson, C.-F. Westin, X. Pennec, S. Joshi, M. Nielsen, T. Fletcher, S. Durrleman, & S. Sommer (Eds.), *Multimodal brain image analysis and mathematical foundations of computational anatomy* (pp. 112–120). Springer.

Master, S. L., Eisenberger, N. I., Taylor, S. E., Naliboff, B. D., Shirinyan, D., & Lieberman, M. D.. (2009). A picture's worth: Partner photographs reduce experimentally induced pain. *Psychological Science*, *20*, 1316–1318. https://doi.org/10.1111/j.1467-9280.2009.02444.x

May, A. (2011). Structural brain imaging: A window into chronic pain. *Neuroscientist*, *17*, 209–220. https://doi.org/10.1177/1073858410396220

McBeth, J., Symmons, D. P., Silman, A. J., Allison, T., Webb, R., Brammah, T., & Macfarlane, G. J. (2008). Musculoskeletal pain is associated with a long-term increased risk of cancer and cardiovascular-related mortality. *Rheumatology*, *48*, 74–77. https://doi.org/10.1093/rheumatology/ken424

McEwen, B. S. (2003). Mood disorders and allostatic load. *Biological Psychiatry*, *54*, 200–207. https://doi.org/10.1016/s0006-3223(03)00177-x

McEwen, B. S. (2010). Stress, sex, and neural adaptation to a changing environment: Mechanisms of neuronal remodeling. *Annals of the New York Academy of Sciences*, *1204*(Suppl.), E38–E59. https://doi.org/10.1111/j.1749-6632.2010.05568.x

McEwen, B. S. (2016). In pursuit of resilience: Stress, epigenetics, and brain plasticity. *Annals of the New York Academy of Sciences*, *1373*, 56–64. https://doi.org/10.1111/nyas.13020

McEwen, B. S. (2017). Neurobiological and systemic effects of chronic stress. *Chronic Stress*, *1*. https://doi.org/10.1177/2470547017692328

McEwen, B. S. (2019). What is the confusion with cortisol? *Chronic Stress*, *3*. https://doi.org/10.1177/2470547019833647

McEwen, B. S., & Milner, T. A. (2017). Understanding the broad influence of sex hormones and sex differences in the brain. *Journal of Neuroscience Research*, *95*, 24–39. https://doi.org/10.1002/jnr.23809

McIlvane, J. M. (2007). Disentangling the effects of race and SES on arthritis-related symptoms, coping, and well-being in African American and White women. *Aging & Mental Health*, *11*, 556–569. https://doi.org/10.1080/13607860601086520

Messier, S. P., Mihalko, S. L., Legault, C., Miller, G. D., Nicklas, B. J., DeVita, P., Beavers, D. P., Hunter, D. J., Lyles, M. F., Eckstein, F., Williamson, J.

D., Carr, J. J., Guermazi, A., & Loeser, R. F.. (2013). Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: The IDEA randomized clinical trial. *JAMA*, *310*, 1263–1273. https://doi.org/10.1001/jama.2013.277669

Mickle, A. M., Garvan, C., Service, C., Pop, R., Marks, J., Wu, S., Edberg, J. C., Staud, R., Fillingim, R. B., Bartley, E. J., & Sibille, K. T. (2020). Relationships between pain, life stress, sociodemographics, and cortisol: contributions of pain intensity and financial satisfaction. *Chronic Stress*, *4*, 247054702097575. http://dx.doi.org/10.1177/2470547020975758

Mills, S. E. E., Nicolson, K. P., & Smith, B. H. (2019). Chronic pain: A review of its epidemiology and associated factors in population-based studies. *British Journal of Anaesthesia*, *123*, e273–e283. https://doi.org/10.1016/j.bja.2019.03.023

Monticone, M., Ferrante, S., Giorgi, I., Galandra, C., Rocca, B., & Foti, C. (2014). The 27-item coping strategies questionnaire-revised: Confirmatory factor analysis, reliability and validity in Italian-speaking subjects with chronic pain. *Pain Research & Management*, *19*, 153–158. https://doi.org/10.1155/2014/956828

Myers, H. F. (2009). Ethnicity- and socio-economic status-related stresses in context: An integrative review and conceptual model. *Journal of Behavioral Medicine*, *32*, 9–19. https://doi.org/10.1007/s10865-008-9181-4

Neugebauer, V., Mazzitelli, M., Cragg, B., Ji, G., Navratilova, E., & Porreca, F. (2020). Amygdala, neuropeptides, and chronic pain-related affective behaviors. *Neuropharmacology*, *170*, 108052. https://doi.org/10.1016/j.neuropharm.2020.108052

Newton-John, T. R. O., Mason, C., & Hunter, M. (2014). The role of resilience in adjustment and coping with chronic pain. *Rehabilitation Psychology*, *59*, 360–365. https://doi.org/10.1037/a0037023

Nickson, C., Procopio, P., Velentzis, L. S., Carr, S., Devereux, L., Mann, G. B., James, P., Lee, G., Wellard, C., & Campbell, I.. (2018). Prospective validation of the NCI Breast Cancer Risk Assessment Tool (Gail Model) on 40,000 Australian women. *Breast Cancer Research*, *20*, 155. https://doi.org/10.1186/s13058-018-1084-x

Ong, A. D., Thoemmes, F., Ratner, K., Ghezzi-Kopel, K., & Reid, M. C. (2020). Positive affect and chronic pain. *Pain*, *161*(6), 1140–1149. https://doi.org/10.1097/j.pain.0000000000001828

Ong, A. D., Zautra, A. J., & Reid, M. C. (2010). Psychological resilience predicts decreases in pain catastrophizing through positive emotions. *Psychology and Aging*, *25*, 516–523. https://doi.org/10.1037/a0019384

Osman, A., Lamis, D. A., Freedenthal, S., Gutierrez, P. M., & McNaughton-Cassill, M. (2014). The multidimensional scale of perceived social support: Analyses of internal reliability, measurement invariance, and correlates across gender. *Journal of Personality Assessment*, *96*, 103–112. https://doi.org/10.1080/00223891.2013.838170

Osório, C., Probert, T., Jones, E., Young, A. H., & Robbins, I. (2017). Adapting to stress: Understanding the neurobiology of resilience. *Behavioral Medicine*, *43*, 307–322. https://doi.org/10.1080/08964289.2016.1170661

Pagliaccio, D., Luby, J. L., Bogdan, R., Agrawal, A., Gaffrey, M. S., Belden, A. C., Botteron, K. N., Harms, M. P., & Barch, D. M.. (2015). Amygdala functional connectivity, HPA axis genetic variation, and life stress in children and relations to anxiety and emotion regulation. *Journal of Abnormal Psychology*, *124*, 817–833. https://doi.org/10.1037/abn0000094

Palmer, R. C., Ismond, D., Rodriquez, E. J., & Kaufman, J. S. (2019). Social determinants of health: Future directions for health disparities research. *American Journal of Public Health*, *109*, S70–S71. https://doi.org/10.2105/ajph.2019.304964

Puterman, E., & Epel, E. (2012). An intricate dance: Life experience, multisystem resiliency, and rate of telomere decline throughout the lifespan. *Social and Personality Psychology Compass*, *6*, 807–825. https://doi.org/10.1111/j.1751-9004.2012.00465.x

Resnick, B. (2014). Resilience in older adults. *Topics in Geriatric Rehabilitation*, *30*, 155–163. https://doi.org/10.1097/TGR.0000000000000024

Reuter, M., Schmansky, N. J., Rosas, H. D., & Fischl, B. (2012). Within-subject template estimation for unbiased longitudinal image analysis. *NeuroImage*, *61*, 1402–1418. https://doi.org/10.1016/j.neuroimage.2012.02.084

Riley, J. L., 3rd, & Robinson, M. E. (1997). CSQ: Five factors or fiction? *Clinical Journal of Pain*, *13*, 156–162.

Riley, J. L. I., Robinson, M. E., & Geisser, M. E. (1999). Empirical subgroups of the coping strategies questionnaire-revised: A MULTISAMPLE STUdy. *The Clinical Journal of Pain*, *15*, 111–116.

Rizzo, G., Milardi, D., Bertino, S., Basile, G. A., Di Mauro, D., Calamuneri, A., Chillemi, G., Silvestri, G., Anastasi, G., Bramanti, A., & Cacciola, A. (2018). The limbic and sensorimotor pathways of the human amygdala: A structural connectivity study. *Neuroscience*, *385*, 166–180. https://doi.org/10.1016/j.neuroscience.2018.05.051

Robinson, M. E., Riley, J. L., Myers, C. D., Sadler, I. J., Kvaal, S. A., Geisser, M. E., & Keefe, F. J.. (1997). The Coping Strategies Questionnaire: A large sample, item level factor analysis. *Clinical Journal of Pain*, *13*, 43–49. https://doi.org/10.1097/00002508-199703000-00007

Rodriguez-Raecke, R., Niemeier, A., Ihle, K., Ruether, W., & May, A. (2009). Brain gray matter decrease in chronic pain is the consequence and not the cause of pain. *Journal of Neuroscience*, *29*, 13746–13750. https://doi.org/10.1523/JNEUROSCI.3687-09.2009

Rodriguez-Raecke, R., Niemeier, A., Ihle, K., Ruether, W., & May, A. (2013). Structural brain changes in chronic pain reflect probably neither damage nor atrophy. *PLoS ONE*, *8*, e54475. https://doi.org/10.1371/journal.pone.0054475

Romeo, R. D. (2017). The impact of stress on the structure of the adolescent brain: Implications for adolescent mental health. *Brain Research*, *1654*, 185–191. https://doi.org/10.1016/j.brainres.2016.03.021

Rosenstiel, A. K., & Keefe, F. J. (1983). The use of coping strategies in chronic low back pain patients: Relationship to patient characteristics and current adjustment. *Pain*, *17*, 33–44. https://doi.org/10.1016/0304-3959(83)90125-2

Rovner, G. S., Sunnerhagen, K. S., Björkdahl, A., Gerdle, B., Börsbo, B., Johansson, F., & Gillanders, D.. (2017). Chronic pain and sex-differences; women accept and move, while men feel blue. *PLoS ONE*, *12*, e0175737. https://doi.org/10.1371/journal.pone.0175737

Russo, S. J., Murrough, J. W., Han, M.-H., Charney, D. S., & Nestler, E. J. (2012). Neurobiology of resilience. *Nature Neuroscience*, *15*, 1475–1484. https://doi.org/10.1038/nn.3234

Salat, D. H., Buckner, R. L., Snyder, A. Z., Greve, D. N., Desikan, R. S. R., Busa, E., Morris, J. C., Dale, A. M., & Fischl, B. (2004). Thinning of the Cerebral Cortex in Aging. *Cerebral Cortex*, *14*(7), 721–730. http://dx.doi.org/10.1093/cercor/bhh032

Sambuco, N., Bradley, M., Herring, D., Hillbrandt, K., & Lang, P. J. (2020). Transdiagnostic trauma severity in anxiety and mood disorders: Functional brain activity during emotional scene processing. *Psychophysiology*, *57*, e13349. https://doi.org/10.1111/psyp.13349

Saygin, Z. M., Osher, D. E., Augustinack, J., Fischl, B., & Gabrieli, J. D. E. (2011). Connectivity-based segmentation of human amygdala nuclei using probabilistic tractography. *NeuroImage*, *56*, 1353–1361. https://doi.org/10.1016/j.neuroimage.2011.03.006

Scheier, M. F., Carver, C. S., & Bridges, M. W. (1994). Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): A reevaluation of the Life Orientation Test. *Journal of Personality and Social Psychology*, *67*, 1063–1078. https://doi.org/10.1037/0022-3514.67.6.1063

Schou-Bredal, I., Heir, T., Skogstad, L., Bonsaksen, T., Lerdal, A., Grimholt, T., & Ekeberg, Ø. (2017). Population-based norms of the Life Orientation Test-Revised (LOT-R). *International Journal of Clinical and Health Psychology*, *17*, 216–224. https://doi.org/10.1016/j.ijchp.2017.07.005

Sibille, K. T., Chen, H., Bartley, E. J., Riley, J., Glover, T. L., King, C. D., Zhang, H., Cruz-Almeida, Y., Goodin, B. R., Sotolongo, A., Petrov, M. E., Herbert, M., Bulls, H. W., Edberg, J. C., Staud, R., Redden, D., Bradley, L. A., & Fillingim, R. B. (2017). Accelerated aging in adults with knee osteoarthritis pain: consideration for frequency, intensity, time, and total pain sites. *PAIN Reports*, *2*(3), e591. http://dx.doi.org/10.1097/pr9.0000000000000591

Sibille, K. T., Kindler, L. L., Glover, T. L., Staud, R., Riley, J. L., & Fillingim, R. B. (2012). Affect balance style, experimental pain sensitivity, and pain-related responses. *The Clinical Journal of Pain*, *28*, 410–417. https://doi.org/10.1097/AJP.0b013e3182324799

Sibille, K. T., King, C., Garrett, T. J., Glover, T. L., Zhang, H., Chen, H., Reddy, D., Goodin, B. R., Sotolongo, A., Petrov, M. E., Cruz-Almeida, Y., Herbert, M., Bartley, E. J., Edberg, J. C., Staud, R., Redden, D. T., Bradley, L. A., & Fillingim, R. B.. (2018). Omega-6: Omega-3 PUFA ratio, pain, functioning, and distress in adults with knee pain. *The Clinical Journal of Pain*, *34*, 182–189. https://doi.org/10.1097/AJP.0000000000000517

Sibille, K. T., Langaee, T., Burkley, B., Gong, Y., Glover, T. L., King, C., Riley, J. L., Leeuwenburgh, C., Staud, R., Bradley, L. A., & Fillingim, R. B. (2012). Chronic pain, perceived stress, and cellular aging: An exploratory study. *Molecular Pain*, *8*, 12. https://doi.org/10.1186/1744-8069-8-12

Sibille, K. T., Steingrímsdóttir, Ó. A., Fillingim, R. B., Stubhaug, A., Schirmer, H., Chen, H., McEwen, B. S., & Nielsen, C. S. (2016). Investigating the burden of chronic pain: An inflammatory and metabolic composite. *Pain Research and Management*, *2016*, 1–11. https://doi.org/10.1155/2016/7657329

Sibille, K. T., Witek-Janusek, L., Mathews, H. L., & Fillingim, R. B. (2012). Telomeres and epigenetics: Potential relevance to chronic pain. *Pain*, *153*(9), 1789–1793. http://dx.doi.org/10.1016/j.pain.2012.06.003

Silverwood, V., Blagojevic-Bucknall, M., Jinks, C., Jordan, J. L., Protheroe, J., & Jordan, K. P. (2015). Current evidence on risk factors for knee osteoarthritis in older adults: A systematic review and meta-analysis. *Osteoarthritis and Cartilage*, *23*, 507–515. https://doi.org/10.1016/j.joca.2014.11.019

Simons, L. E., Moulton, E. A., Linnman, C., Carpino, E., Becerra, L., & Borsook, D. (2014). The human amygdala and pain: Evidence from neuroimaging. *Human Brain Mapping*, *35*, 527–538. https://doi.org/10.1002/hbm.22199

Son, S. J., Park, B., Choi, J. W., Roh, H. W., Kim, N.-R., Sin, J. E., Kim, H., Lim, H. K., & Hong, C. H.. (2019). Psychological resilience enhances the orbitofrontal network in the elderly with mild cognitive impairment. *Frontiers in Psychiatry*, *10*, 615. https://doi.org/10.3389/fpsyt.2019.00615

Srikanth, V. K., Fryer, J. L., Zhai, G., Winzenberg, T. M., Hosmer, D., & Jones, G.. (2005). A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthritis and Cartilage*, *13*, 769–781. https://doi.org/10.1016/j.joca.2005.04.014

Stone, A. A., Broderick, J. E., Junghaenel, D. U., Schneider, S., & Schwartz, J. E. (2016). PROMIS fatigue, pain intensity, pain interference, pain behavior, physical function, depression, anxiety, and anger scales demonstrate ecological validity. *Journal of Clinical Epidemiology*, *74*, 194–206. https://doi.org/10.1016/j.jclinepi.2015.08.029

Strand, E. B., Zautra, A. J., Thoresen, M., Ødegård, S., Uhlig, T., & Finset, A.. (2006). Positive affect as a factor of resilience in the pain-negative affect relationship in patients with rheumatoid arthritis. *Journal of Psychosomatic Research*, *60*, 477–484. https://doi.org/10.1016/j.jpsychores.2005.08.010

Sturgeon, J. A., & Zautra, A. J. (2010). Resilience: A new paradigm for adaptation to chronic pain. *Current Pain and Headache Reports*, *14*, 105–112. https://doi.org/10.1007/s11916-010-0095-9

Terry, E. L., Tanner, J. J., Cardoso, J. S., Sibille, K. T., Lai, S., Deshpande, H., Deutsch, G., Goodin, B. R., Bradley, L. A., Price, C. C. (2020). Associations of pain catastrophizing with pain-related brain structure in individuals with or at risk for knee osteoarthritis: Sociodemographic considerations. *Brain Imaging and Behavior*, https://doi.org/10.1007/s11682-020-00372-w

Thompson, J. M., & Neugebauer, V. (2017). Amygdala plasticity and pain. *Pain Research and Management*, *2017*, 1–12. https://doi.org/10.1155/2017/8296501

Thompson, K. A., Bulls, H. W., Sibille, K. T., Bartley, E. J., Glover, T. L., Terry, E. L., Vaughn, I. A., Cardoso, J. S., Sotolongo, A., Staud, R., Hughes, L. B., Edberg, J. C., Redden, D. T., Bradley, L. A., Goodin, B. R., & Fillingim, R. B.. (2018). Optimism and psychological resilience are beneficially associated with measures of clinical and experimental pain in adults with or at risk for knee osteoarthritis. *Clinical Journal of Pain*, *34*, 1164–1172. https://doi.org/10.1097/ajp.0000000000000642

Tottenham, N., Hare, T. A., Quinn, B. T., McCarry, T. W., Nurse, M., Gilhooly, T., Millner, A., Galvan, A., Davidson, M. C., Eigsti, I.-M., Thomas, K. M., Freed, P. J., Booma, E. S., Gunnar, M. R., Altemus, M., Aronson, J., & Casey, B. (2010). Prolonged institutional rearing is associated with atypically large amygdala volume and difficulties in emotion regulation. *Developmental Science*, *13*, 46–61. https://doi.org/10.1111/j.1467-7687.2009.00852.x

Vachon-Presseau, E., Tétreault, P., Petre, B., Huang, L., Berger, S. E., Torbey, S., Baria, A. T., Mansour, A. R., Hashmi, J. A., Griffith, J. W., Comasco, E., Schnitzer, T. J., Baliki, M. N., & Apkarian, A. V.. (2016). Corticolimbic anatomical characteristics predetermine risk for chronic pain. *Brain*, *139*, 1958–1970. https://doi.org/10.1093/brain/aww100

Vartiainen, N., Perchet, C., Magnin, M., Creac'h, C., Convers, P., Nighoghossian, N., Mauguière, F., Peyron, R., & Garcia-Larrea, L.. (2016). Thalamic pain: Anatomical and physiological indices of prediction. *Brain*, *139*, 708–722. https://doi.org/10.1093/brain/awv389

Vaughn, I. A., Terry, E. L., Bartley, E. J., Schaefer, N., & Fillingim, R. B. (2019). Racial-ethnic differences in osteoarthritis pain and disability: A meta-analysis. *Journal of Pain*, *20*, 629–644. https://doi.org/10.1016/j.jpain.2018.11.012

Viniol, A., Jegan, N., Leonhardt, C., Brugger, M., Strauch, K., Barth, J., Baum, E., & Becker, A.. (2013). Differences between patients with chronic widespread pain and local chronic low back pain in primary care—A comparative cross-sectional analysis. *BMC Musculoskeletal Disorders*, *14*, 351. https://doi.org/10.1186/1471-2474-14-351

Von Korff, M., Ormel, J., Keefe, F. J., & Dworkin, S. F. (1992). Grading the severity of chronic pain. *Pain*, *50*, 133–149. https://doi.org/10.1016/0304-3959(92)90154-4

Vos, T., Barber, R. M., Bell, B., Bertozzi-Villa, A., Biryukov, S., Bolliger, I., Charlson, F., Davis, A., Degenhardt, L., Dicker, D., Duan, L., Erskine, H., Feigin, V. L., Ferrari, A. J., Fitzmaurice, C., Fleming, T., Graetz, N., Guinovart, C., Haagsma, J., … Murray, C. J. L. (2015). Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet*, *386*, 743–800. https://doi.org/10.1016/s0140-6736(15)60692-4

Wager, T. D., Phan, K. L., Liberzon, I., & Taylor, S. F. (2003). Valence, gender, and lateralization of functional brain anatomy in emotion: A meta-analysis of findings from neuroimaging. *NeuroImage*, *19*, 513–531. https://doi.org/10.1016/s1053-8119(03)00078-8

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology*, *54*, 1063–1070. https://doi.org/10.1037/0022-3514.54.6.1063

Wellman, C. L., Bangasser, D. A., Bollinger, J. L., Coutellier, L., Logrip, M. L., Moench, K. M., & Urban, K. R. (2018). Sex differences in risk and resilience: Stress effects on the neural substrates of emotion and motivation. *Journal of Neuroscience*, *38*, 9423–9432. https://doi.org/10.1523/jneurosci.1673-18.2018

World Health Organization. (2011). Waist circumference and waist-hip ratio: Report of a WHO expert consultation, Geneva, 8–11 December 2008.

Wilson, T. D., Valdivia, S., Khan, A., Ahn, H.-S., Adke, A. P., Martinez Gonzalez, S., Sugimura, Y. K., & Carrasquillo, Y.. (2019). Dual and opposing functions of the central amygdala in the modulation of pain. *Cell Reports*, *29*, 332–346.e335. https://doi.org/10.1016/j.celrep.2019.09.011

Zald, D. H. (2003). The human amygdala and the emotional evaluation of sensory stimuli. *Brain Research Reviews*, *41*, 88–123. https://doi.org/10.1016/s0165-0173(02)00248-5

Zautra, A. J., Johnson, L. M., & Davis, M. C. (2005). Positive affect as a source of resilience for women in chronic pain. *Journal of Consulting and Clinical Psychology*, *73*, 212–220. https://doi.org/10.1037/0022-006X.73.2.212

Zhang, L., Zhang, Z., Zhang, Y., Hu, G., & Chen, L. (2014). Evaluation of finnish diabetes risk score in screening undiagnosed diabetes and prediabetes among U.S. adults by gender and race: NHANES 1999–2010. *PLoS ONE*, *9*, e97865. https://doi.org/10.1371/journal.pone.0097865

Zimet, G. D., Dahlem, N. W., Zimet, S. G., & Farley, G. K. (1988). The multidimensional scale of perceived social support. *Journal of Personality Assessment*, *52*, 30–41. https://doi.org/10.1207/s15327752jpa5201_2

Zimet, G. D., Powell, S. S., Farley, G. K., Werkman, S., & Berkoff, K. A. (1990). Psychometric characteristics of the multidimensional scale of perceived social support. *Journal of Personality Assessment*, *55*, 610–617. https://doi.org/10.1207/s15327752jpa5503&4_17

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

Transparent Peer Review Report

Transparent Science Questionnaire for Authors

How to cite this article: Tanner, JJ, Johnson, AJ, Terry, EL, et al. Resilience, pain, and the brain: Relationships differ by sociodemographics. *J Neurosci Res*. 2021;99:1207–1235. https://doi.org/10.1002/jnr.24790