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No man is an island: Living in a disadvantaged neighborhood influences chronic pain development after motor vehicle collision

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ABSTRACT

Living in a lower socioeconomic status neighborhood has been shown to alter stress system function and is associated with a number of adverse health outcomes, but its influence on musculoskeletal pain (MSP) outcomes after traumatic stress exposures such as motor vehicle collision (MVC) has not been assessed. We performed a multicenter, prospective study that enrolled 948 European-American individuals within 24 hours of MVC who were discharged home after emergency department evaluation. Follow-up evaluations were completed via telephone or Internet survey 6 weeks, 6 months, and 1 year after MVC on 91%, 89%, and 91% of participants, respectively. A robust aggregate measure of census tract neighborhood disadvantage was derived, and individual-level characteristics assessed included socioeconomic and demographic characteristics, pain prior to MVC, litigation status, and opioid use. MSP was assessed in the emergency department; MSP and pain interference with daily activity were assessed at 6 weeks, 6 months, and 1 year. After adjustment for individual-level factors, living in more disadvantaged neighborhoods was associated with increased MSP ($P = 0.0009$) and increased pain interference with daily function ($P < 0.0001$). The relationship between neighborhood disadvantage and MSP was moderated by a common single nucleotide polymorphism, *rs2817038*, 5′ of the gene encoding FKBP5, a functional regulator of glucocorticoid receptor sensitivity (interaction P-value = 0.0015). These data support the hypothesis that low neighborhood socioeconomic status increases the likelihood of worse MSP outcomes after traumatic stress exposures such as MVC, and that this influence is mediated in part via its influence on stress system function.

1. Introduction

Motor vehicle collisions (MVCs) are among the most common life-threatening experiences, resulting in 50 million injuries worldwide and almost four million U.S. emergency department (ED) visits each year [44,54]. Approximately 90% of individuals presenting

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to U.S. EDs for care after MVC are discharged home after ED evaluation [46]. Persistent musculoskeletal pain (MSP) after MVC in this population is a common and costly public health problem in the US and other industrialized nations [18,24].

Available evidence suggests that individuals seen in the ED after MVC who live in a lower socioeconomic status neighborhood may experience worse pain outcomes [7,11,19,23,41]. Lower neighborhood socioeconomic status (nSES) has been associated with a range of adverse health outcomes [15,20,32–34,37,50], and studies of patients with pain conditions suggest that those living in lower socioeconomic status areas have worse pain severity and pain-related disability [7,11,19,23]. However, these studies were cross-sectional and/or had only limited ability to adjust for individual-level characteristics.

In this study, we investigated the influence of nSES on chronic MSP severity and MSP-related disability in a large cohort of European Americans enrolled in the ED in the early aftermath of MVC and followed longitudinally for 1 year. We hypothesized that individuals in low SES neighborhoods would have more severe MSP and MSP-related disability after MVC. In addition, we also hypothesized that this effect is due in part to the influence of low nSES on stress system function, and therefore, that living in a disadvantaged neighborhood environment would have a particularly deleterious effect on pain outcomes among those with stress system-related genetic vulnerability factors. We hypothesized that this is because lower nSES has been shown to cause alterations in stress system function [42,49] (eg, dysregulated cortisol levels [14,27]) and because increasing evidence indicates that stress systems are involved in the pathogenesis of persistent MSP after traumatic events such as MVC [2,6,39]. To test this hypothesis, we investigated common genetic variation in the locus of the gene coding for co-chaperone FK506 binding protein 51 (*FKBP5*), because this protein is known to influence hypothalamic-pituitary adrenal (HPA) axis function [47,59] (an important component of the stress response system), and because *FKBP5* variants have been shown to predict persistent neck and overall pain severity after MVC [6].

2. Methods

2.1. Study population and design

2.1.1. Design and setting

This prospective longitudinal study enrolled patients presenting to the ED within 24 hours of MVC. Data were collected at 8 EDs in 4 no-fault MVC litigation/insurance states (Michigan, Massachusetts, New York, and Florida) between February 2009 and October 2011. Participants were not required to reside in the enrollment state. The study was approved by the Institutional Review Boards of all participating hospitals, and each participant provided written informed consent. Complete information regarding study design, procedures, and methods has previously been described [6,40,45].

2.1.2. Participant eligibility criteria and study sites

In brief, patients aged 18 to 65 years who presented to the ED within 24 hours after an MVC and were unlikely to require hospitalization were screened for eligibility. Patients who were admitted to the hospital, had fractures other than phalangeal fractures, had more than 4 lacerations requiring sutures or a single laceration more than 20 cm in length, or had intracranial or spinal injuries were excluded. Enrollment was also limited to non-Hispanic whites (the most common ethnicity at study sites) because the study included the collection of genetic data, and genetic analyses are potentially biased by population stratification [13]. Patients who were not alert and oriented were also excluded, as were pregnant patients, prisoners, patients unable to read and understand English, patients taking a β-adrenoreceptor antagonist, or patients taking opioids above a total daily dose of 20 mg of oral morphine or equivalent.

2.2. Study procedures

Eligible and consenting participants completed ED interview evaluations regarding pre-MVC health status, the details of the MVC, and current symptoms. Research assistants conducted interviews at the time of the ED visit using a Web-based survey with explicit definitions of variables. Injury characteristics and medications administered in the ED were obtained by data extraction from the ED medical record. Follow-up time points were 6 weeks, 6 months, and 1 year after the MVC. At each follow-up, participants completed an interview online, by telephone, or via mail. Participants were compensated $50 for completing the ED interview, $60 for completing each of the 6-week and 6-month interviews, and $70 for completing the 1-year interview.

2.2.1. DNA collection and genotyping

Research assistants collected blood samples from participants at the time of enrollment using PAXgene DNA tubes. Following DNA purification (PAXgene blood DNA kit, QIAGEN, Valencia, CA, USA), genotyping was performed using the Sequenom platform (Sequenom Inc., San Diego, CA, ISA); 2 Hapmap samples and 2 repeat samples were included in each genotyping batch (96 samples) to ensure accuracy and reliability. All single nucleotide polymorphisms (SNPs) out of Hardy-Weinberg equilibrium were discarded ($P < 0.05$). Fifteen FKBP5 tag SNPs previously identified using the Tagger procedure in Haploview [3] ($r^2 \geqslant 0.8$ [12]) were selected for gene-by-environment interaction analyses.

2.2.2. Outcome variables

At each follow-up interview, participants responded to a question about their overall pain level during the week prior on a 0–10 numeric rating scale (NRS) where 0 was defined as no pain, and 10 was defined as pain "as bad as it can possibly be" [58]. Additionally, participants were asked to respond to questions from the Brief Pain Inventory (BPI) [10] about how much pain related to the MVC interfered with their daily lives during the past week. In particular, they were asked on a 0–10 NRS, where 0 is no interference and 10 is complete interference, how much this pain during the past week interfered with their general activity, mood, walking ability, normal work (including both work outside the home and housework), relations with other people, sleep, and enjoyment of life. The 7 items were summed to obtain a total interference score. Participants were also asked at each interview whether they had been seen by a physician for MVC-related complaints since their ED visit.

2.2.3. Individual-level variables

Pain during the month prior to the MVC (0–10 NRS), acute pain in the ED (0–10 NRS), and sociodemographic variables were obtained from participant self-report during the ED interview. Participant age, sex, height, weight, and opioid receipt at discharge were obtained from a medical record abstraction completed within 2 weeks of discharge. Mental health status prior to the MVC was determined from participant response in the ED to the Short-Form 12 and scored as previously described [57]. Similarly, at-risk drinking was determined from response in the ED to the TWEAK and scored as previously described [9]. Patient injuries were scored using the Abbreviated Injury Scale [1]. At each follow-up interview, participants were asked if they were working with a lawyer to pursue damages or compensation related to the MVC.