INTRODUCTION

Traumatic events are common in life. While most individuals recover following trauma exposure, a substantial proportion develop chronic posttraumatic pain (CPTP). Consistent with data from other types of pain conditions, women are at greater risk of CPTP than men.1

Previous studies suggest that the relationship between the endogenous opioid system following trauma exposure and CPTP development may differ in women vs. men.2,3

In the current prospective observational study we evaluated for potential sex differences in the relationship between CPTP development and endogenous opioid receptor expression (OPRM1, OPRD1, OPOR1) in women and men following one of the most common types of trauma exposure in industrialized nations, motor vehicle collision (MVC).

In secondary analyses, based on previous studies demonstrating that opioid receptor binding can be influenced by sex hormones4,5, we explored the relationship between opioid receptor expression and circulating 17β-estradiol levels.

METHODS

Cohort - African American (AA) individuals ≥ 18 and ≤ 65 years of age presenting to one of ten emergency departments (EDs) within 24 hours of MVC who did not have fracture or require hospital admission were enrolled. In this longitudinal study, CPTP severity (0-10 NRS) was assessed 6 weeks, 6 months, and 1 year following MVC. Exogenous opioid use in the week prior to each visit was recorded.

Statistics – The association between OPRM1, OPRD1, and OPOR1 mRNA expression levels and post-MVC CPTP development was assessed using repeated measures mixed models adjusted for age, ED study site, and exogenous opioid use. The relationship between 17β-estradiol and OPRM1 mRNA expression levels was assessed via an interaction term in the model adjusted for age and ED study site.

RESULTS

mRNA and plasma samples were obtained from study participants enrolled following MVC at 10 US Emergency Department sites across the Eastern US (Figure 1). All individuals were African American and between the ages of 18-65 (Table 1).

A significant interaction between participant sex and OPRM1, OPRD1 mRNA expression levels was observed (p = 0.039 and 0.001, respectively). In women, high expression levels of either of these opioid receptors was associated with low CPTP (Figure 2).

Women with high expression levels of both OPRM1 and OPRD1 mRNA report the least CPTP in the months following MVC (Figure 3).

Women with high circulating levels of 17β-estradiol in the early aftermath of MVC report the lowest CPTP severity 6 weeks and 1 year following MVC (Figure 4).

The lowest CPTP severity was reported by women with high levels of both OPRM1 mRNA expression and 17β-estradiol (Figure 5).

CONCLUSIONS

The results of this study suggest that opioid receptor expression levels influence CPTP outcomes differently in men and women and that the sex hormone 17β-estradiol may influence opioid receptor levels and their effect on CPTP in women following MVC.

REFERENCES


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