**Background**

Catechol-O-methyltransferase (COMT), encoded by COMT gene, is the primary enzyme that metabolizes catecholamines: COMT exists in both soluble and membrane-bound (MB-COMT) isoforms. Three haplotypes in the central haplotype of the COMT gene code for different levels of COMT enzymatic activity and influence vulnerability to persistent pain. However, two large population-based studies have failed to demonstrate an association between central haplotype COMT polymorphisms and chronic widespread pain. In addition, other studies suggest that SNPs in the distal promoter P2 (controlling MB-COMT expression) influence transcription and pain outcomes after MVC: U-shaped dose-response curve between COMT activity and post-MVC pain vulnerability. We hypothesized that interactions between three functionally important COMT loci (promoter P2, coding region, and 3′ untranslated region) affect vulnerability to persistent pain after motor vehicle collision (MVC).

**Methods**

**Study design:** Prospective multicenter observational cohort study of individuals experiencing MVC.

**Study population:** European Americans 18-85 years old presenting to the ED within 24 hours of MVC who did not have injuries requiring hospital admission: 1,416 individuals were eligible and 948 were enrolled. Sixty one percent were females.

**Outcome measures:**
1. Overall pain intensity (SE) assessed via verbal 0-10 numeric rating scale (NRS); 2) Pain interference with life functions assessed via a telephone interview or web questionnaire using a verbal 0-10 numeric rating scale (NRS); 3) Pain interference only among individuals with one or two copies of the A3 allele (left panels).

**Results**

**COMT polymorphisms were grouped in three haplotype blocks** (promoter P2, coding region, and 3′ untranslated region)

All SNPs were in Hardy-Weinberg equilibrium (p > .05).

Haplotype and haplotype population frequencies were estimated using the expectation-maximization algorithm (below).

**Haplotypes from the three COMT haplotype blocks were associated with pain outcomes after MVC**

**Conclusions**

Results of this study suggest that the potential influence of COMT polymorphisms on pain outcomes is best evaluated using a haplotype-based approach that takes into account interactions between distal promoter, coding, and 3′ untranslated region haplotypes and sex differences in these interactions. Further studies are needed to investigate the biological substrate for these interactions.

**References**