COMT haplotypes predict pain intensity and interference 6 weeks after motor vehicle collision

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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 haploblock of the COMT gene code for different levels of COMT enzymatic activity and influence vulnerability to persistent pain.1 However, two large population-based studies have failed to demonstrate an association between central haplotype haplotypes and chronic widespread pain.2,3 In addition, other studies suggest that SNPs in the distal promoter P2 (controlling MB-COMT expression) influence transcriptomic4 and modify the effects of SNPs in the central haploblock on enzymatic activity.5

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

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RESULTS
COMT polymorphisms were grouped in three haploblock groups: (promoter P2, coding region, and 3' untranslated region)

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

Results of the present 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
1 Diatchenko et al. (2005) Hum Mol Genet, 14, 135-143.

CONCLUSIONS
Results of the present 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.

RESULTS (Cont.)
Low pain sensitivity (LPS) haplotype had a protective effect on pain and pain interference only among individuals with one or two copies of the A3 allele (left panels).

COMMENTS
Hypothesized mechanistic explanation for the interacting influence of haplotypes in the promoter P2 and COMT coding regions on pain outcomes after MVC: U-shaped dose-response curve between COMT activity and post-MVC pain vulnerability.

RESULTS
Haplotypes from the three COMT haploblocks were associated with pain outcomes after MVC

82 haplotype was associated with increased pain and pain interference only among men (left panels).

CONCLUSIONS
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