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LETTER TO THE EDITOR

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The functional Val158Met variant of the COMT gene is not associated with migraine with or without aura

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Dear Dr Martelletti,

Similar to Dr Hagen and colleagues [1] in *The Journal of Headache and Pain*, we were intrigued by the observation that genetic variants influence pain sensitivity in humans [2]. The enzyme catechol-O-methyltransferase (COMT) degrades catecholamines including dopamine. The functional variant of COMT, Val158Met, determines COMT enzyme activity, with the Met variant leading to a 3–4-fold lower enzyme activity, compared to the Val variant. The finding that the Val158Met genotype influences experimental pain sensitivity [2] led us to query whether this variant may contribute to the polygenic aetiology of migraine. The COMT activity of the genotypes is paralleled by the pain threshold, being lowest in met/met, intermediate in met/val and highest in val/val [2]. We assessed a sample of 92 patients with migraine with aura, 127 patients with migraine without aura and 144 headache-free controls. Inclusion and exclusion criteria were as described previously [3]. Val158Met genotypes were in Hardy-Weinberg equilibrium for the patient and control groups. The frequency of the met/met genotype was 25% in migraine with aura, 23.6% in migraine without aura and 28.5% in controls. Conversely, val/val frequency was 30.4% in migraine with aura, 27.6% in migraine without aura and 25.7% in controls. There were no significant differences between groups as assessed by logistic regression, adjusted for sex differences (migraine with aura: Wald χ^2=0.86, 2 degrees of freedom, p=0.65; migraine without aura: Wald χ^2=0.51, 2 degrees of freedom, p=0.77). Thus, similar to the finding of Dr Hagen and colleagues in this journal, we do not find a contribution of the functional Val158Met variant of the COMT gene to the pathogenesis of migraine. This variant may be more important in tumour pain [4] and in tension headache [1] than in neuropathic pain [5] or in migraine.

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