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Arthritis Care Res (Hoboken). 2010 Oct 28. [Epub ahead of print]

Role of the Na(V)1.7 R1150W amino acid change in susceptibility to symptomatic knee osteoarthritis and multiple regional pain.

Valdes AM, Arden NK, Vaughn FL, Doherty SA, Leaverton PE, Zhang W, Muir KR, Rampersaud E, Dennison EM, Edwards MH, Jameson KA, Javaid MK, Spector TD, Cooper C, Maciewicz RA, Doherty M.

Dept of Twin Research and Genetic Epidemiology Unit, St. Thomas' Hospital, King's College London, London, UK.

OBJECTIVE: To assess the genetic association of pain in patients with knee osteoarthritis (OA) and those with multiple regional pain with the R1150W variant in the alpha subunit of the voltage-gated sodium channel Na(V)1.7.

METHODS: Knee OA patients from two UK cohorts (1411 from the GOAL study and 267 from the Hertfordshire cohort study, 74% with symptomatic OA) with West Ontario and McMaster University OA (WOMAC) pain scores were genotyped for rs6746030 (encoding the R1150W change). 176 knee OA patients (53% symptomatic) from the Clearwater Osteoarthritis Study were also tested. 4295 samples in total (both OA affected and unaffected) from all three studies with data on multiple regional pain were tested. Fixed effects meta-analyses were carried out with WOMAC, symptomatic OA (adjusting for radiographic severity) and multiple regional pain as outcomes.

RESULTS: No association with WOMAC was seen in the UK cohorts. Overall the meta-analysis of WOMAC yielded a summary statistic $\beta=0.47$ (95%CI 0.04-0.89) $p=0.030$ for the variant allele. The meta-analysis of symptomatic versus asymptomatic OA did not demonstrate an association with rs6746030 (odds ratio (OR) = 0.90 95% CI 0.71-1.15 $p=0.38$). The meta-analysis of multiple regional pain resulted in a significant OR=1.40 (95% CI 1.08-1.80) $p=0.0085$. No inter-study heterogeneity was seen for any of the analyses.

CONCLUSIONS: We find evidence that the R1150W amino-acid change in Na(V)1.7alpha-chain is associated with multiple regional pain. This variant is confirmed to be involved in genetic susceptibility to pain but it does not appear to have a major role in OA-specific pain.

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