DECIPHERING THE ROLE OF MELANOCORTIN 1 RECEPTOR IN PAIN THROUGH SINGLE NUCLEOTIDE POLYMORPHISMS

K.S. Lichtenwalter, Ph.D. Candidate
McGill University
Student/Trainee

INTRODUCTION / AIM

Melanocortin 1 receptor, encoded by the gene MC1R, has been demonstrated to contribute to pain sensitivity. Previous reports provide conflicting evidence regarding the role of its genetic variants. Here we query the possible differential contribution of MC1R to nociceptive and chronic pain conditions by analyzing its single nucleotide polymorphisms (SNPs) for association with phenotypes of baseline pain sensitivity and chronic pain conditions. Additionally, we analyze for association with psychological stress factors to determine whether they modify susceptibility to either nociception or chronic pain.

METHODS

We genotyped all common non-synonymous MC1R SNPs in a cohort of 1,082 chronic cases of temporomandibular disorder (TMD) and 2,144 TMD-free controls in the OPPERA (Orofacial Pain: Prospective Evaluation and Risk Assessment) project. Both groups underwent clinical examination and quantitative sensory testing to evaluate sensitivity to thermal, cutaneous, and deep pressure pain. Presence of chronic pain conditions other than TMD and psychological distress phenotypes was assessed with questionnaires. We then performed regression analysis on individual SNPs and phenotypes as well as haplotype analysis and principal component analysis on phenotypes to reduce multiple testing and assay for multivariate contribution.

RESULTS

Our analysis shows that loss-of-function variants in MC1R are positively associated with chronic pain and baseline pain sensitivity as measured by thermal stimuli. Additionally, loss-of-function in MC1R is positively associated with phenotypes of psychological distress.

DISCUSSIONS / CONCLUSIONS

Loss of function MC1R variants appear to contribute to chronic pain conditions, possibly by increasing the risk of psychological distress and/or decreasing the nociceptive thresholds.

OTHER AUTHORS

R.N. Lichtenwalter
G.D. Slade
R. Dubner
R.B. Fillingim
J.D. Greenspan
R. Ohrbach
C. Knott
W. Maixner
L.B. Diatchenko