TRPV1 in the Dorsolateral Periaqueductal Grey Differentially Modulates Formalin-evoked Nociceptive Behaviour in Sprague-Dawley and Wistar-Kyoto Rats

Manish K. Madasu[1, 3], Bright N. Okine[1, 3], Weredeselam M. Olango[1, 3], Róisín Lenihan, Michelle Roche[1, 2, 3] and David P. Finn[1, 3]

[1]Pharmacology and Therapeutics, [2]Physiology, School of Medicine, [3] Galway Neuroscience Centre and Centre for Pain Research, NCBES, National University of Ireland Galway, University Road, Galway, Ireland

m.madasu1 @nuigalway.ie

Keywords: Biomedical Science; Biology & Life Sciences

Abstract

The study was designed to study the role of the transient receptor potential vanilloid receptor 1 (TRPV1) in the dorsolateral (DL) periaqueductal grey (PAG), of two rat strains, Sprague-Dawley (SD) and Wistar-Kyoto (WKY), which differ in their responses to stress and pain. Expression of TRPV1 mRNA was higher in the DLPAG of SD rats versus WKY rats, and pharmacological blockade/desensitisation of TRPV1 in the DLPAG increased formalin-evoked nociceptive behaviour in SD but not WKY rats. Thus, altered expression and/or functionality of TRPV1 in the DLPAG may underlie phenotypic differences of relevance to pain.

1. Introduction

The Wistar-Kyoto (WKY) rat is a stress-hyperresponsive strain that exhibits a hyperalgesic phenotype, compared with the Sprague-Dawley (SD) strain[1]. Transient receptor potential vanilloid receptor 1 (TRPV1) within the midbrain periaqueductal grey (PAG) plays a key role in regulating nociceptive behaviour via modulation of neuronal activity in the rostral ventromedial medulla[2]. The present study tested the hypothesis that pharmacological modulation of TRPV1 in the dorsolateral (DL) PAG would differentially regulate formalin-evoked nociceptive behaviour in SD versus WKY rats.

2. Methods:

Adult male WKY and SD rats (n=5-7 per group; 260-290g) received intra-DLPAG injections of either vehicle (100% DMSO), the TRPV1 agonist capsaicin (6nmoles/0.2µL), the TRPV1 antagonist 5'-IRTX (0.5nmoles/0.2µL) or co-administration of capsaicin and 5'-IRTX via bilaterally implanted stainless steel guide cannulae, 10 minutes prior to intra-plantar formalin injection (2.5%, 50µl). Nociceptive behaviour was assessed for 60 minutes using EthoVision XT. In a separate experiment, we used qRT-PCR to compare levels of TRPV1 mRNA in the DLPAG of SD and WKY rats (with and without formalin administration). Data were analysed by two-way ANOVA (with or without repeated measures) followed by Fisher's LSD post-hoc test. $P<0.05$ was considered statistically significant.

3. Results

In SD rats, intra-DLPAG administration of 5'-IRTX or capsaicin significantly increased formalin-evoked nociceptive behaviour, in the later phase of the formalin trial compared with vehicle-treated rats. These effects of 5'-IRTX or capsaicin were not observed in WKY rats. WKY rats receiving either intra-DLPAG vehicle or capsaicin injection, but not 5'-IRTX, exhibited higher nociceptive behaviour over the entire formalin trial compared with SD counterparts. Co-administration of capsaicin with 5'-IRTX had no effect on formalin-evoked nociceptive behaviour when compared with vehicle treatment in either SD or WKY rats. TRPV1 mRNA levels were significantly higher in the DLPAG of non-formalin treated SD rats compared with WKY rats. Formalin administration decreased the TRPV1 mRNA levels in SD rats but not in WKY rats.

4. Conclusion

Pharmacological blockade/desensitisation of TRPV1 in the DLPAG results in elevation of formalin-evoked nociceptive behaviour in SD but not WKY rats. These data, together with evidence for higher expression of TRPV1 mRNA in the DLPAG of SD rats, suggest a differential role of TRPV1 in the DLPAG in nociceptive responding between the two rat strains.

5. Acknowledgement

This work was funded by grants from Science Foundation Ireland (10/IN.1/B2976) and College of Science, National University of Ireland, Galway.

6. References

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