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NSAIDs attenuate agonist-evoked activation of TRP channels

Transient receptor potential (TRP) cations channels are the largest group of sensory detector proteins expressed in the nerve terminals of many receptors including nociceptors and are activated by temperature and chemicals that elicit hot or cold sensations. Antagonists of these channels are likely promising targets for new analgesic drugs at the peripheral and central levels. Because some non-steroidal anti-inflammatory drugs (NSAIDs) are structural analogs of prostaglandins and NSAIDs attenuate heat nociception and mechanical allodynia in models of inflammatory and neuropathic pain, we investigated whether three widely used NSAIDs (diclofenac, ketorolac, and xefocam) affect thermal and mechanical hyperalgesia following the activation of TRPA1 and TRPV1 channels. We measured nociceptive thermal paw withdrawal latencies and mechanical thresholds bilaterally at various time points following intraplantar injection of the TRPA1 agonists, cinnamaldehyde (CA) and allyl isothiocyanate (AITC) or the TRPV1 agonist capsaicin, or vehicle. When pretreated with vehicle, intraplantar injection of CA, AITC and capsaicin each resulted in significant decreases in thermal withdrawal latency and mechanical threshold in the ipsilateral hindpaw that did not return to baseline for more than 2 hr. To test effects of NSAIDS either diclofenac, ketorolac or xefocam was pre-injected in the same hindpaw 35 min prior to CA, AITC or capsaicin. Pretreatment with each of the three NSAIDs produced strong antinociceptive and antihyperalgesic effects lasting approximately 60 min. Thus, we show for the first time that local administration of NSAIDs suppresses thermal and mechanical hyperalgesia following TRPA1 or TRPV1 activation.

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Biography

Merab G Tsagareli is graduated from Tbilisi State University, Georgia (1977) and completed his PhD from Lomonosov State University of Moscow, Russia (1982) and then postdoctoral studies from Serbsky Research Institute for General and Forensic Psychiatry in Moscow, Russia (1985-1990). He is the Director of the Pain and Analgesia Laboratory at Ivane Beritashvili Center for Experimental Biomedicine in Tbilisi, Georgia. His research focuses on the behavioral studies of TRP channels and analgesic and tolerance effects of NSAIDs in relation with the descending pain modulation system. He has published more than 100 papers in peer-reviewed journals.

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