P5.07.

Effect of sphingomyelinase on TRP ion channel activation of trigeminal sensory neurons and transfected cell line

Szőke, É.[1*]; Tóth, D. M.[2]; Helyes, Z.[1]; Sándor, Z.[2]; Szolcsányi, J.[1, 2]

1: Department of Pharmacology and Pharmacotherapy, Faculty of Medicine, University of Pécs, Hungary
2: Analgesic Research Laboratory, University of Pécs and Gedeon Richter Plc., Pécs, Hungary

Transient Receptor Potential ion channels, such as TRP Vanilloid 1 and Ankyrin repeat domain 1 (TRPV1 and TRPA1), are expressed in primary sensory neurones. TRPV1 can be activated by capsaicin and resiniferatoxin (RTX). Pungent molecules such as mustard oil (MO) can be activated TRPA1 receptors. Lipid rafts are membrane microdomains rich in cholesterol, sphingomyelin and gangliosides. Sphingomyelinase (SMase) decreases membrane sphingomyelin by hydrolization of sphingomyelin to phosphocholine and ceramide. The aim of the present study is to analyse the effects of lipid raft disruption by SMase. Ratiometric technique of [Ca2+]i measurement on cultured trigeminal cells and radioactive calcium-45 uptake experiments in TRPV1-expressing CHO cells were performed. SMase (30 mUN) significantly diminished the intracellular Ca2+ influx induced by capsaicin (330 nM), but had no significant effect on the Ca2+ uptake caused by RTX (3 nM) on TRPV1-expressing CHO cells. Whereas SMase caused significant inhibition in TRPV1 receptor activation evoked by capsaicin as well as RTX on cultured trigeminal neurons. Similarly, SMase diminished the MO-evoked (200 μM) TRPA1 activation on cultured trigeminal neurons. These data suggest that disruption of lipid rafts inhibits the opening properties of the TRP channels, and the role of hydrophobic interactions of ligands at the TRPchannel/lipid raft interface might play more important role in drug action than it has previously been taken into account.