

## **Transient receptor potential vanilloid type-1 (TRPV1) in the human trigeminal system and arteries of the scalp**

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The non selective cation channel transient receptor potential vanilloid type-1 (TRPV1) is expressed by sensory neurons and triggered by a wide variety of activating factors, with depolarisation leading to burning pain. TRPV1 activation also leads to release of sensory neuropeptides calcitonin gene-related peptide (CGRP) and substance P (SP) which, in turn, activate their effector cell receptors and contribute to the process of neurogenic inflammation and sensitization of nociceptors. In view of the possible involvement of TRPV1 in headache disorders, we undertook the analysis of the occurrence of TRPV1 in the trigeminal sensory system and here relate on the localization of TRPV1 immunoreactivity in the human scalp arteries and trigeminal ganglion and spinal nucleus, and compare it to the distribution of CGRP and SP.

Surgical specimens of temporal, frontal and occipital arteries and autoptic specimens of trigeminal ganglion and caudal brainstem were fixed in 4% phosphate buffered paraformaldehyde and processed for avidine-biotin-peroxidase complex (ABC) or fluorescence immunohistochemistry.

Arteries of the scalp showed a consistent TRPV1-like immunoreactivity (LI) in form of varicose nerve fibres running at the media-adventitia border. In the trigeminal ganglion, a subpopulation of predominantly small- to medium-sized neurons showed a distinct TRPV1-LI in the perikaryon, sometimes extending to the proximal process. Coexistence with CGRP-LI was observed sporadically, whereas coexistence with SP-LI was never detected. Centrally, TRPV1-LI labelled extensive fiber tracts and punctate terminal-like elements distributed in the spinal tract and in lamina I, inner lamina II and deep magnocellular part of the spinal trigeminal nucleus. Neuronal cell bodies with membrane-like immunostaining were also detectable in the superficial layers of the nucleus. While TRPV1-LI was widely codistributed with both SP-LI and CGRP-LI, no colocalization was detectable in double immunostaining with SP-LI. The results obtained will be discussed and compared to the available data in literature.