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### Antinociceptive tolerance to NSAIDs: The role of opioid mechanism

The most important signaling mechanism for imminent harm is the pain system to minimize tissue damage. This system illustrates the complex process by which the brain constructs the sensory and emotional sensation of pain. The mainstay of mild pain therapy remains drugs that have been around for decades, like non-steroidal anti-inflammatory drugs (NSAIDs). Over the past decade, we have intensively studied the effects of antinociceptive tolerance to NSAIDs injected intraperitoneally or microinjected into pain-matrix structures like as the central nucleus amygdala, the periaqueductal grey matter, the dorsal hippocampus, the anterior cingulate and the rostral insular cortices. In this presentation, we review that repeated microinjections of NSAIDs like as analgin, clodifen, ketorolac and xefocam into above mentioned structures of rats over a 4-5 days period resulted in progressively less antinociception compared to the vehicle control, testing in the battery of behavioral tests (the tail-flick, hot plate, thermal and mechanical withdrawal). Hence, tolerance develops to these drugs and cross-tolerance to morphine. These findings strongly support the suggestion of endogenous opioid system involvement in NSAIDs antinociception. Pre-treatment with an opioid antagonist naloxone completely prevented, as well as post-treatment with naloxone abolished, the analgesic effects of these non-opioid drugs in all behavioral assays. These findings support the notion that the development of tolerance to the antinociceptive effects of NSAIDs is mediated via an endogenous opioid system possibly involving descending pain modulatory circuits.

### Biography

Merab G Tsagareli 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 National 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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