**Contribution of membrane receptors to visceral pain sensation**

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Chronic pain is a major, but underappreciated, clinical issue affecting >1.5 billion people globally. Chronic abdominal pain is the most common and debilitating feature of Irritable Bowel Syndrome (IBS), a chronic gastrointestinal disorder affecting approximately 15 % of the Western Population. As IBS occurs in the absence of bacterial infection or obvious pathology, the etiology of IBS symptoms remain unknown, and efficacious therapeutic options are limited. Current analgesics are not suitable to treat chronic visceral pain; as long term opioid use is associated with serious side effects including addiction, dependence and constipation. Pre-clinical and clinical studies show that exaggerated responses of sensory afferent innervating the colon (visceral hypersensitivity) underlie pain signalling in IBS. Using animal models of chronic visceral pain, we find that alterations in the balance of pro- and anti- nociceptive membrane receptor function on colonic nociceptors is a key factor in the development of visceral hypersensitivity and the maintenance of chronic visceral pain. Results from both rodent and human sensory neurons show that activation of γ-aminobutyric acid receptor B (GABABR) reduces nociceptive signalling via downstream inhibition of the voltage-gated calcium channels CaV2.2 and CaV2.3. Conversely, activation of protease activated receptor-1 on sensory neurons is involved in sensory response to mediators associated with IBS in humans. Thus, our results indicate that specific targeting of receptors or ion channels at the periphery is an advantageous strategy in the pharmacological treatment of chronic visceral pain, in clinical conditions such as IBS.