

Table 1. Neural Mechanisms of Pain: Facilitating and Inhibiting Factors

Anatomical Structure	Neurotransmitters, Neurochemicals or Receptors	Modulatory Effect on Transduction or Transmission (Facilitates { F } Inhibits { I })	Therapy Enhancing Effect (Relieves Pain Sensation)	Therapy Inhibiting Effect (Relieves Pain Sensation)
Peripheral Nervous System PAN Terminal	Leukotriene Prostaglandins Potassium Histamine Bradykinin Serotonin Substance P Endorphin	Transduction F, sensitizes F, sensitizes F, sensitizes F, sensitizes F, sensitizes F, sensitizes F, sensitizes I	Opioids	corticosteroids, ketoprophen ASA, NSAIDs n/a antihistamines n/a n/a capsaisin
Fiber	Na ⁺ , K ⁺ exchange across the cellular membrane	F, Transmission of action potential to CNS		mexiletine, tocainide, EMLA
Autonomic Nervous System	Norepinephrine	Transduction F, sensitizes nociceptive state F, activates neuropathic state		anxiolytics, relaxation
Spinal Cord	Substance P, glutamate, and others serotonin (5HT _{1B} and 5HT ₃) norepinephrine mu delta kappa GABA _A GABA _B	F, Transmission to projection cell (2 nd order neuron) F, Transmission with wind-up	TCAs TCAs TCAs, clonidine opioid agonists (e.g. morphine) opioid agonists opioid antagonist-agonists baclophen benzodiazapines	opioids ketamine dextromethorphan
Brain	Substance P, glutamate, and others	F, Transmission to 3 rd or 4 th order neuron		opioids

Key: PAN=primary afferent nociceptor; ASA=aspirin; NSAIDs=nonsteroidal antiinflammatory drugs; n/a=not available or not applicable; Na⁺=sodium; K⁺=potassium; CNS=central nervous system; TCAs=tricyclic antidepressant drugs or other re-uptake inhibitor drugs. © 2001 D.J. Wilkie, used with permission.