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The lower limb flexion reflex in humans

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Abstract

The flexion or flexor reflex (FR) recorded in the lower limbs in humans (LLFR) is a widely investigated neurophysiological tool. It is a polysynaptic and multisegmental spinal response that produces a withdrawal of the stimulated limb and resembles (having several features in common) the hind-paw FR in animals. The FR, in both animals and humans, is mediated by a complex circuitry modulated at spinal and supraspinal level.

At rest, the LLFR (usually obtained by stimulating the sural/tibial nerve and by recording from the biceps femoris/tibial anterior muscle) appears as a double burst composed of an early, inconstantly present component, called the RII reflex, and a late, larger and stable component, called the RIII reflex.

Numerous studies have shown that the afferents mediating the RII reflex are conveyed by large-diameter, low-threshold, non-nociceptive A-beta fibers, and those mediating the RIII reflex by small-diameter, high-threshold nociceptive A-delta fibers. However, several afferents, including nociceptive and non-nociceptive fibers from skin and muscles, have been found to contribute to LLFR activation.

Since the threshold of the RIII reflex has been shown to correspond to the pain threshold and the size of the reflex to be related to the level of pain perception, it has been suggested that the RIII reflex might constitute a useful tool to investigate pain processing at spinal and supraspinal level, pharmacological modulation and pathological pain conditions.

As stated in EFNS guidelines, the RIII reflex is the most widely used of all the nociceptive reflexes, and appears to be the most reliable in the assessment of treatment efficacy. However, the RIII reflex use in the clinical evaluation of neuropathic pain is still limited.

In addition to its nocifensive function, the LLFR seems to be linked to posture and locomotion. This may be explained by the fact that its neuronal circuitry, made up of a complex pool of interneurons, is interposed in motor control and, during movements, receives both peripheral afferents (flexion reflex afferents, FRAs) and descending commands, forming a multisensorial feedback mechanism and projecting the output to motoneurons. LLFR excitability, mediated by this complex circuitry, is finely modulated in a state- and phase-dependent manner, rather as we observe in the FR in animal models.

Several studies have demonstrated that LLFR excitability may be influenced by numerous physiological conditions (menstrual cycle, stress, attention, sleep and so on) and pathological states (spinal lesions, spasticity, Wallenberg's syndrome, fibromyalgia, headaches and so on). Finally, the LLFR is modulated by several drugs and neurotransmitters.

Abbreviations: A, adrenaline; CH, cluster headache; CNS, central nervous system; CPH, chronic paroxysmal hemicrania; CPT, cold pressor test; CTTH, chronic tension-type headache; DNICs, diffuse noxious inhibitory controls; EMG, electromyography, electromyographic; FM, fibromyalgia; LLFR, lower limb flexion reflex; FR, flexion or flexor reflex; FRAs, flexion reflex afferents; HNCS, heterotopic noxious conditioning stimulation; IBS, irritable bowel syndrome; IFT, interferential therapy; MCS, motor cortex stimulation; NA, noradrenaline; NFR, nociceptive flexion reflex; NRM, nucleus raphe magnus; NSAIDs, non-steroidal anti-inflammatory drugs; PAG, periacqueductal gray; PECs, piezo-electric currents; PLMs, periodic limb movements; RRF, reflex receptive field; TENS, transcutaneous electrical nerve stimulation; T_p/T_r, pain threshold/reflex threshold ratio; VIP, vasoactive intestinal peptide; WDR, wide dynamic range; WS, whiplash syndrome

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In summary, study of the LLFR in humans has proved to be an interesting functional window onto the spinal and supraspinal mechanisms of pain processing and onto the spinal neural control mechanisms operating during posture and locomotion.

Keywords: Flexion reflex; Flexor reflex; Withdrawal reflex; Flexor reflex afferents

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