Changes in Biochemical Markers of Pain Perception and Stress Response After Spinal Manipulation

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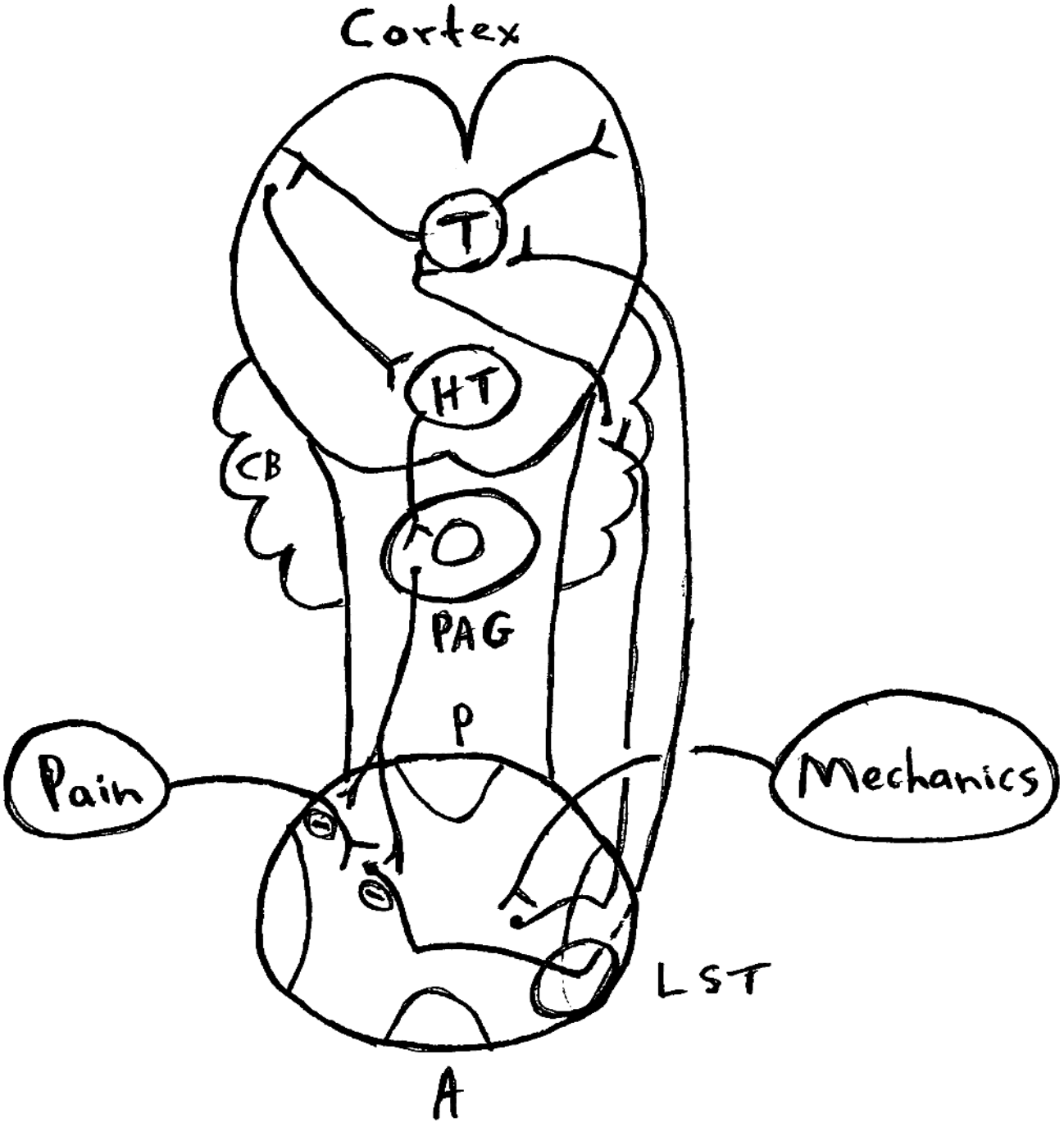

A	=	Anterior	CB	=	Cerebellum
HT	=	Hypothalamus	LST	=	Lateral Spinal Thalamic Tract
P	=	Posterior	PAG	=	Periaqueductal Gray

The thoracic manipulation description and picture used in this study appeared to be a standard anterior thoracic joint cavitation procedure delivered to T4-5.

The cervical manipulation description and picture used in this study appeared to be a standard joint cavitation procedure involving supine ipsilateral lateral flexion with contra-lateral rotation delivered to the C4-C5 level.

KEY POINTS FROM THIS STUDY:

1) The aim of this study was to evaluate the effects of cervical and thoracic spinal manipulation (SM) on the plasmatic concentration of biochemical markers [that are known to suppress pain as well as have other physiological influences] ***neurotensin***, ***oxytocin***, and ***cortisol***):

Neurotensin, is implicated in analgesia via its actions within central and peripheral pain modulatory circuits. "Neurotensin is a 13-amino acid produced in several regions of the central nervous system, such as the substantia nigra, amygdala, hypothalamus, prefrontal cortex, periaqueductal gray matter, and the spinal cord, and it has several actions, including analgesia."

Oxytocin, plays an antinociceptive role in the central nervous system. Oxytocin plays a major neuroendocrine role, "modulating several physiological functions including somatosensory transmission, nociception, and pain."

Cortisol, correlates inversely with pain intensity; specifically, an increase of cortisol is proven to have an antinociceptive effect.

2) This study used 30 asymptomatic subjects who were randomly divided into 3 groups: cervical manipulation (n = 10), thoracic manipulation (n = 10), and non-manipulation (control) (n = 10). Blood samples were extracted before, immediately after, and 2 hours after each intervention.

3) Immediately after SM, significantly higher values of *neurotensin* levels were observed with both cervical and thoracic manipulation. "Our data indicate an increase in neurotensin plasmatic concentration after an SM, suggesting that the mechanical stimulus provided by SM is enough to modulate the liberation of this neuropeptide."

Also, there is interaction between neurotensin and serotonergic neurons. Neurons of the rostral part of the raphe synthesize neurotensin, and neurotensin receptors are widely expressed in most of the raphe. [The raphe magnus nucleus is an important relay of the descending pain inhibitory control system, and its main neurotransmitter is serotonin].

"The anti-nociceptive effect of neurotensin after SM may increase the mechanical stress threshold that cervical tissues can tolerate."

4) Immediately after SM, significantly higher values of *oxytocin* levels were observed with both cervical and thoracic manipulation.

Oxytocin is synthesized and secreted by a subpopulation of the paraventricular and supraoptic nuclei of the hypothalamus. [This is important because it suggests that SM influences the hypothalamus].

"Oxytocin exerts a potent anti-nociceptive control after its release in the spinal cord from hypothalamo-hypophysal descending projections." This "anti-nociceptive action is mediated, in part, by an increase in synaptic inhibition within the most superficial layers of the spinal cord."

Also, oxytocin inhibits sensory glutamate transmission between afferent fibers and dorsal horn neurons. [Glutamate is known to cause chronic pain sensitization].

An increase of oxytocin may result in a greater synthesis of endogenous opioids.

Human subjects with central neurogenic pain and low back pain have pain relief after the intra-cerebro-ventricular and intrathecal administration of oxytocin.

"Our results suggest that the increase of the plasmatic concentration of oxytocin following an SM could be partly responsible for the analgesic effect linked to manual therapy techniques due to the activation of descending pain-inhibitory pathways."

5) Immediately after SM, significantly higher values of *cortisol* were observed, but only in the cervical manipulation group. "The cervical SM group showed a significant increase in cortisol plasma concentration immediately post intervention compared with baseline values." Two hours later cortisol levels had returned to pre-manipulation levels.

Cortisol acts to decrease local edema and pain by blocking early stages of inflammation.

These authors "found a significant increase of cortisol plasmatic concentration following cervical manipulation."

6) Two hours after the intervention, no significant differences were observed in between-group analysis. [The results were phasic, not tonic]

7) "Spinal manipulation is a common treatment approach for pain reduction in low back and neck disorders." Evidence from Cochrane reviews suggests that SM provides improvements in neck and back pain relief.

8) Pain induces changes in the anatomy and function of the central and peripheral nervous systems.

9) The mechanisms through which SM alters musculoskeletal pain may be by direct stimulation of the periaqueductal gray matter.

10) "Several studies currently support the idea that the analgesic effect of manual therapy is mediated by central mechanisms of pain modulation through the modulation of neuropeptide production."

11) "The results of this study show that cervical and thoracic manipulation resulted in an increase in neurotensin, oxytocin, and plasmatic cortisol concentration in asymptomatic individuals. These neuropeptides are related to the modulation of nociception and stress-induced analgesia."

12) "These findings suggest that descending inhibitory pathway mechanisms may be involved in the physiological effects that follow SM."

13) "The effect size for the cervical manipulation group was larger than that for the thoracic manipulation group. This suggests an increase in the activation of the possible descending inhibitory pathway mechanisms after cervical manipulation compared to thoracic manipulation."

14) "The mechanical stimulus provided by spinal manipulation triggers an increase in neurotensin, oxytocin, and cortisol blood levels. Data suggest that the initial capability of the tissues to tolerate mechanical deformation affects the capacity of these tissues to produce an induction of neuropeptide expression."

COMMENTS FROM DAN MURPHY:

The evidence that cervical spinal manipulation significantly phasically (but not tonically) increases cortisol levels is important. Because this occurs only following cervical spine manipulation and not following thoracic spine manipulation suggests the spinal manipulation is influencing suprasegmental control relays (the adjustment is influencing the brain and probably the hypothalamus).

The evidence that spinal manipulation activates the descending pain inhibitory control systems through the hypothalamic-periaquecductal gray-raphe magnus nucleus relays is not new; there are many supporting studies for this. I heard Ted Carrick, DC go over this mechanism nearly 2 decades ago in neurology diplomate class. This article adds to the evidence and refines the mechanisms.

The most important thing in this article for me is mounting evidence that spinal adjusting, particularly cervical spine adjusting, influences the hypothalamus, as the hypothalamus controls not only pain perception, but also all of visceral physiology.