Treating Inflammation

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Inflammation underlies most of the common diseases that we see in our medical practices. We can trace the effects of inflammation as a basic component in many diseases, such as diabetes, cancer, arthritis, cardiovascular disease, autoimmune disorders, inflammatory bowel disease and others.[1, 2] We know that increased production of inflammatory cytokines results from multiple causes that are commonplace in our culture: trauma from accidents as well as surgery, infection and chronic ergonomic strain; acidic diets; extreme exercise; toxic exposure; and, of course, emotional stressors.[2, 3] Being able to control the inflammatory process in our patients would be a great advantage in the management of many common diseases and crucial to the restoration of homeostasis.[1] Although untested, but promising from early clinical experience, osteopaths have the opportunity, with OMT, to modulate the production of inflammatory cytokines.[7] Such modulation of the production of cytokines putatively would have not only local cellular effects but also global, systemic effects through central nervous system modulation. This paper provides anatomical and physiological reasoning behind a proposed protocol of OMT to achieve a reduction of inflammation.

Recent studies have illuminated new pathways and mechanisms of action of the parasympathetic function of the vagus nerve.[4,9] These studies point towards the influence of the autonomic nervous system on the immune system and one of its resulting products - inflammation. These studies project the possibility of modulating the immune system through stimulating the vagus nerve with pharmaceuticals and implanted electrodes.[1,2,4] For those of us who treat the brain and nerves directly through osteopathic manipulation, these studies point to an opportunity for us, through palpatory means, to influence the immune system, bypassing drugs and surgery.

It is interesting to note that a nerve with such extensive reach also connects the nervous and immune systems. From reviewing these recent studies, we now understand what a vital role the vagus nerve plays in regulating not only our heart and gut, but also our immune function, specifically inflammation.[1,2,3,4,8,9]

CENTRAL AUTONOMIC NETWORK (CAN)

The CAN provides input to and output from the vagus. Connection of the vagus nerve to higher centers includes the medial prefrontal cortex, insular cortex, anterior cingulate cortex, as well as the central nucleus of the amygdala, periaqueductal gray region, and parabrachial region.[4] Communication in these neural circuits of the Central Autonomic Network is bidirectional. Connection of the vagus nerve to distal regions includes the heart, lungs, and gastrointestinal organs. With regard to inflammation, we are specifically interested in the immune functioning organ, the spleen.

Within our culture, characterized by our separation from nature, noise and other forms of pollution, mental and emotional stressors everywhere, we see ongoing clinical evidence of increased sympathetic tone. Palpating the central nervous system, we find overstimulation of the amygdalae in many of our patients. This singular finding is characteristic of many of the patients that we see in our clinics. There are other signs of increased tone of the sympathetic nervous system: increased function of the sympathetic chain ganglia and increased tone of the autonomic plexi (cardiac, celiac, and hypogastric). We might also see imbalances of other autonomic-related nuclei in the brain: hypothalamus, cingulate cortex and frontal cortex, for example.[7]

Because the sympathetic nervous system operates in conjunction with the parasympathetic system, we need to consider both sides of the autonomics in any strategy to affect the vagus nerve. By treating the CAN with osteopathic manipulation and using the intelligence of the tide, we can promote balance between both the sympathetic and parasympathetic nervous systems.

Parasympathetic output from the vagus originates in the medulla from the dorsal motor vagal nucleus.[6] (The nucleus ambiguus, not part of the CAN, but efferent vagal fibers, nonetheless, sends special visceral fibers to the palate, pharynx and larynx for swallowing and gag reflex). Parasympathetic vagal efferents originate in the medulla and proceed out through the jugular foramina where the two vagal ganglia exist, bilaterally: the superior (jugular) and the inferior (nodose) ganglia. These ganglia contain the cell bodies for visceral afferents traveling via the vagus back to the CNS. The efferents pass through the ganglia without synapsing and proceed through the carotid sheath into the anterior neck with the jugular vein laterally in front and carotid artery medially and behind down to the great vessels where the cardiac plexus exists. Here the parasympathetic efferents join fibers from the sympathetic nervous system emanating from the stellate ganglion and other sympathetic chain ganglia from as low as T4 and as high as the superior cervical sympathetic ganglion.[6,7]

The connection of the autonomic nervous system (CAN) to immune function follows a particular route from here. On the sympathetic side, autonomic nerves in the lateral horn of the thoracic spinal cord from T5-T9 send fibers through the ventral root and the white rami communicantes to the sympathetic chain ganglia at each level of the sympathetic trunk.[6] Here they synapse with post-ganglionic sympathetic fibers that then travel through

the grey rami communicantes out the spinal nerves to the celiac plexus. Here they meet with the vagal fibers delivering parasympathetic influence. Fibers of the vagus nerve carry these parasympathetic impulses from the dorsal vagal nucleus in the medulla continuing from the region of the cardiac plexus traveling down the exterior part of the esophagus through the diaphragm to the celiac plexus.[6] The celiac plexus can be palpated when dysfunctional in the epigastrium below the xiphoid process and between the costal margins. A dysfunction of the plexus will feel as though it is lacking vitality, lagging, dragging or heavy.[7]

The celiac plexus is composed of autonomic fibers just anterior and lateral to the abdominal aorta where sympathetic fibers emerge from the aortic hiatus of the diaphragm into the abdomen.[6] The celiac plexus controls the functions of the kidneys and adrenal glands as well as many gastrointestinal organs: liver, pancreas, stomach, and small intestine down as far as the transverse colon. The celiac plexus also sends information to the spleen through the splenic nerve.[1] Research has shown that the vagus nerve has influence over the immune system via the reticuloendothelial system, especially the spleen. When acetylcholine is released from the vagal nerve endings into the white pulp of the spleen, the macrophages there cease their release of TNF alpha.[1] This has a profound effect on the state of inflammation within the body as a whole. TNF alpha is at the head of the inflammatory cascade. Thus, the spleen has influence over the level of inflammation of the entire body.[3]

The intensity of the stimulation of the vagus required to reduce the production of cytokines is less than that required to change heart rate variability, the marker usually monitored for judging the effects on the autonomic nervous system.[3,8]

THE INFLAMMATORY REFLEX (Cholinergic anti-inflammatory pathway)

The cholinergic anti-inflammatory pathway is associated with efferent activity of the vagus.[3] Pharmacologic agents and neuroimaging have been used to demonstrate parasympathetic control of the heart via its connections through the right vagus nerve and the right hemisphere of the brain.[3,4] Neuroimaging studies also support the predominant role of the right hemisphere in the regulation of vagal tone during emotion.[4] Convention has it that the right brain controls the spleen through the vagus, as well.

The amount of pro-inflammatory cytokines, such as interleukin (IL-1 and IL-6), has important implications in the balance of health and disease.[4] These cytokines are inhibited by acetylcholine and parasympathetic tone under the vagus nerve's tonic inhibitory control. The acetylcholine release from the vagus acts on the reticuloendothelial system in the liver, heart, spleen and gastrointestinal tract.[1] Acetylcholine inhibits the release of pro-inflammatory cytokines but not the anti-inflammatory cytokines (IL-10).[4] The vagus nerve's efferent activity, with its release of acetylcholine, inhibits the release of tumor necrosis factor (TNF-alpha) from macrophages, the beginning of the inflammatory cascade.[4]

Amazingly, for a nerve that has such an extensive efferent influence, approximately 80% of vagus nerve fibers are afferent/sensory.[7] They convey signals to the brain regarding many functions of these organs including the presence of pro-inflammatory cytokines. The amount of pro-inflammatory cytokines needed to elicit a response from the efferent vagus is below the concentration required to demonstrate an elevation of cytokines in the blood stream.[3] If the afferent vagus reports a slight localized elevation of cytokines, these signals will arrive in the nucleus solitarius. From here the signals are conveyed to the dorsal motor vagal nucleus completing the afferent/efferent circuit.[8] Tonic control of the production of TNF-alpha will persist when the dorsal vagus sends acetylcholine signals to the spleen.[3]

The sympathetic nervous system and the endocrine system (the hypothalamic-pituitary axis) also regulate cytokines. The sympathetic nervous system has both pro- (IL-1, IL-6) and anti- (IL-10, IL-6) inflammatory influences, including IL-6, which can do both via a negative feedback mechanism, which promotes the production of C-reactive protein (CRP) in the liver.[4] Therefore a potential therapeutic strategy to mediate inflammatory diseases should involve therapies to activate the cholinergic anti-inflammatory pathway and short-circuit this inflammatory cascade.

As osteopaths, we can employ strategies aimed at stimulating the vagus nerve and quieting the sympathetic nervous system to affect the inflammatory pathways. We can alter the activity of the vagus nerve by several simple osteopathic maneuvers: the pussyfoot technique to influence the vagus as it transits the jugular foramen; balancing the atlas in its articulation with the occiput where the vagus descends into the carotid sheath; the frontal lift to influence the prefrontal cortex; and the release of the anterior dural girdle to release the frontal part of the brain. These less specific techniques might provide adequate stimulation of the vagus by themselves. However, utilizing specific techniques to address the nuclei of the central nervous system and the nerve ganglia and plexi can produce results with even greater specificity.

The specific techniques involve working directly with the nuclei of the CAN. The protocol could start with the insular cortex. Clinically, we usually find the right side of the brain to be dysfunctional in these cases of inflammation. One feels a lagging, pulling, and lack of vitality of the nucleus in question when dysfunctional. As we discover the dysfunction and then follow the intelligence of the tide, we feel an improvement of motility of the insular cortex. Then, we might perceive the intelligence of the tide taking our attention to the anterior cingulate and prefrontal cortices. Next might appear the central nucleus of the amygdala. As these display improved motility, the hypothalamus and the parabrachial nuclei as well as the periaqueductal gray regions might appear in our awareness. This sequence is often what occurs under treatment. Such a sequence seems to be consistent with the manner in which the circuits operate as the brain communicates within itself and modulates its performance under changing circumstances.[7]

Then comes the outflow from the medulla: nucleus tractus solitarius communicates with the dorsal vagus nucleus, which emits parasympathetic impulses. Finally, we feel the improved motility in the vagus nerve and follow its course through the jugular foramen and down the carotid sheaths and esophagus to the cardiac and celiac plexi. There we will observe a softening and vitalizing for a time until the splenic nerve becomes activated and we can feel the spleen itself being nourished by the acetylcholine. Soon the whole dynamic comes to an end with a stillpoint. Then, when the Primary Respiratory Mechanism re-emerges, we are finished.[7]

By working directly and specifically on the CAN through osteopathic manipulation we have the potential to influence patient health with wide reaching benefits in many disease processes. Specific attention to the relevant CNS nuclei, ganglia and plexi, as described above, alongside more basic osteopathic protocols can potentially reduce inflammation in our patients.

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Dental Corner

Dental Cranial Management of Head Pain

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The dental physician that applies osteopathic cranial principles, better serves the patient's full spectrum of health concerns. Below is the first of three case reports concerning the dental cranial management of a patient's chronic head pain.

This report is reflective of a mindful assessment of a chronic-pain-patient as a means to educate, diagnose and initiate the lengthy, and often arduous task, of restructuring patient beliefs, anatomical relationships, and the re-patterning of associated para-functional movements. Cognitive behavioral therapy, facilitated positional release, clinical hypnosis and biodynamic osteopathy are integrated to prepare the patient for this journey and the fabrication, delivery and acceptance of a balanced oral orthotic.

INITIAL EVALUATION AND MANAGEMENT

GM presented, complaining of weekly disabling head pain. He reported to be 59 years old, married, father of four grade-school children, and owner of multiple metropolitan retail outlets; he spends many hours in the car driving to and from those outlets throughout the work week.

He was physically fit, health-conscious and non-medicated. He did not use recreational drugs and was a moderate weekend social drinker.

As documented in his cell phone diary, his head pain started 48 months ago, and continues to occur during the cool-down from his weekly cross-fit workout routine. The cardiac goal of his routine is to progressively achieve a target heart rate of 160 beats per minute. His targeted rate is achieved by performing a "kettlebell swing," whereby, while standing, a handle connected to a weight is grasped by both hands and elevated from the floor in front of the body as fast, as high, and as many times as possible until exhaustion sets in. Upon exhaustion and achievement of the targeted heart rate, the "cool-down" period would ensue. However, 10 to 15 minutes into the cool-down, the heart rate remained fixed at the targeted rate, a low-pitched hum within his head would arise, followed by a dull pressure behind his left ear. A visual pixilation of the right eye would occur and the left ear pressure would escalate from dull pain to that of radiating sharp pain within the right temple region and behind the right eye. These episodes confined him to bed rest for eight to twelve hours, disabling him from work and family life until the pain would subside.

At the time of the first episode, because the patient experienced transient right eye blindness, a consulting neurologist advised him that he had experienced a stroke behind the left ear. However, the MRI brain scan was negative for stroke. The neurologist advised him on follow-up that this recurrent workout-related head pain was a migraine headache due to the stroke, and that because of