

## Laryngeal symptoms may be caused by cranial nerve 9 and 10 compression at the brain stem

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While a sudden coughing fit is a protective reflex to clear the airway, chronic cough can be caused by multiple factors that must be investigated to determine treatment. Cough is just one of several laryngeal symptoms including hoarseness and dysphoric breathing that can become debilitating. Until recently, the cause of these severe laryngeal symptoms could not be identified in many patients, and the only treatments were to manage them with medication and rehabilitation therapy.

A team of MUSC researchers can now offer these patients some hope. Lucinda Halstead, M.D., associate professor of medicine in MUSC's Department of Otolaryngology: Head & Neck Surgery and medical director of the Evelyn Trammell Institute for Voice and Swallowing, led her team to uncover a new cause for these symptoms and an effective treatment.

"Symptoms like hoarseness may not seem serious, but if you are a singer, teacher or a preacher, or have a job at a call center, it's exhausting to push your voice every day," explained Halstead. "Chronic cough is not just a little throat-clearing. We're talking about a very forceful cough. These people can break ribs or become incontinent from the force. It's very debilitating. They're afraid to go out in public—to church, or a concert, or a restaurant-because it's so disruptive."



When a patient presents with chronic laryngeal symptoms (persisting for more than eight weeks and not improving with standard treatment), physicians follow a step-by-step protocol to look at the most common causes. For example, over 86% of chronic coughs are caused by postnasal drainage, asthma or gastroesophageal reflux disease.

If a full history and exam do not identify the cause, an otolaryngologist evaluates the larynx. In some patients, this turns up asymmetrical movement of the vocal fold (the vocal cords) or vocal fold paralysis. The cause is usually a lesion or another structure pressing on one of the nerves that activates the vocal fold and swallowing (cranial nerves nine and ten). Because these nerves run from the brain stem through the neck and into the chest, further investigation is needed to pin-point exactly where the compression is occurring.

"The laryngeal exam tells us that the vocal fold is not opening, lengthening or shortening correctly," said Halstead. "For people with vocal fold paralysis, we look right away in the chest and neck. Maybe a mass in the thyroid gland is pressing on a nerve and interfering with the signal. Maybe it's a lesion in the chest or a mass along the carotid sheath that's causing the laryngeal weakness."

But sometimes the cause remains elusive. "If the usual scans don't show anything that could cause it, we usually assume that it had a viral originviruses do sometimes cause these problems—or we simply say that the etiology is unknown."

Then, Halstead's team met their index case who would inspire the study that led to their recent discovery. A medical student presented at their clinic with severe difficulty swallowing and "breathy" speech. A laryngeal exam found vocal fold paralysis, but further investigations didn't identify a cause.



"The patient just wasn't going to take, 'I don't know' for an answer and refused to believe we couldn't find an etiology for what was happening," recalled Halstead. "We kept investigating but there were no masses in the neck or chest—everything looked good. So, we went back through the history and saw that the symptoms all started during a bad migraine, which is a vascular event in brain. A migraine wouldn't cause cranial nerve compression, but many blood vessels in the brain can press on these nerves. Based on some vagal nerve symptoms that the patient reported while exercising, we hypothesized that maybe when blood vessels dilated during the migraine, it exacerbated some ongoing vascular compression at the brain stem."

When this was confirmed by MRI, the patient chose to have surgery to move the vessel off the nerve (a procedure similar to what is done to relieve trigeminal neuralgia). It was a success. Partial motion of the paralyzed vocal fold occurred, and swallowing ability was recovered completely.

The team wondered how many of their other patients with unexplained symptoms might also have compression at the brain stem. Could this neurosurgical procedure also help them? They used retrospective chart reviews to identify 149 study candidates and, after extensive work-ups to eliminate all other causes, they found that 33% (49/149) had nerve compression at the brainstem. Their symptoms included dysphonia (51%), chronic cough (39%), dysphoric breathing (6%) and dysphagia (4%). After explaining the potential risks and benefits, 49% elected neurosurgical decompression and 51% chose non-surgical/standard-of-care treatment.

Results showed that surgical decompression significantly improved quality of life on all measures. The change in Voice-Related Quality of Life (V-RQOL) was p=0.02, Reflux Symptom Index (RSI) was p=0.02 and Glottal Closure Index (GCI) was p=0.01. Results comparing surgical



and non-surgical groups showed significantly (p=0.02) greater improvement in V-RQOL in the surgical group and trends toward statistical significance on the RSI (p=0.20) and GCI (p=0.17).

42% of the surgical group reported near-complete or complete symptom resolution compared to 8% in the non-surgical group (p=0.008). Over a mean follow-up of three years, non-surgical patients (60%) experienced no significant improvement or worsening symptoms, compared to surgical patients (13%) (p=0.001). Finally, none of the non-surgical patients demonstrated improved laryngeal exam findings, while 43% of surgical patients demonstrated improvements and 29% demonstrated resolution of their laryngeal exam findings.

"Our study shows that when we can't identify a cause for vocal fold weakness based on the standard work up, the next step may be to look at the brain stem," Halstead said. "It's so important that we now have one more thing to look at and one more thing we can offer as definitive treatment."

The team hopes that their findings will benefit more <u>patients</u> soon and that their study might point others to investigate <u>nerve</u> compression at the brain stem as a possible cause for other unexplained symptoms.

**More information:** Robert J. Taylor et al, Laryngeal manifestations of cranial nerve IX/X compression at the brainstem, *The Laryngoscope* (2018). DOI: 10.1002/lary.27678

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