

Editorial

Acute Solitary Tract Nucleus Insufficiency in Chronic Heart Failure

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Editorial

The typical neurologist with a clinical office practice on Main Street in Peoria probably does not spend very much time thinking about chronic heart failure -yet. Whether that will change in the future may depend on how much researchers are able to discover about an obscure site in the brainstem called the solitary tract nucleus. Ischemia there has been identified as a likely causal factor in many cases of sudden unexpected death during the course of a variety of common cardiorespiratory illnesses including sleep apnea and heart failure. The deaths are thought to be preventable.

Schematically on a drawing board, the heart is an electric pump. The brain is a computerized electronic guidance system. The vagus nerve is an electric cable cord attached to the heart, utilized to plug the heart into the brain, just as an electric pump cord be would plugged into a wall socket. The cable holds 2 wires, each insulated from the other: an up-stream wire from the heart to the brain and a down-stream wire from the brain to the heart. At the end of the cable cord are 2 metal prongs that fit into an electric socket in the brain. Each metal prong attaches to one of the 2 wires in the vagus nerve. The 2 metal prongs that are 'plugged into' the brain are thereby imbedded in the brain and receive their blood supply from the brain vessels, which are significantly influenced by carbon dioxide (CO₂) levels. The solitary tract nucleus is the up-stream wire prong. The dorsal motor nucleus of the vagus nerve is the down-stream wire prong.

When someone initially begins to develop heart failure, the myocardium begins to suffer from lack of oxygen. The heart then sends distress signals to the brain through the vagus nerve up-stream wire. The brain then makes adjustments in the heart rate and contractility through the down-stream wire. As heart failure becomes progressively more severe, the 2 metal prongs are unable to handle the high volume of signaling which occurs, and they begin to overheat, and require increased blood flow. Respiratory therapy given to improve myocardial oxygenation, or to manage concurrent sleep apnea, may inadvertently lower CO₂ levels, causing vasoconstriction

in the brain, and reducing blood flow to the metal prongs. In the absence of a treatment modality which offers increased blood flow in the brain, an electrical short circuit may occur between the metal prongs, sending abnormal electrical discharges from the prongs through the down-stream wire to the heart -sometimes causing cardiac arrest.

Researchers studying 'low-level' vagus nerve stimulation [1] are making an important contribution to basic science regarding vagus nerve stimulation in heart failure -an area which has recently incurred setbacks in human clinical trials [2], with some investigators asking whether it may be 'time to pull the plug' [3]. Meanwhile, an important segment of the heart failure population, 'sleep apnea with heart failure', has recently failed clinical trials with other treatment modalities (Adaptive Servo-Ventilation) [4] leaving a therapeutic void in medical care, which low-level vagus nerve stimulation might potentially fill, at least in part.

The 'low-level' researchers [1] focused most of their attention on the effects of electrical impulses proceeding down-stream on efferent fibers traveling toward the heart from the point of stimulation of the vagus nerve -which ultimately improved left ventricular ejection fraction in their 'heart failure rats'. And some clinical investigators have reported that vagus nerve stimulation in epilepsy patients has reduced cardiac electrical instability [5] a potential trigger for lethal arrhythmias -probably by a down-stream mechanism. Others [6,7] have considered the effects of electrical impulses proceeding up-stream on afferent fibers toward the brain medulla from the point of stimulation of the vagus nerve. The latter travel directly into the solitary tract nucleus, the 'central receiving station' for sensory afferent autonomic messaging from the heart.

The solitary tract nucleus is regarded by some [6,7] as an important target for nerve stimulation therapy because it is believed to commonly develop very small ischemic lesions during the course of chronic cardio-respiratory illnesses like heart failure [8] and sleep apnea [9]. These ischemic lesions are thought to form as a result of excitotoxic neural input from thoracic organs during illness which causes increased metabolism in dendritic regions of solitary tract nucleus parenchymal tissue in the setting of a limited watershed vasculature. The ischemic lesions then seem capable of triggering life-threatening cardiac arrhythmias [10] by an unknown mechanism. Vagus nerve stimulation indirectly stimulates the solitary tract nuclei, where it has been shown in epilepsy patients to increase blood flow locally [11] and where it might potentially stabilize autonomic discharges, thereby preventing lethal arrhythmias.

Citation: Howard Jaster J. Acute Solitary Tract Nucleus Insufficiency in Chronic Heart Failure. *Neurol Curr Res.* 2018; 1(1): 1001.

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Publisher Name: MedText Publications LLC

Manuscript compiled: August 23rd, 2018

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The 'low-level' researchers [1], while preparing their Sprague-Dawley 'heart failure rat' model, may have induced not only 'post-myocardial infarction heart failure', but also ischemic lesions in the solitary tract nucleus. Another basic science research group [12] has used an animal model similar to that of the 'low-level' researchers [1] to study the solitary tract nucleus during 'chronic myocardial infarction' simulating angina pectoris- a phenomenon in humans possibly overlapping what some investigators have called 'chest pain from the brain' [7]. It would be interesting to see the 'low-level' researchers' [1] experiment repeated with the solitary tract nucleus examined microscopically for ischemic lesions when the animals are euthanized for testing of myocardial tissues. The 'low-level' researchers' [1] model of 3 subgroups should be able to reveal the differences in histopathology of the solitary tract nucleus in different settings. The control group, with no coronary ligation, would be expected to show no solitary tract nucleus lesions. The 'heart failure rats' without 'low-level' vagus nerve stimulation should show solitary tract nucleus ischemic lesions. The rat group with 'both heart failure and 'low-level' vagus nerve stimulation' should show the therapeutic value of 'low-level' vagus nerve stimulation on the solitary tract nucleus- if there is any.

Also interesting would be a similar experiment using the 'low-level' researchers' [1] 'heart failure rat' model to test stimulation of the chorda tympani nerve rather than the vagus nerve. The chorda tympani nerve in the mouth just as the vagus nerve in the chest travels directly to the solitary tract nucleus. But electrical stimulation of the chorda tympani nerve does not directly impact the heart. Stimulation of the chorda tympani nerve indirectly stimulates the rostral third of the solitary tract nucleus of the medulla via functional connections, just as vagus nerve stimulation indirectly stimulates the caudal 2/3 of the solitary tract nucleus [7]. The chorda tympani nerve mediates taste sensation on the anterior 2/3 of the tongue.

Short-term stimulation of the chorda tympani nerve might potentially be accomplished using some version of small floating microelectrical stimulators [13], implantable wireless neural stimulators [14], or neuro-monitors [15]. Possible mechanisms for long-term stimulation have been described elsewhere [7]. Data from chorda tympani nerve stimulation might also help the 'low-level' researchers [1] to sort out whether the beneficial cardiac end-organ effects from their experiment were caused by direct down-stream efferent stimulation of the vagus nerve or rather by up-stream afferent stimulation traveling to the solitary tract nucleus and then triggering a down-stream efferent response through the dorsal motor nucleus of the vagus nerve.

Chorda tympani nerve stimulation may potentially be an option in managing heart failure -even if clinical trials of low-level vagus nerve stimulation were to reveal down-stream efferent adverse effects on the heart that force clinicians to 'pull the plug'. And low-level vagus nerve stimulation may still have a significant role in the management of patients with ischemic medullary brain lesions [16-30], or sleep apnea, who do not have heart failure.

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