Neuromodulation of the Autonomic Nervous System for Regulation of Cerebral Blood Flow

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Learning Objective

1. Describe open surgical approach to the superior cervical ganglion in human cadaver.
2. Predict the cerebrovascular response when the superior cervical ganglion is electrically stimulated and pharmacologically blocked in Yorkshire Swine.

Background

To ensure adequate brain perfusion, multiple mechanisms tightly regulate cerebral blood flow (CBF) through myogenic, neurogenic, metabolic and endothelial factors in a process known as autoregulation[1]. Cerebral vasospasm is a disease of impaired autoregulation, resulting in reversible narrowing of blood vessels, often leading to stroke and poor patient outcomes[2-5]. It occurs in up to 50-90% of patients with aneurysmal subarachnoid hemorrhage (SAH)[6], and 60% of patients with traumatic brain injury[7], making it one of the leading causes of preventable morbidity in these patients[8-10]. Yet, there are limited durable treatment modalities for patients experiencing cerebral vasospasm. Hence, targeted therapies to augment cerebral blood flow in disease states such as cerebral vasoconstriction are of immediate clinical importance. I sought to investigate the feasibility of augmenting CBF during cerebral vasospasm by pharmacologically blocking sympathetic outflow from the superior cervical ganglion (SCG).

Methods

Specific Aim 1 Methods: to determine a repeatable dissection procedure for exposing the superior cervical ganglion in human cadavers to verify accurate anesthetic drug delivery post-injection, by performing practice SCG dissections on human cadavers to develop a repeatable dissection protocol.

Specific Aim 2 Methods: to assess the degree of cerebral vasoconstriction resulting from SCG stimulation compared to vasoconstriction caused by models of SAH-induced vasospasm, by exposing the superior cervical ganglion of a Yorkshire Swine and stimulating it with direct electrical current with subsequent CT perfusion analysis of CBF.

Specific Aim 3 Methods: to evaluate the efficacy of minimally invasive SCG anesthetic block in treating cerebral vasospasm and restoring CBF, a Bullfrog catheter was utilized to administer a local anesthetic directly to the SCG in a Yorkshire Swine through the internal carotid artery during SCG electrical stimulation. The methods described in specific aims 2 and 3 have thus far been implemented exclusively to collect the preliminary data of this study.

Results

A dissection protocol for surgically locating the superior cervical ganglion in human was established through summer dissection of human cadavers. This protocol follows: 1) an incision is made along the medial border of the sternocleidomastoid; 2) fat and fascia are removed to expose the sternocleidomastoid muscle and external jugular veins; 3) the carotid sheathe is breached and its contained structures are medialized; 4) the sympathetic chain is located and tracked superiorly to the superior cervical ganglion.

Data collected in Yorkshire swine (to meet specific aims 2 and 3) are limited to preliminary experimental data due to covid-19 restrictions slowing the approval of animal protocols and delaying the execution of non-survival Yorkshire swine experiments. These results are illustrated in Figures 1, 2, and 3.

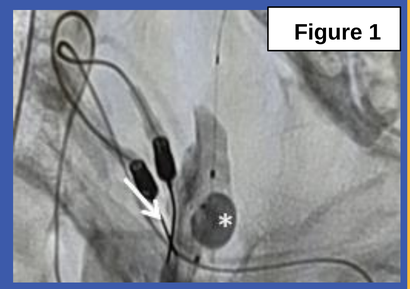

Figure 1

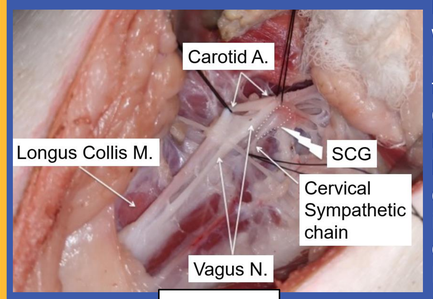

Figure 2

Figure 1 illustrates digital subtraction angiography of the lateral neck of Yorkshire Swine with catheter placed in the ascending pharyngeal artery. Two electrode stimulators are placed in the SCG from an open surgical lateral neck dissection. Asterisk (white) shows the inflated Bullfrog device in the ascending pharyngeal artery that has been used to deliver contrast-stained lidocaine. Arrow (white) shows the location of the SCG near the Bullfrog device. The results from carotid neck dissection of a Yorkshire swine shown in Figure 2 indicate that the SCG is readily accessible for electrical stimulation from a common surgical approach to the lateral neck. Figure 3 illustrates axial CT perfusion images of Yorkshire Swine. (A): Baseline symmetric blood flow. (B): Right superior cervical ganglion stimulation (via surgical access shown in Figure 2) showing reduced blood flow to the right cerebral hemisphere. (C): Right superior cervical ganglion stimulation after direct administration of local anesthetic agent to the right superior cervical ganglion showing restored cerebral blood flow.

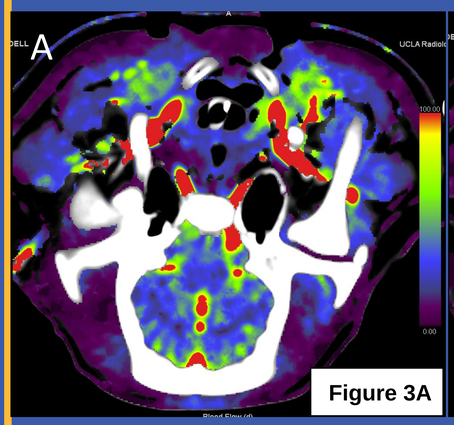

Figure 3A

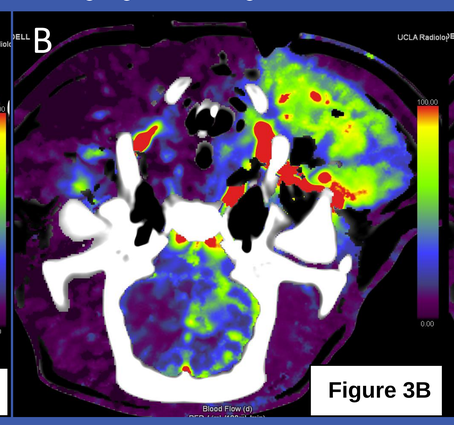

Figure 3B

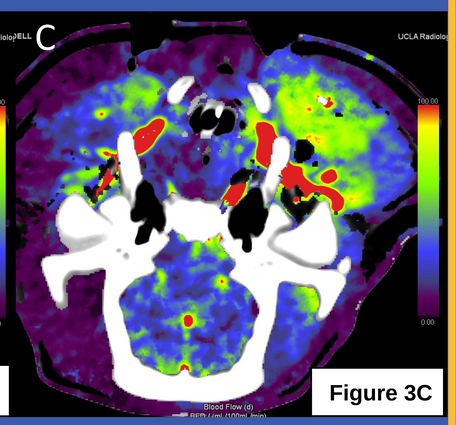

Figure 3C

Discussion

Specific Aim 1 was achieved through practice human cadaveric dissection to expose the superior cervical ganglion. In the next phase of this study, this dissection procedure will be used to reliably confirm successful targeting of the SCG in humans with dye delivered through a Bullfrog catheter. If Specific Aim 2 is achieved and electrical stimulation of the SCG is shown to be an acceptable model for cerebral vasospasm based on perfusion measurements, future studies of vasospasm will be able to use the same model. Given the notable convenience this method which can induce and remove cerebral vasospasm on-demand, it has the potential to be adopted by other researchers in the field. If Specific Aim 3 is achieved, we will be one step closer to introducing a targeted therapy for cerebral vasospasm to the clinical setting. With cerebral vasospasm occurring in up to 50-90% of patients with aneurysmal SAH[6] and 60% of patients with traumatic brain injury[7], the introduction of a safe and effective therapy for cerebral vasospasm which integrates easily into exiting clinical workflow has the potential to reduce morbidity in the cerebral vasospasm patient population[8-10].

Limitations

This study is limited primarily by the assumption that electrical direct current stimulation of the superior cervical ganglion and subsequent vasospasm is an accurate animal model for subarachnoid hemorrhage-induced vasospasm. Indeed, electrically stimulating the superior cervical ganglion does not replicate the accumulation of blood in the subarachnoid space as is the case in true subarachnoid hemorrhage and in animal models which induce subarachnoid hemorrhage by mechanically inducing stroke. Furthermore, specific aims 2 and 3 have currently only been partially achieved through preliminary data which is not sufficient in quantity to power statistically significant findings in CT perfusion data. Additional experiments with Yorkshire swine will meet this limitation.

Conclusion

A dissection protocol was developed to ensure the repeatable exposure of the superior cervical ganglion in human cadavers for verification of successful delivery of an anesthetic agent to the superior cervical ganglion. Preliminary data is promising in that appreciable restoration of cerebral perfusion was observed in response to targeted administration of local anesthetic to an electrically stimulated SCG. These findings encourage further investigation into the development of this novel targeted therapy for cerebral vasospasm which would fit well into the existing clinical management of cerebral vasospasm.

References

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