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Protocol for vagus nerve stimulation in awake pigs (subject-4)

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Protocol status: Working

We use this protocol and it's working

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Abstract

The Vagus nerve innervates a number of thoracic and visceral organs. Exogenous nervous signal, for example, Vagus nerve stimulation (VNS) provides a route to modulating their function for therapeutic purposes. However, the relationship between VNS parameters and organ responses is poorly understood as evidenced by a number of failed human trials, for example, in the heart failure space.

This protocol is for a chronic study that builds upon a previous acute study (<https://doi.org/10.26275/dm5l-tspb>) in which the pigs were under anesthesia. It maps VNS parameters to their immediate neural and cardiac effects in 2 freely moving pigs. By exploring the changes in heart rate responses from acute to chronic periods, we aim to gain a more comprehensive understanding of the effects of VNS on organ function.

Subjects

- 1 Female swine of adult age and weight between 35—55 kg for the experimental design were used.

Surgery

- 2 Measure the weight of the pig, then administer anesthesia. Intubate the animal and start mechanical ventilation.
- 3 Position pig prone and mark neck where the skin implant is to be placed along with the incisions on the neck. Mark where the ECG leads will go on the backside of the subject.
- 4 Cut out circle for skin implant to go through and make an incision where the implant will be inserted.
- 5 Place skin implant in position. Take both ECG leads and tunnel them along the back to each side of the animal. Coil the ECG leads and sew them into place. Sew the skin implant into muscle and skin.
- 6 Tunnel the cuffs and leads to an open incision halfway down the neck.
- 7 Position the pig supine with neck extended and make a single incision through the skin and superficial fat layers between the mandible and sternal notch. Use blunt dissection to expose the carotid sheath and isolate the vagus nerve from the carotid artery.
- 8 Use blunt dissection to locate the superior and recurrent laryngeal branches of the vagus nerve.
- 9 Use blunt dissection to expose as much length of the vagus trunk as possible. Ideally at least 8 cm from the superior laryngeal branch insertion point to a more caudal location.
- 10 Tunnel the leads and cuffs from the incision in the neck to where the vagus nerve is exposed.
- 11 Place cuffs on vagus nerve such that there is at least 4 cm between each cuff, but ideally 5.5 cm.



- 12 Sew EMG patch on laryngeal muscle and the ground lead in a pocket next to the caudal cuff. Tack down the wires.
- 13 Validate system works before closing incisions.
- 14 Close incisions.

Stimulation Protocol

- 15 Connect BIOS Neurotool software to implant.
- 16 Set the the following stimulation parameters in BIOS Neurotool software:
 - Pulse width: 260us
 - Train duration: 3s
 - Stimulation shape: monophasic
 - Polarity: cathodic
- 17 Conduct a grid search by doing the cartesian product of the frequency and current parameters.
 - Frequency: {2Hz, 5Hz, 10Hz, 20Hz}
 - Current: {0.05mA, 0.5mA, 1mA, 1.5mA, 2.5mA}After each stimulation, wait for the physiological signals to return to baseline.