Mapping single digit cortical representation in the rat using systematic nerve transection and fMRI at 9.4T

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Purpose

There are two novel aspects of this study. The first involves the electrical stimulation of a single digit, and the second involves transecting nerves in rat brachium such that only one nerve can provide the somatosensory transmission to the rat cortex when the digit is stimulated. Four main nerves of the brachial plexus, the ulnar, median, radial and musculocutaneous nerves, are collectively responsible for the sensory innervation of the rat forepaw. Traditional forepaw experiments with electrical stimulation during fMRI acquisitions have focused on varying the stimulation parameters such as the current, duration, or frequency. To our knowledge, there have been little or no studies that aim to refine the cortical response to an individual digit or the response of an individual nerve of a single digit. This study aims to develop a methodology for single sensory nerve stimulation of a single digit of the rat forepaw. In this experiment, the radial, ulnar and musculocutaneous nerves are surgically transected in the rat brachium, while leaving the median nerve intact. In doing so, we can isolate the somatosensory component of the median nerve of a single digit. This effort is part of a larger goal of developing a cortical map for motor and sensory nerves of the rodent upper extremity and developing a rodent model for brachial plexus injuries and surgical nerve repair.

Methods

4 Sprague Dawley rats were used in this study. The brachial plexus of 3 rats were exposed on the right upper arm. The radial, ulnar and musculocutaneous nerves were surgically transected with care to preserve the median nerve. A fourth rat did not have any surgical procedure involving the brachii, and was used to conduct a forepaw experiment to serve a control. For every rat, the right femoral artery and vein were used for invasive blood pressure monitoring and for continuous IV drug administration. A tracheotomy allowed for mechanical ventilation during the fMRI acquisition. Isoflurane (1%) was administered during the surgical portions of the procedure. Once the rat was transferred to the scanner the Isoflurane was turned off. A continuous infusion of Pancurium Bromide (2mg/kg/hr) and Domitor (0.1mg/kg/hr) was used during the fMRI acquisition. For 3 rats, stainless steel electrodes were implanted on the right and left fourth digits. For the fourth rat, stainless steel electrodes were placed in the left and right forepaws in the second and fourth webspaces. Four separate protocols that differed in current level (0.5 mAmp or 1.0 mA) or frequency (5 Hz or 10 Hz), but with a constant duration of 1ms were used for the digital stimulation. The forepaw stimulation varied in frequency (5Hz or 10Hz), but had a constant current of 2mA and duration of 3ms. Each stimulation sequence began with an OFF period of 40 seconds followed by three repetitions of ON for 20 seconds and OFF for 40 seconds (total scan time 3minutes 40seconds). Gradient echo scans (Single shot EPI, TE = 18.39 ms, TR = 2 ms, MTX 96 x 96, FOV = 4 cm, number of repititions = 110, 10 contiguous 1mm scans, acquisition time = 3 minutes 40 seconds) were acquired on a 9.4T Bruker MRI scanner. Physiologic monitoring included invasive blood pressure, arterial blood gases, pulse oximetry, pulse, temperature, respiratory rate, inspired / expired O2 and CO2. These parameters were maintained within normal physiologic ranges. Activation was determined by an F-test with a P-value threshold of 0.02 using AFNI.

Results and Discussion

The cortical response to electrical stimulation of the forepaw has been well studied and was repeated in this study as means to compare to single digit stimulation. Four nerves originate in the brachial plexus and provide the sensory input to the forepaw, including the individual digits. In humans, there are predictable patterns of innervation for each individual digit; however anatomic variations are well documented. In rats, the fourth digit is innervated by the median and ulnar nerves volarly, and the radial nerve dorsally, but variations may also be present across different rats. Though the muculocutaneous nerve is known to provide the dorsal sensory innervation to the first and second digits, it does communicate with the radial nerve as it travels distally in the antebrachium, and for this reason it was also transected in this experiment.). Lower current levels were used for digital stimulation given the smaller size of the digits compared to the forepaw. The cortical response to the stimulation of the left fourth digit is shown in Figure 1A and B. The ulnar, radial, musculocutaneous nerves were transected in the right brachium, leaving the median nerve intact. The surgery ensures that the cortical response to the right fourth digit stimulation is purely derived from the median nerve. The response is smaller than the response to corresponding left fourth digit stimulation, which has an intact brachial plexus (compare Figure 1A and B to Figure 1C and D). Both responses are smaller than the forepaw well-studied forepaw signal (not shown). This technique shows a method to identify solitary nerve innervation to a single digit, an important means of refining our understanding of the detailed cortical responses to somatosensory stimulation of the rat forelimb. This method can be used to provide a cortical map of the rat digits with and without systematic nerve transection.

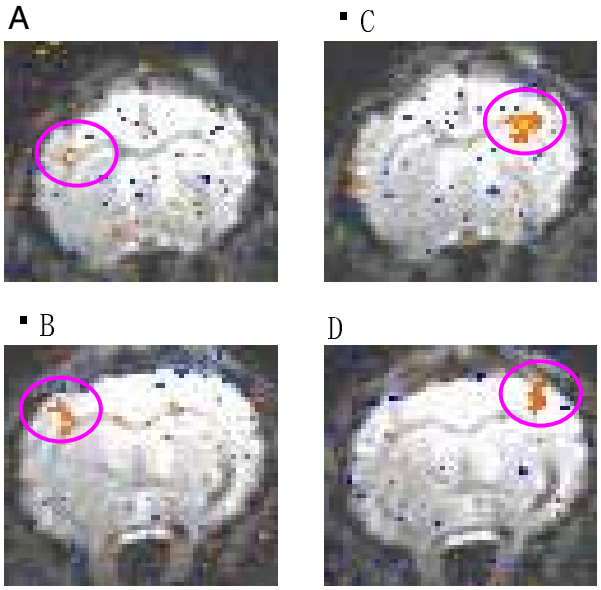

Figure 1: **A** - Left fourth digit with nerve transection (1ms, 10 Hz, 0.5mA); **B** - Left fourth digit with nerve transection (1ms, 10Hz, 1mA); **C** - Right fourth digit with no nerve transection (1ms, 10Hz, 0.5mA); **D -** Right fourth digit with no nerve transection (1ms, 10Hz, 1mA).