

# VIBROTACTILE AND ELECTROCUTANEOUS STIMULI ACTIVATE DISTINCT BUT OVERLAPPING AREAS IN PRIMARY SOMATOSENSORY CORTEX THAT DIFFER IN THEIR STIMULUS-RESPONSE PROPERTIES

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## Introduction

The adult primate brain retains a remarkable capacity for functional reactivation and reorganization following spinal cord injury (SCI). Appropriate reactivation of somatosensory areas is an important determinant of functional recovery following SCI. However this process remains poorly understood. Little is known about the functional adaptations of higher order somatosensory areas to loss of sensory inputs. Furthermore, the influence of different spinal cord pathways (dorsal, spino-thalamic) on cortical (particularly somatosensory and sensory-motor) and sub-cortical remodeling and reactivation remain unclear. By comparing the responsiveness of somatosensory cortices to vibrotactile (VS; activate dorsal column pathways) and electrical stimuli (ES; activate dorsal column and spinothalamic pathways) before, and after a partial dorsal column section, we can begin to study the role of these different spinal cord pathways in cortical remodeling and functional recovery. In this study, we used high-resolution CBV-fMRI to compare the patterns and stimulus-response characteristics of cortical and thalamic activation elicited by VS and ES stimulation of sensory afferents in a single digit in anesthetized squirrel monkeys with both dorsal and spinothalamic spinal cord pathways intact.

## Methods

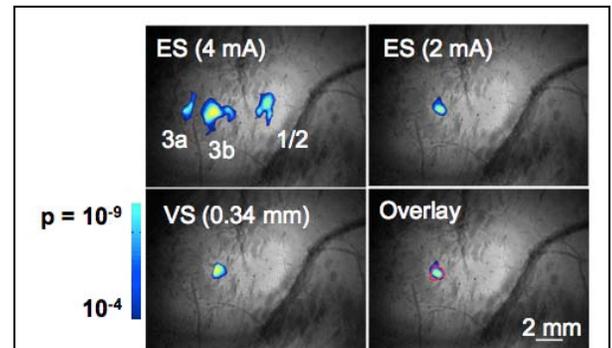
Squirrel monkeys were anesthetized (isoflurane 0.5-0.8%), mechanically ventilated, and the head stabilized in an MR compatible frame. Vital signs were monitored and maintained throughout the imaging session. MR images were acquired with a 9.4T Varian magnet using a 3 or 6 cm surface transmit-receive coil positioned over primary somatosensory cortex. T2\*-weighted gradient echo structural images (TR/TE 200/16 ms, 16 slices, 512x512 matrix; 78x78x500  $\mu\text{m}^3$  resolution) were acquired to identify cortical landmarks used to locate SI cortex and coregister fMRI maps across imaging sessions. ES was delivered to a single finger tip by a Grass S88 stimulator and constant current unit. ES was a square wave pulse (duration 2 ms, frequency 8 Hz; pulse amplitude 0-6 mA). VS, delivered with piezoceramic actuators (Noliac), consisted of 8 Hz trains of 20 ms duration taps. Seven alternating 30 s blocks of baseline and stimulation were delivered per imaging run. Multi-slice GE-EPI (2-shot, TR/TE 750/10 ms, in-plane resolution 273x273  $\mu\text{m}^2$ ) was used for CBV mapping, beginning 10 minutes following a slow i.v. bolus of MION (12-16 mg/kg). Data were identically analyzed: individual imaging runs were pre-conditioned using standard high- and low-pass filters for drift correction and removal of high frequency noise, then runs using the same functional contrast were combined to generate functional maps thresholded at  $p < 10^{-4}$  (uncorrected),  $k=2$ . The amplitude and area of single digit activation in different cortical areas was then determined and compared. All study procedures were approved by the Vanderbilt IACUC.

## Results

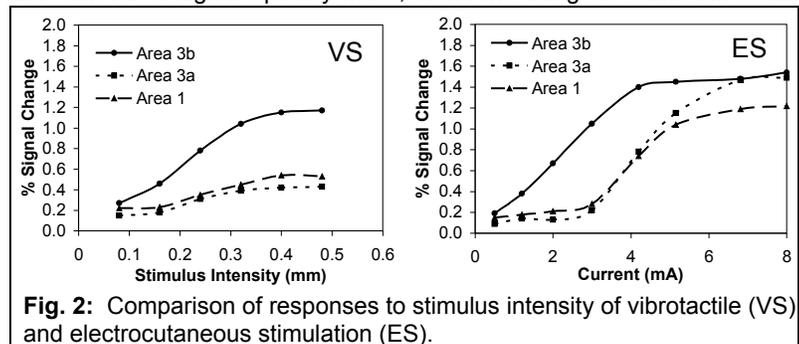
Low intensity (2mA) ES activation in area 3b colocalized with, and had areas and fractional signal changes similar to high intensity (near saturating) VS (Fig 1). However cortical response properties differed significantly for ES compared with VS in areas 3a and 1 (Fig 2). Responses in areas 3b, 3a and 1 increased with increasing VS intensity, but saturated at  $\sim 0.35$  mm, and peak responses in areas 3a and 1 were significantly smaller than in 3b. Area 3b activation increased monotonically with increasing ES current, plateauing at 4 mA. Areas 3a and 1 were unresponsive for ES < 3 mA, but showed increasingly robust activation above 3 mA, plateauing at 5-6 mA, with activations comparable in amplitude to area 3b. Finally, there was strong bilateral activation in VPM and unilateral activation in VPL at high ES, but little activation with VS or low ES (Fig 3).

## Discussion

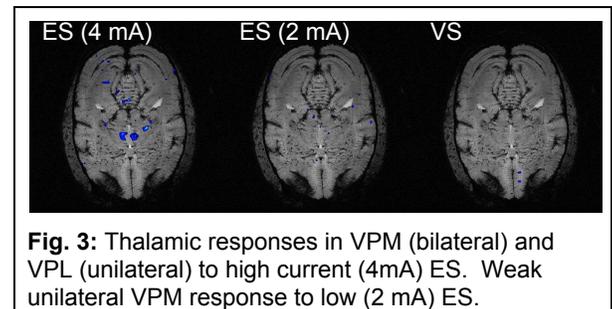
ES and VS elicit distinctly different patterns of SI cortical activation, reflecting differences in the afferent pathways engaged by high intensity ES and VS. Thus VS engages principally the dorsal pathways, as does weak ES, while strong ES engages both dorsal and spinothalamic pathways. These results are consistent with a role for areas 3a and/or 1 in coding of nociceptive stimuli, and suggest that VS and ES can be used to probe the integrity of dorsal and spinothalamic pathways and their roles in cortical reorganization and functional recovery following SCI.



**Fig. 1:** Primary somatosensory cortex responses to ES and VS. Areas 3a, 1 are engaged by ES > 3mA.



**Fig. 2:** Comparison of responses to stimulus intensity of vibrotactile (VS) and electrocutaneous stimulation (ES).



**Fig. 3:** Thalamic responses in VPM (bilateral) and VPL (unilateral) to high current (4mA) ES. Weak unilateral VPM response to low (2 mA) ES.