

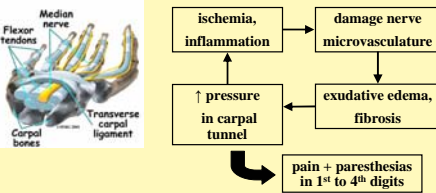
# Central Processing of Acupuncture Stimuli in Carpal Tunnel Syndrome

Vitaly Napadow, J Liu, M Li, N Kettner, KK Kwong, M Vangel, N Makris, J Audette, KKS Hui  
 Massachusetts General Hospital, Boston, MA; Logan College of Chiropractic, Chesterfield, MO., Spaulding  
 Rehabilitation Hospital, Medford, MA U.S.A.



## Introduction

### CTS Pathophysiology



### CTS doesn't just affect the wrist

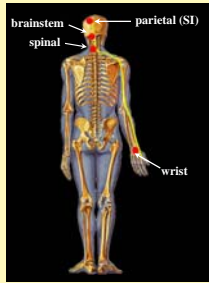
Tinazzi et al. reported somatosensory evoked potentials (SSEPs) abnormally amplified with stimulus to affected side – spinal N13, brainstem P14, parietal N20, P27<sup>1</sup>

Tecchio et al. reported cortical ECD amplification with MEG<sup>2</sup>

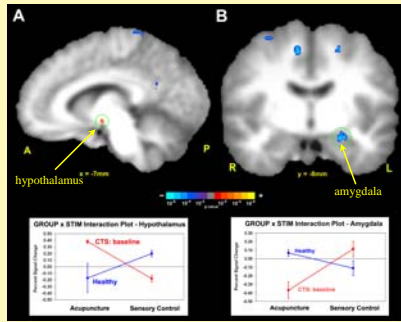
Napadow et al. reported SMC hyperactivation and blurred digit representations with fMRI<sup>3,4</sup>

While acupuncture processing in the brain of healthy adults has been studied in the past, these data cannot be easily extrapolated to chronic pain patients.

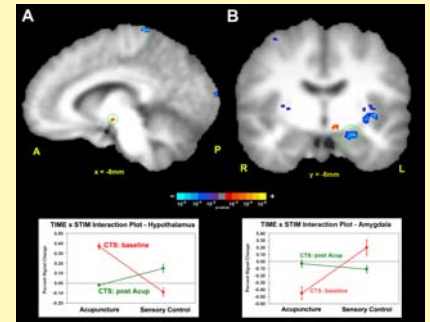
As clinical acupuncture is typically applied to patients and not normal subjects, we used fMRI to evaluate differences in brain processing of acupuncture stimulation in CTS patients vs. healthy adults.



## Results

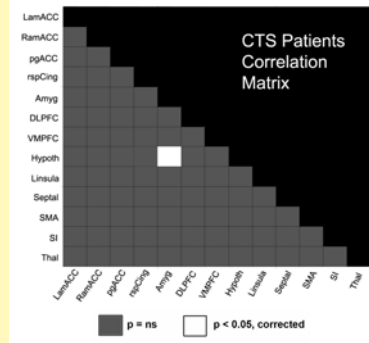


**X-sectional Baseline Analysis: (CTSbase.acup – CTSbase.ctl) – (Healthy.acup – Healthy.ctl).** A positive ANOVA interaction was found in the hypothalamus, while a negative interaction was found in the amygdala. Interaction plots demonstrated that the main driver of the significant interaction was CTS patients at baseline with acupuncture stimulation



**Longitudinal CTS analysis: (CTSbase.acup – CTSbase.ctl) – (CTSpost.acup – CTSpost.ctl).** Similar to baseline analysis, a positive interaction was found in the hypothalamus, while a negative interaction was found in the amygdala.

### Functional Connectivity: Correlated fMRI response to acupuncture in hypothalamus and amygdala

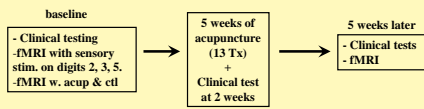


Region (Brodmann Area)	Side	Talairach			Z-score
		X (mm)	Y (mm)	Z (mm)	
amACC (24)	L	-3	13	34	-3.70
(24)	R	8	26	27	-3.42
pgACC (24)	R	13	40	6	-3.30
rspCing (31)	L	-7	-53	25	-3.30
Amyg	L	-21	-8	-13	-4.33
DLPFC	L	-20	49	9	-3.00
VMPFC	R	8	41	-6	-4.15
LathHypothA	L	-7	-6	-8	2.88
ainsula	L	-34	7	-4	-3.16
Septal Area	R	2	0	8	-3.57
SMA	L	-6	-19	51	-4.15
SI (3b/1)	L	-42	-32	45	-4.08
Thalamus	R	13	-12	13	-2.85

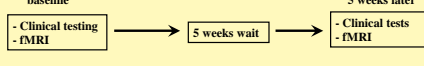
(Left) Functional connectivity was explored by calculating the percent signal change correlation matrix for CTS patients at baseline responding to acupuncture stimulation. Potential brain regions (13) were drawn from those demonstrating a significant cross-sectional ANOVA interaction (table, left). The only two regions which demonstrated a significant correlation were the amygdala and hypothalamus.

## Methods

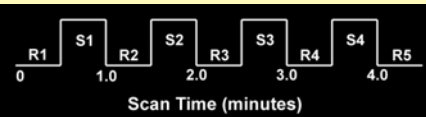
### CTS (n=10)



### Healthy Adults (n=9)

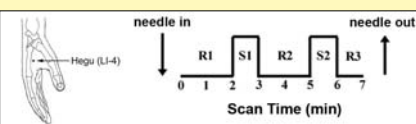


**Finger Cortical Mapping and Somatotopy**  
 fMRI Stimulation: 100Hz electro-stimulation on digits 2, 3, and 5 (pseudo-random order); just below pain threshold.



### Acupuncture fMRI Protocol

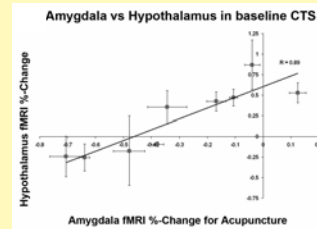
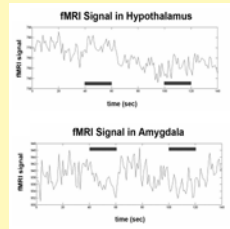
fMRI Stimulation: manual acupuncture at LI-4 (1Hz twisting stim. with 0.23x30mm pure silver needle) OR somatosensory/cognitive control stimulation with 5.88 Von Frey monofilament (1Hz tapping).



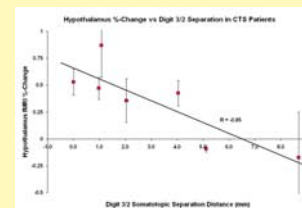
### Data Analysis

- Single subject GLM analysis performed with FEAT, FSL (motion correction with FLIRT; spatial smoothing, FWHM=5mm)  
 - Surface-based analyses performed with FreeSurfer & SUMA (AFNI) → group & difference maps thresholded at p<0.05 FDR corrected and minimum cluster size of 5 voxels.  
 - Acupuncture neuroimaging: Two 2x2 ANOVA interactions with factors GROUP and STIM (x-sec), and factors STIM and TIME (longitudinal).

(Right) fMRI signal time course for the hypothalamus in baseline CTS patients with predominant hypothalamic activation and for the amygdala in patients with predominant amygdala deactivation. Note more pronounced response to the first stimulation block.



(Above) The less deactivation in the amygdala, the more activation in the hypothalamus for CTS patients at baseline in response to acupuncture.



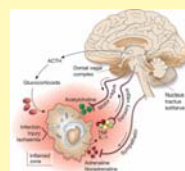
(Above) The magnitude of hypothalamic activation in response to acupuncture for CTS patients at baseline was found to correlate negatively with their digit 2 / digit 3 cortical representation separation distance in contralateral SI. The worse a patient's central maladaptive neuroplasticity, the more they respond to acupuncture with hypothalamic activation.

## Conclusions

• Patients with CTS respond to acupuncture with more pronounced fMRI signal decrease in the amygdala and signal increase in the hypothalamus, compared to healthy subjects.

• These brain regions in CTS patients were also more affected by acupuncture stimulation at baseline compared to after a 5 week course of acupuncture therapy.

• Acupuncture may benefit CTS patients via both peripheral (e.g. increased blood flow to median n. via vasodilative peptide release) and central mechanisms (e.g. the cholinergic anti-inflammatory pathway<sup>5</sup> via hypothalamic activity).



## References

- 1 Tinazzi, et al. *Brain*, 1998. **121 (Pt 9)**:1785-94.
- 2 Tecchio, et al. *HBM*, 2002. **17**: 28-36.
- 3 Napadow, et al. *Neuroimage*, in press.
- 4 Napadow, et al. *HBM*, in press.
- 5 Tracey (2002) *Nature* 420(6917):853-9

pdf's available at: [www.nmr.mgh.harvard.edu/~vitaly](http://www.nmr.mgh.harvard.edu/~vitaly)

## Acknowledgements

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