

# Functional Imaging of Magnetic Field Therapy

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# Declaration of Conflict of Interest

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John Robertson: Partial student support from Fralex Therapeutics Inc, and minor shareholder.

Alex Thomas: Co-founder, major shareholder, and VP-Research of Fralex Therapeutics Inc.

Frank Prato: Co-founder, major shareholder, and Chair of Scientific Advisory Board of Fralex Therapeutics Inc.

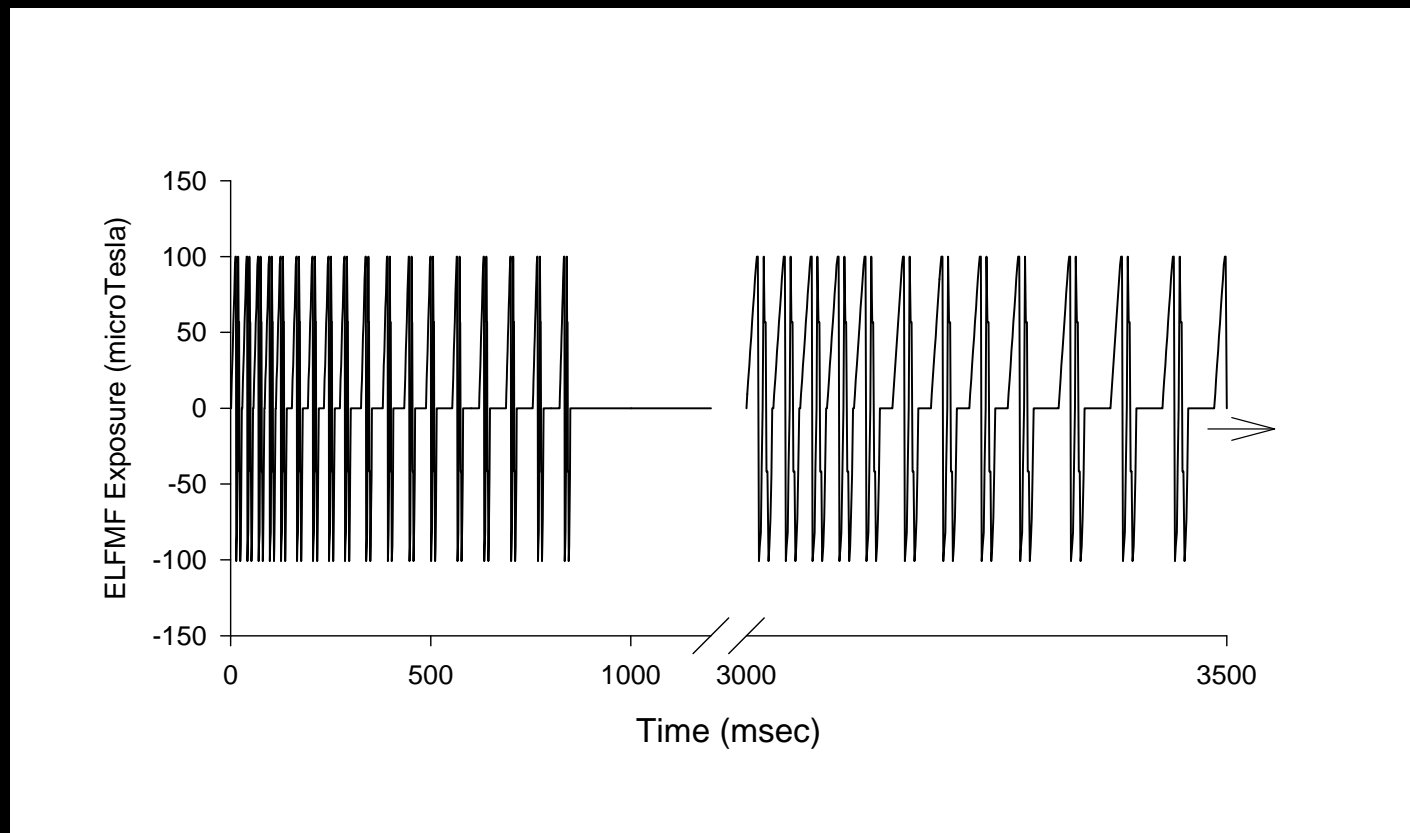
# Background

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- Our lab has developed a specific magnetic field known as the Complex Neuroelectromagnetic Pulse (CNP)
- This pulsed extremely low frequency magnetic field has analgesic properties in snails, mice, and humans
- Previous studies have indicated that the CNP affects nociception without altering sensory thresholds

# The CNP

- A specific pulsed magnetic field with analgesic effects



# Analgesia from CNP

- Head-only exposures have been effective in producing analgesia



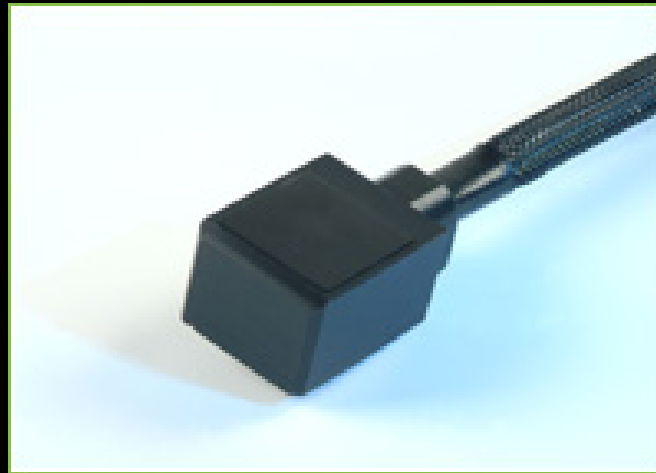
# fMRI

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- Functional MRI allows us to image changes in blood oxygenation
- Changes in brain activation -> changes in brain blood flow
- Compare sets of images taken during different activities to see blood flow changes

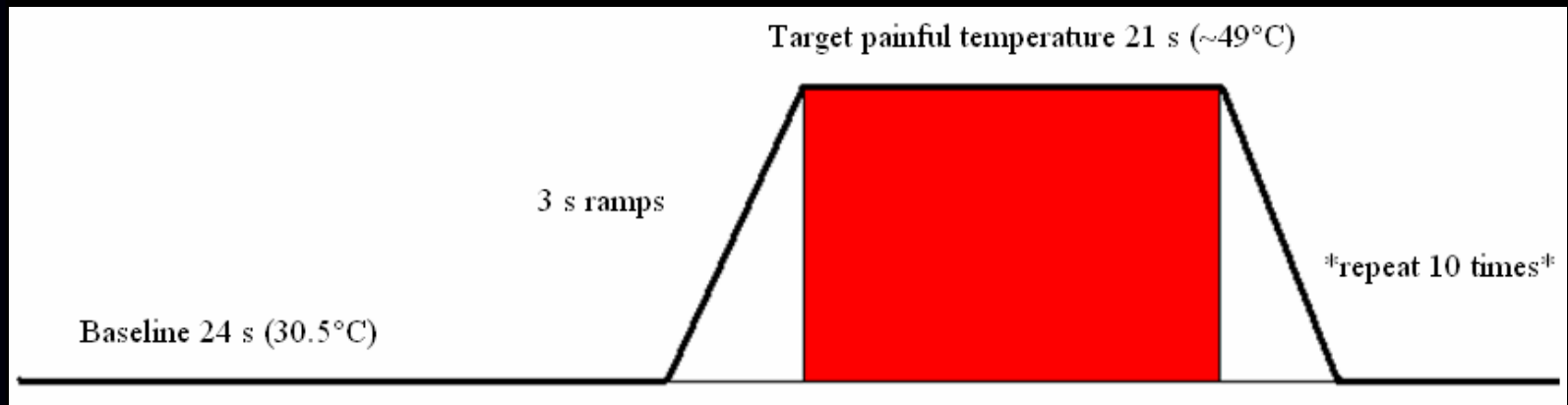
# Experimental Protocol

- Normal volunteers
- Acute thermal pain delivered using a small thermode attached to the **right hand** [Medoc TSA-II]



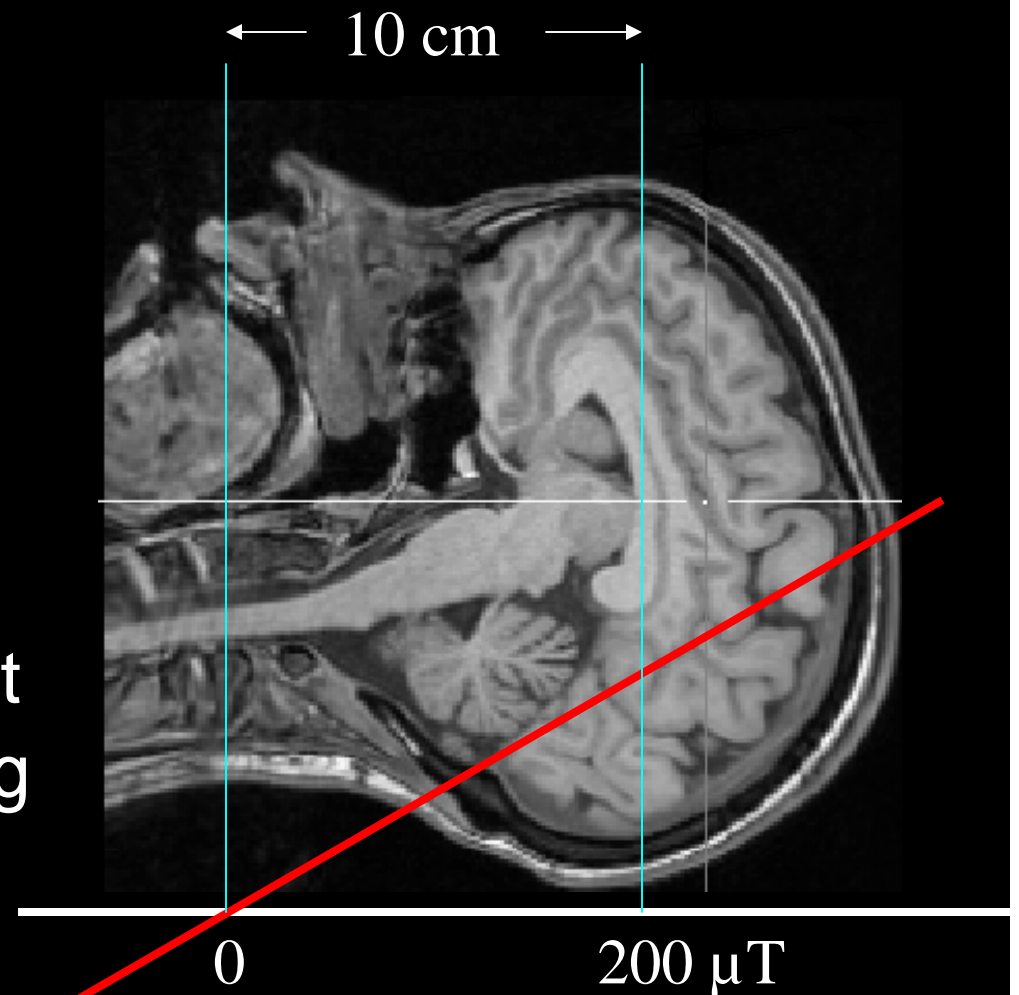
# Experimental Protocol

- Heat stays on for 21s, 3s ramps, 24s off; repeat 10 times pre and post
- For analysis consider heat on to be pain (may be some neural delay)



# Introduced CNP

- CNP delivered with the gradient coils of the MRI
- CNP is delivered between imaging sessions
- Subjects have not reported detecting the field



# fMRI Protocol

- Determine temperature needed for individual subject's pain tolerance
- Image baseline pain processing with 1.5 T Siemens Avanto
  - Single-shot EPI 64x64 slice
  - 16 slices, 3x3x5 mm voxels
  - 2.5s TR, 50 ms TE, 192 mm FOV
- 15 minute exposure inside magnet
- Image post exposure pain processing

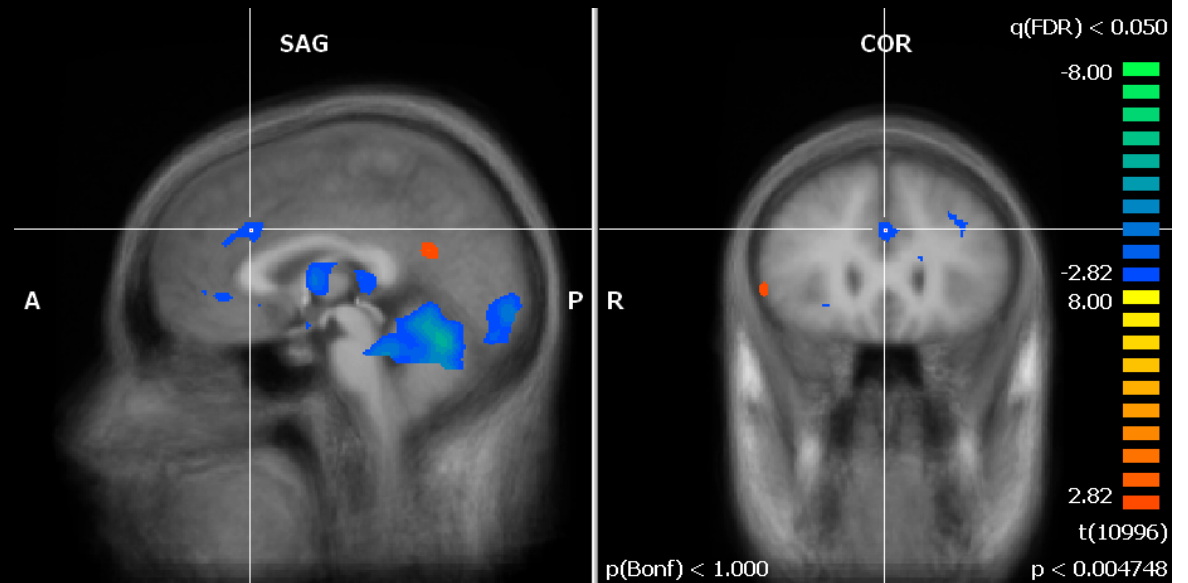
# Results

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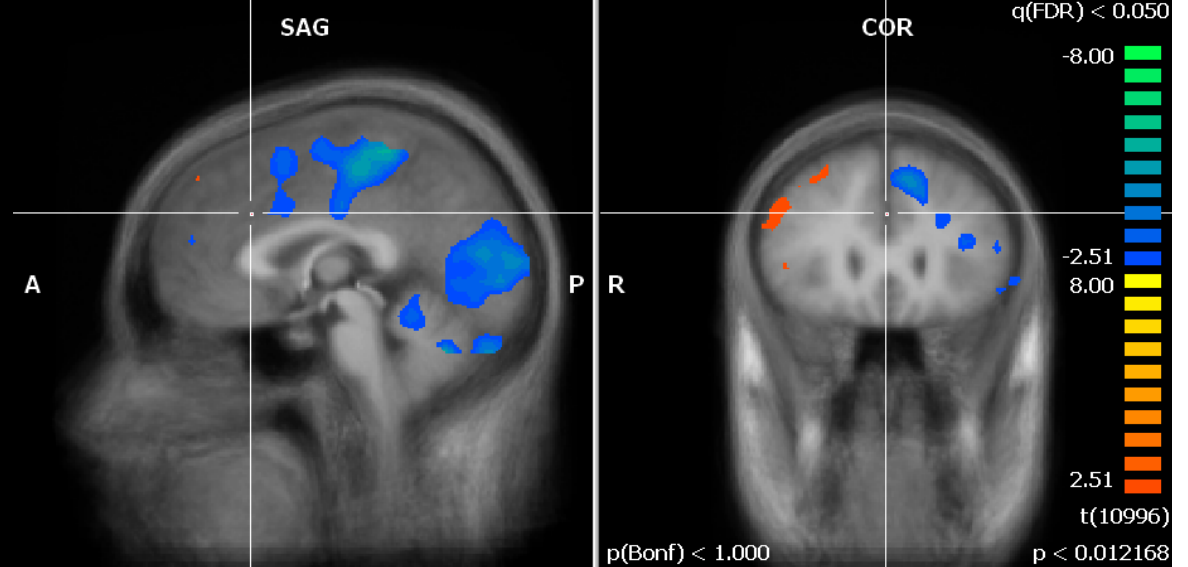
- 31 subjects analysed (17 sham, 14 CNP)
- Group differences seen in the processing within anterior cingulate, bilateral hippocampus/caudate, as well as the ipsilateral insula

# Anterior Cingulate

CNP Post-Pre

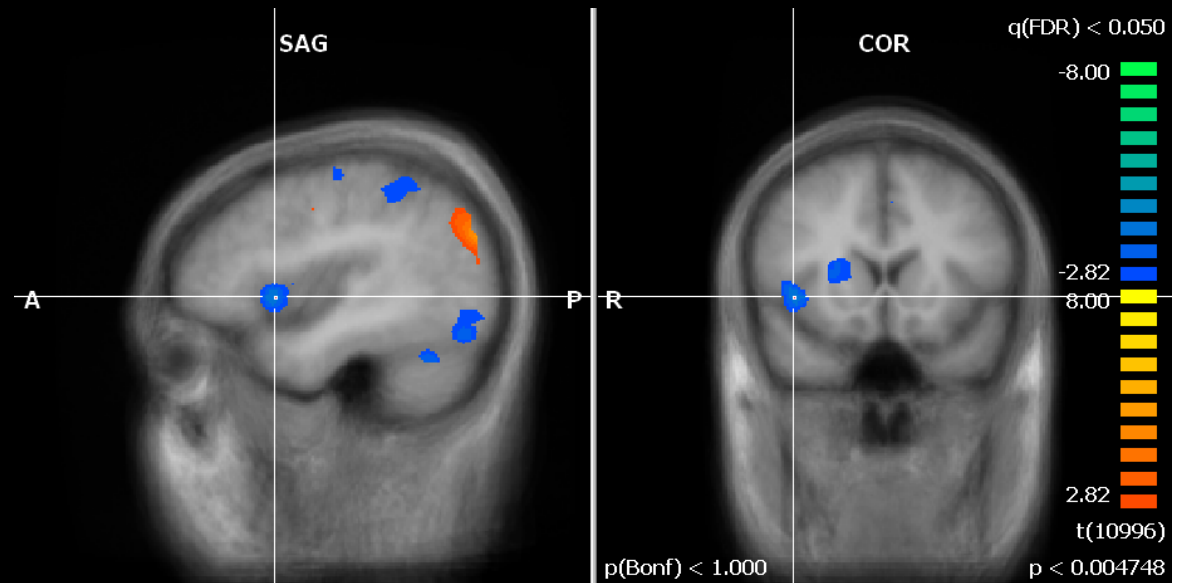


Sham Post-Pre

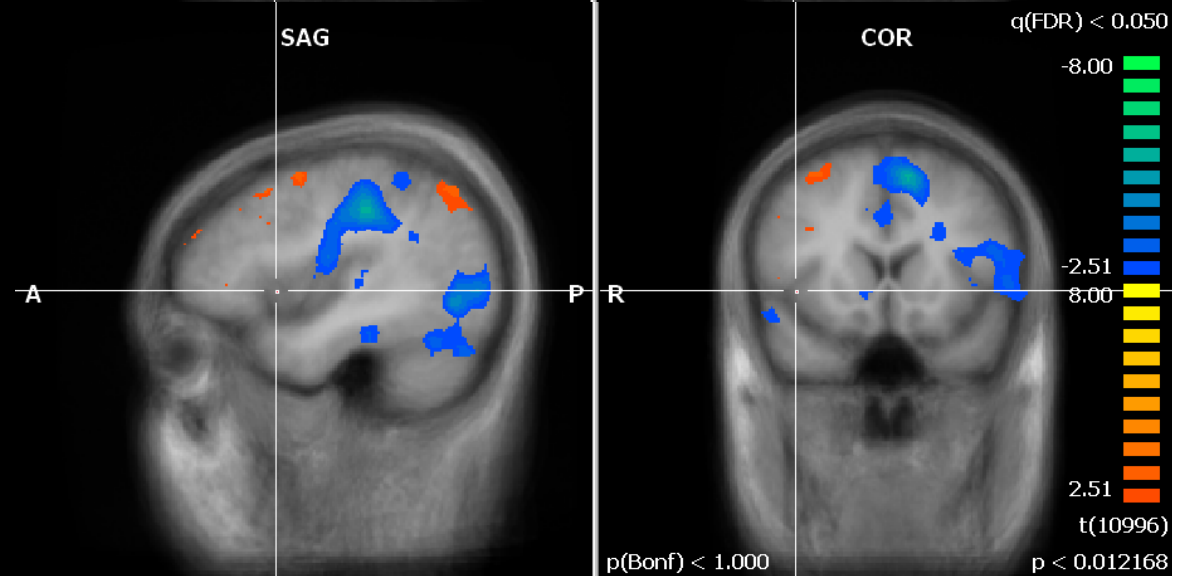


# Insula

CNP Post-Pre

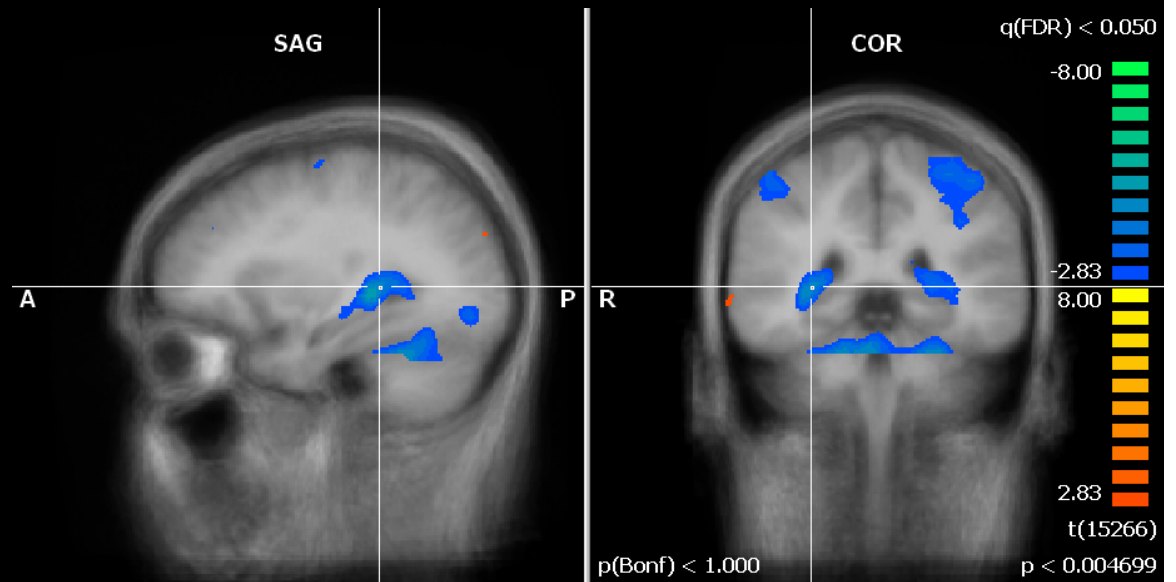


Sham Post-Pre

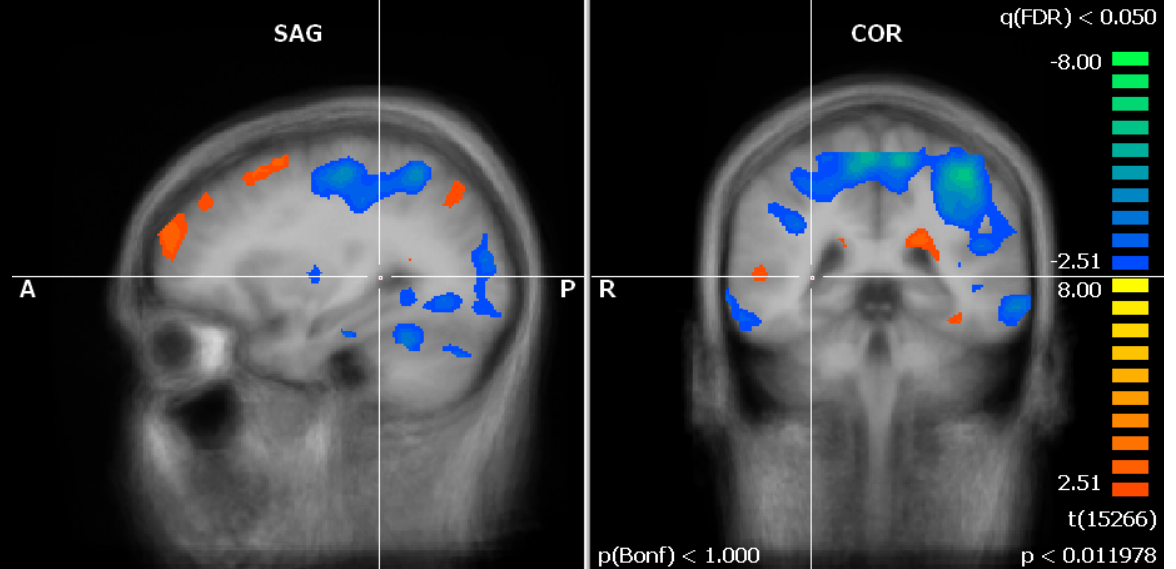


# Hippocampus/Caudate

CNP Post-Pre



Sham Post-Pre

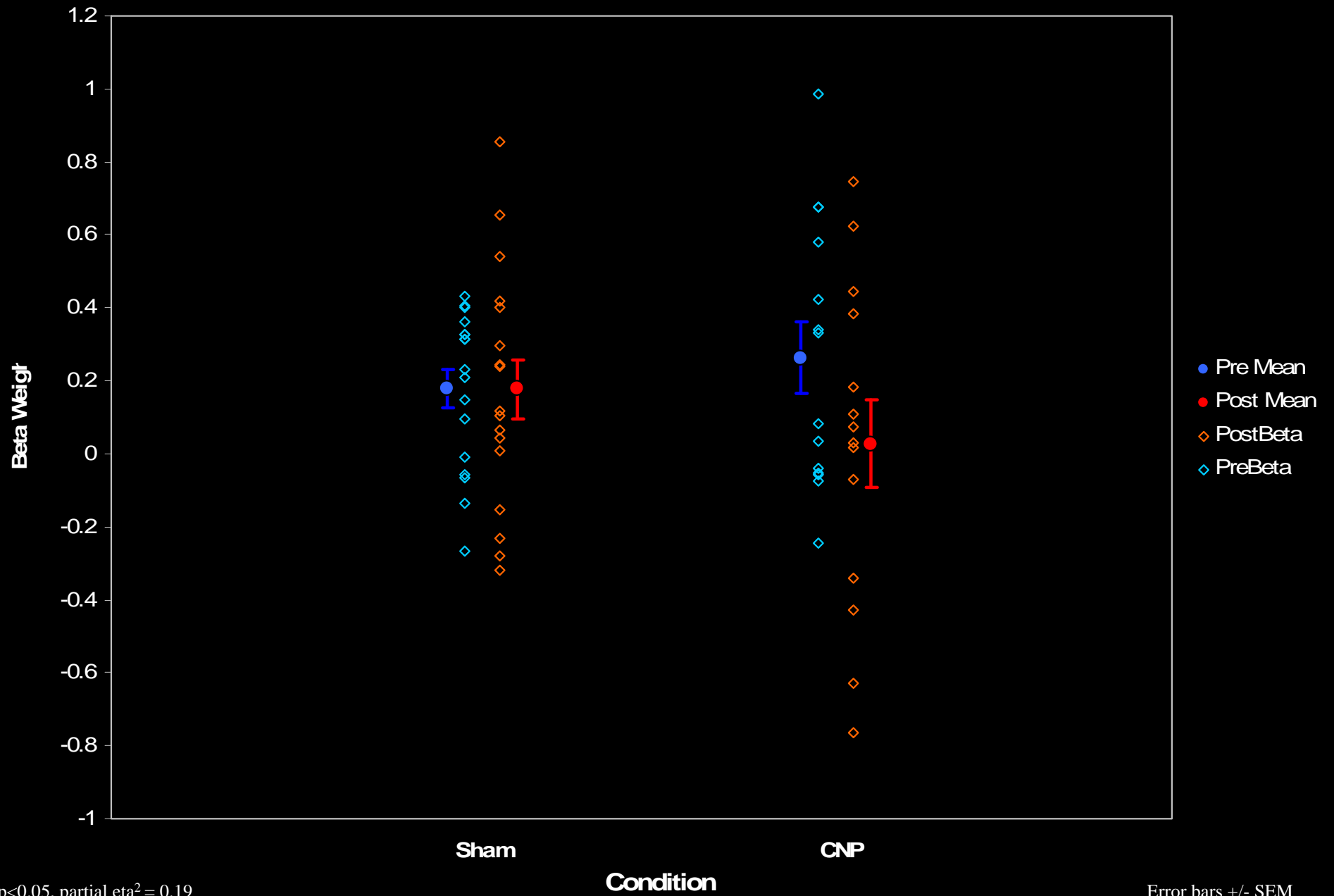


# Post Hoc Analysis

- Volumes of Interest (VOIs) taken from BrainVoyager images (1 cm<sup>3</sup>)
- Beta weights analyzed in SPSS
- Significant interactions found for several areas

<u>Region</u>	<u>Interaction F</u>	<u>Interaction p</u>	<u>Partial eta-squared</u>	<u>Observed power</u>
Anterior cingulate	$F_{1,29} = 6.834$	$p < 0.05$	0.19	0.72
Insula (ipsilateral)	$F_{1,29} = 5.204$	$p < 0.05$	0.15	0.60
Hippocampus/Caudate (ipsilateral)	$F_{1,29} = 13.803$	$p < 0.01$	0.32	0.94
Hippocampus/Caudate (contralateral)	$F_{1,29} = 6.055$	$p < 0.05$	0.17	0.66

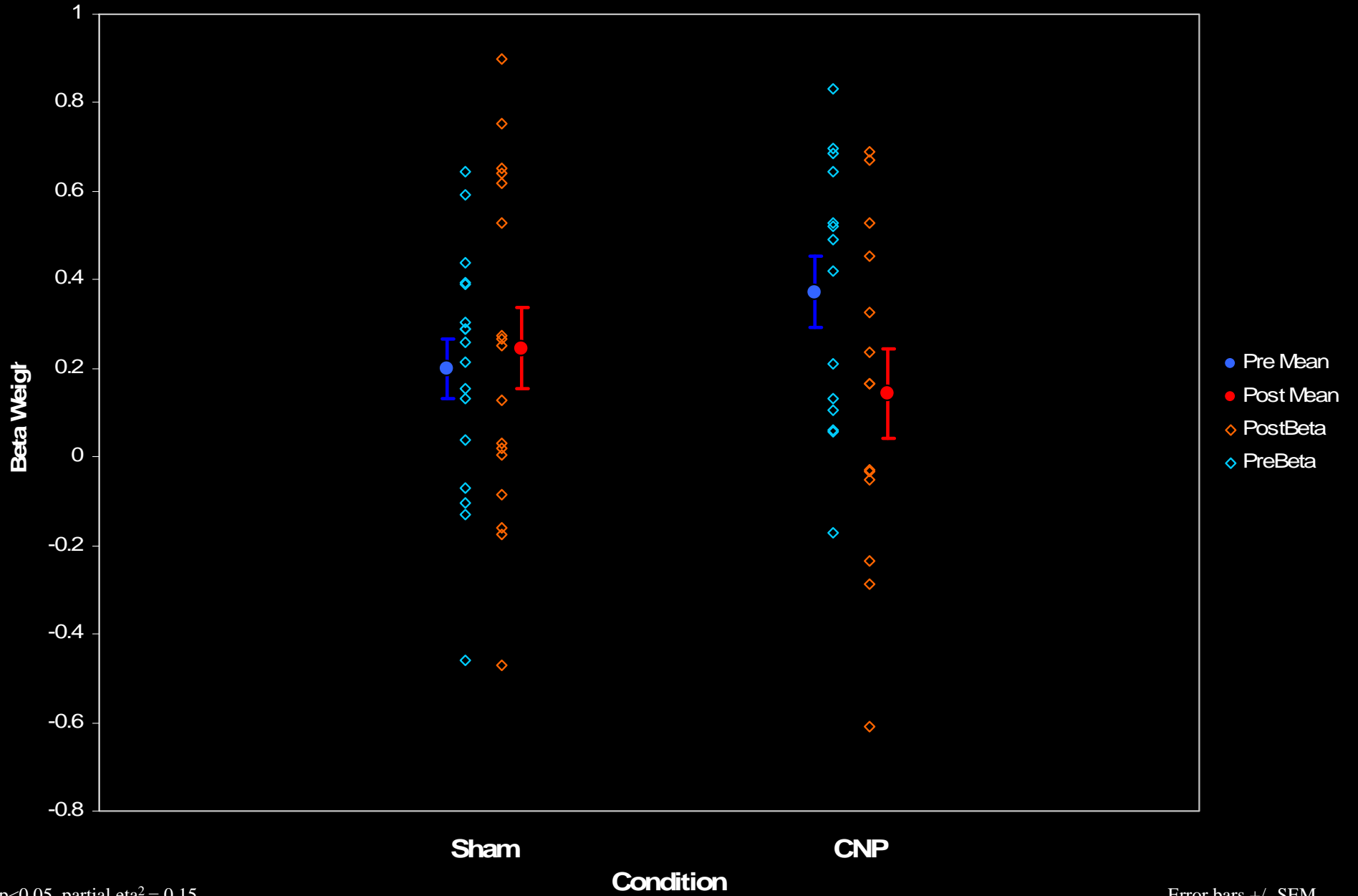
# Anterior Cingulate Beta Weight ROI



p<0.05, partial eta<sup>2</sup> = 0.19

Error bars +/- SEM

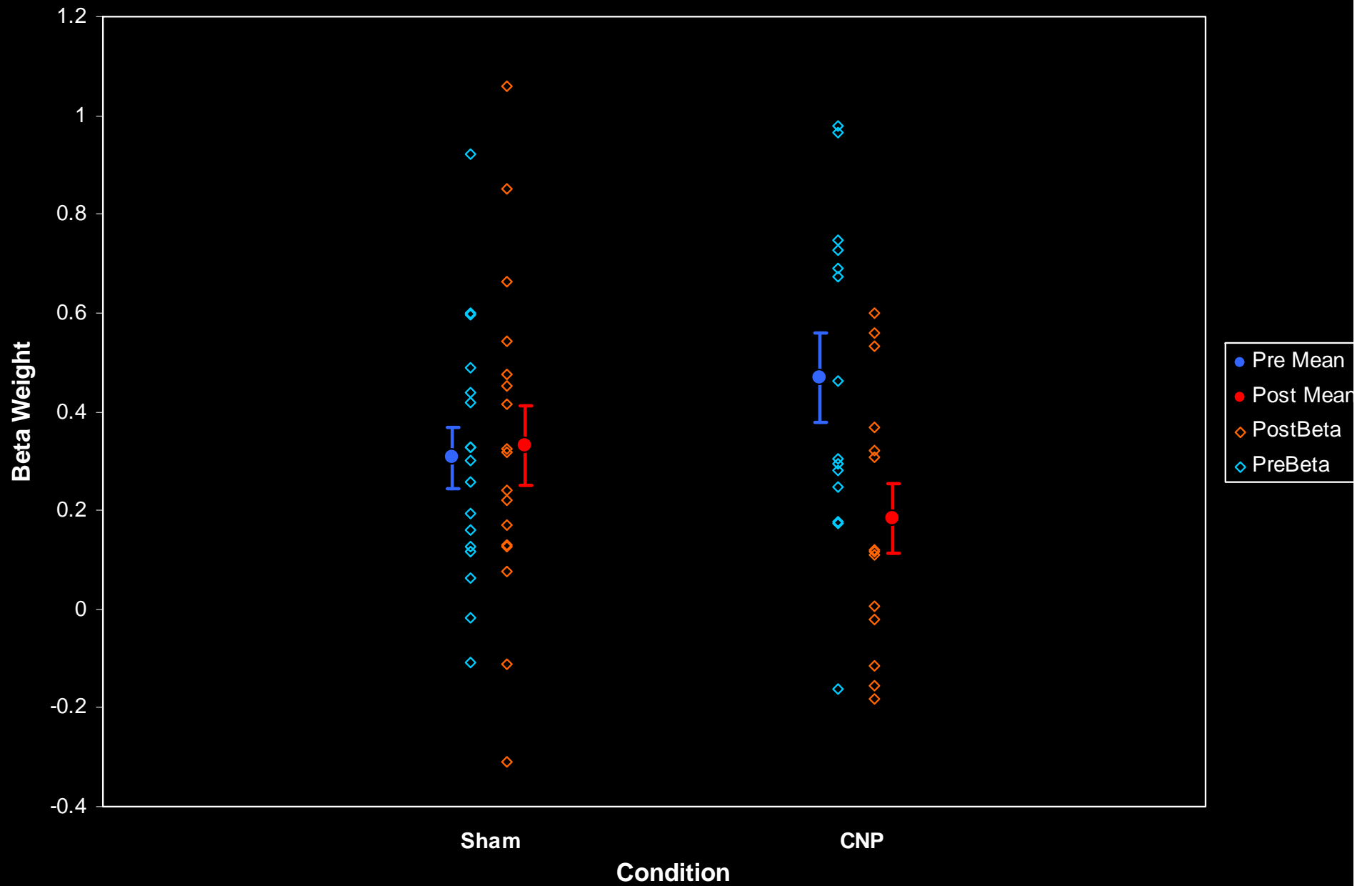
# Insula Beta Weight ROI



p<0.05, partial eta<sup>2</sup> = 0.15

Error bars +/- SEM

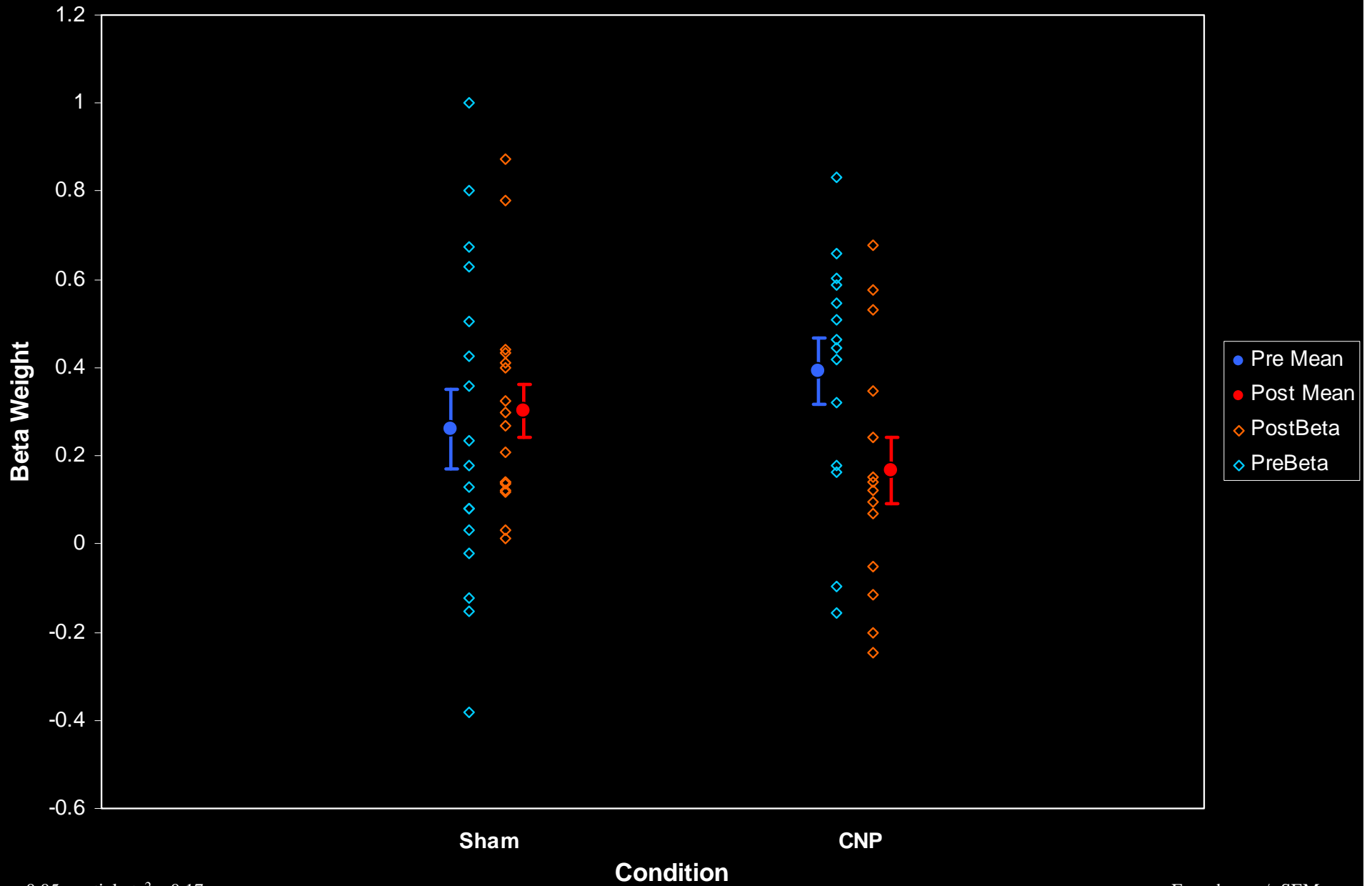
# Ipsilateral Hippocampus/Caudate Beta Weight ROI



$p < 0.01$ , partial  $\eta^2 = 0.32$

Error bars +/- SEM

# Contralateral Hippocampus/Caudate Beta Weight ROI



$p < 0.05$ , partial  $\eta^2 = 0.17$

Error bars +/- SEM

# Conclusions

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- Using the CNP within an MRI system, differences were seen in the processing of pain
- fMRI appears to be more sensitive to pain processing changes than subjective ratings
- The activation changes may shed some light on the CNP's mechanism and specificity

# Acknowledgments

- **Committee:**
  - Alex Thomas, PhD
  - Dick Drost, PhD
  - Dwight Moulin, MD
  - Keith St. Lawrence, PhD
  - Frank Prato, PhD
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# Thank You!

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- If you have any questions, feel free to contact me:

John Robertson

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# Confounds to Remember

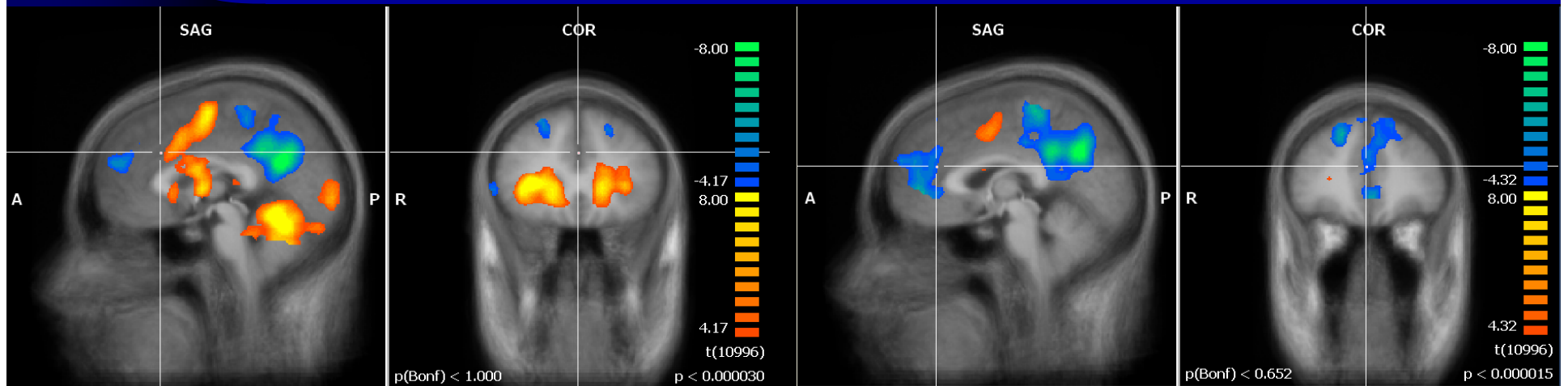
- The MRI produces a lot of electromagnetic fields for the imaging process
  - Static magnetic field (1.5 T)
  - Gradient switching (~mT/m fields changing in ms)
  - Radiofrequency pulses (~64 MHz)
- The spatial gradient is a different profile from fields used previously
- 15 minutes is the shortest CNP exposure tested to date

# Pre-Processing

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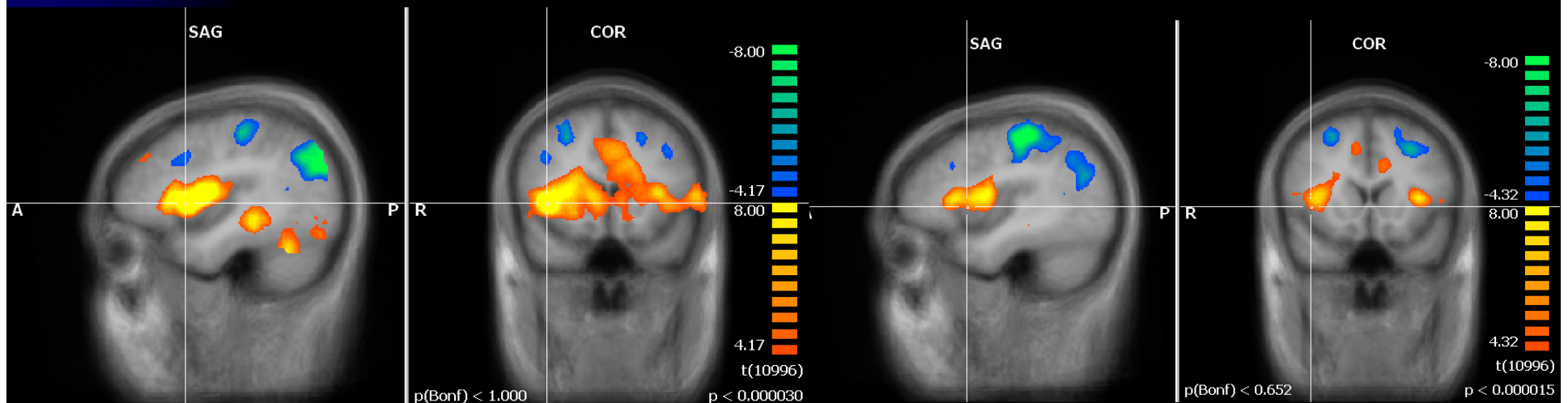
- “Reverse” 3D motion correction
- Temporal filtering (>3 cycles/run)
- Talairach transformation
- Spatial smoothing (8mm Gaussian FWHM)

# CNP pre + post

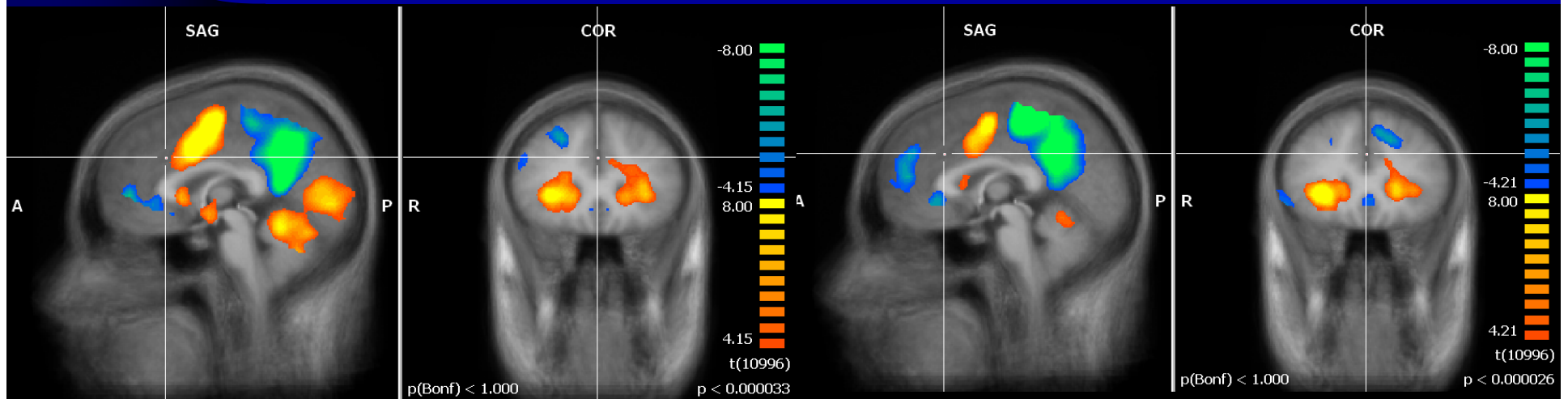


Pre

Post

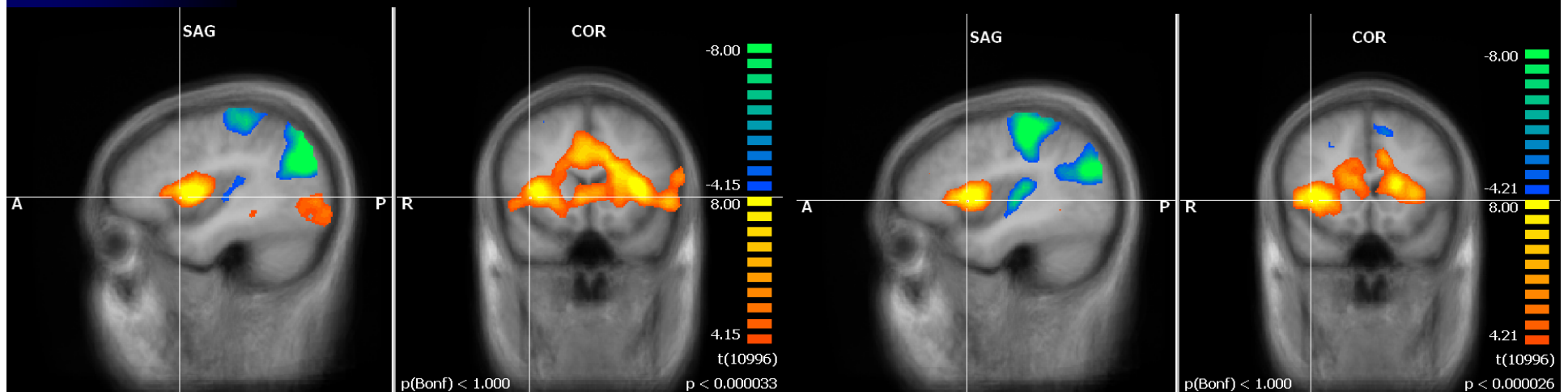


# Sham Pre + Post



Pre

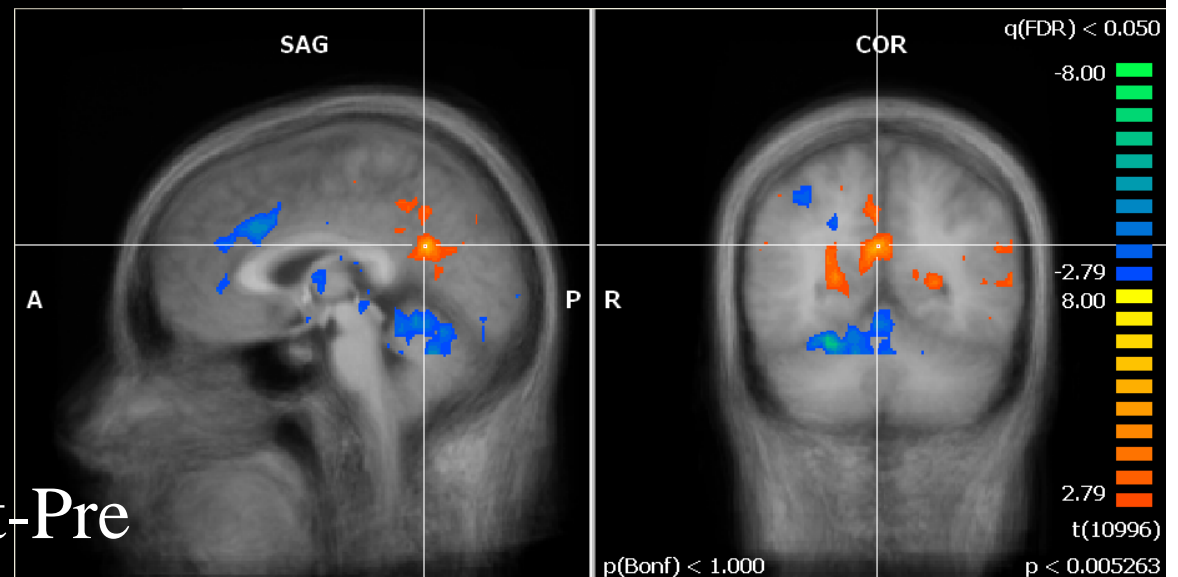
Post



# Posterior Cingulate

- No significant interaction in post-hoc analysis

CNP Post-Pre



Sham Post-Pre

