Can integrated Pain Management Strategies of CBT and Relapse Prevention Alter CNS Function and Structure?

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CBT

- Cognitive-Behavioral Therapy (CBT) is effective for chronic pain management

- However, maintenance of coping skills after completing CBT is variable and patients often experience decline in therapeutic benefit within several weeks

- The transition from skills used under the therapist's guidance to long term maintenance without guidance is difficult

- Interactive Voice Response (IVR) is a promising technology for this transition

Study purpose:

To test if:

1. Interactive Voice Response (IVR) can be used as a therapeutic tool to enhance and extend the use of coping skills patients learn in group CBT.

2. To test if the use of Therapeutic IVR (TIVR) could significantly reduce relapse into pain behavior.

3. To test if TIVR use could decrease opioid analgesic medication use

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Interventions:

1. Group Behavioral/Cognitive therapy (CST-coping skills training)

2. Therapeutic Interactive Voice Response Program

Group Behavioral/Cognitive therapy teaches pain coping skills:

a. relaxation techniques
b. cognitive coping strategies
c. challenge pain beliefs,
d. setting treatment goals,
e. increase self monitoring (pain diaries),
f. enhance social support.

What is Therapeutic IVR (TIVR)?

- IVR is a method for interaction between an individual and a computer through a telephone. An automated script poses questions and the caller enters responses using the telephone keypad.

- The TIVR was created as an extension of CBT group therapy and is based on a relapse prevention model of behavior change.

Therapeutic IVR

There are four components of Therapeutic IVR:

Component 1--Self-monitoring 21-item Daily Questionnaire

Component 2—Prerecorded didactic skills review

Component 3—Prerecorded behavioral skills practice

Component 4—Monthly therapist feedback

Recorded personalized message summarizing clinical progress based on TIVR daily reports

Monthly Message data analysis:

Correlation between:

1. pain level and coping skills
2. pain and daily relaxation practice
3. pain, sleep quality and activity level
4. pain vs sadness, anger, catastrophizing, and perception of control
5. coping skills and relationships
6. others…

Results then are formulated as a monthly "special message" (therapeutic feedback).

Single Subject Daily Pain TIVR Data

Four-Month Trends 7-Day Moving Averages

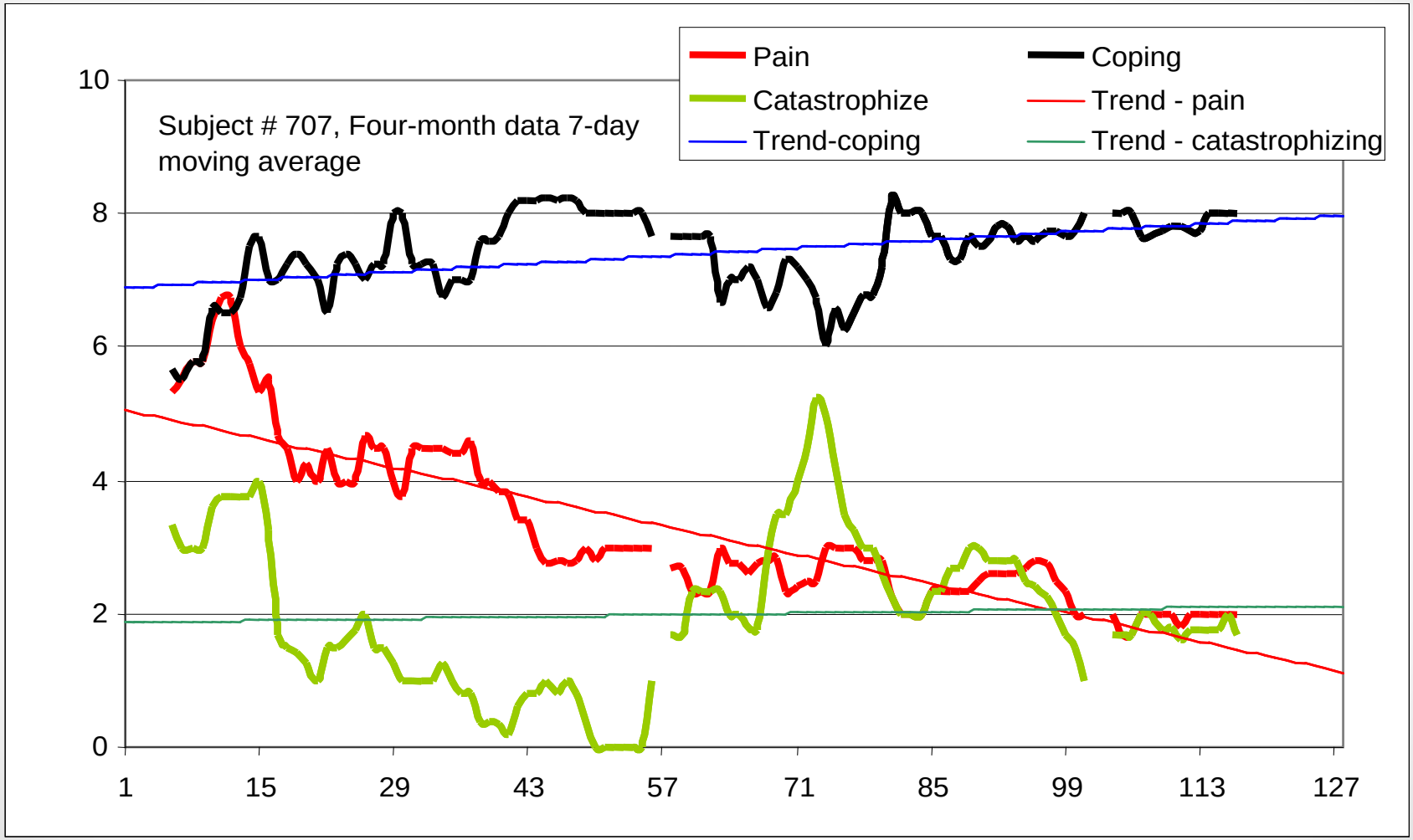
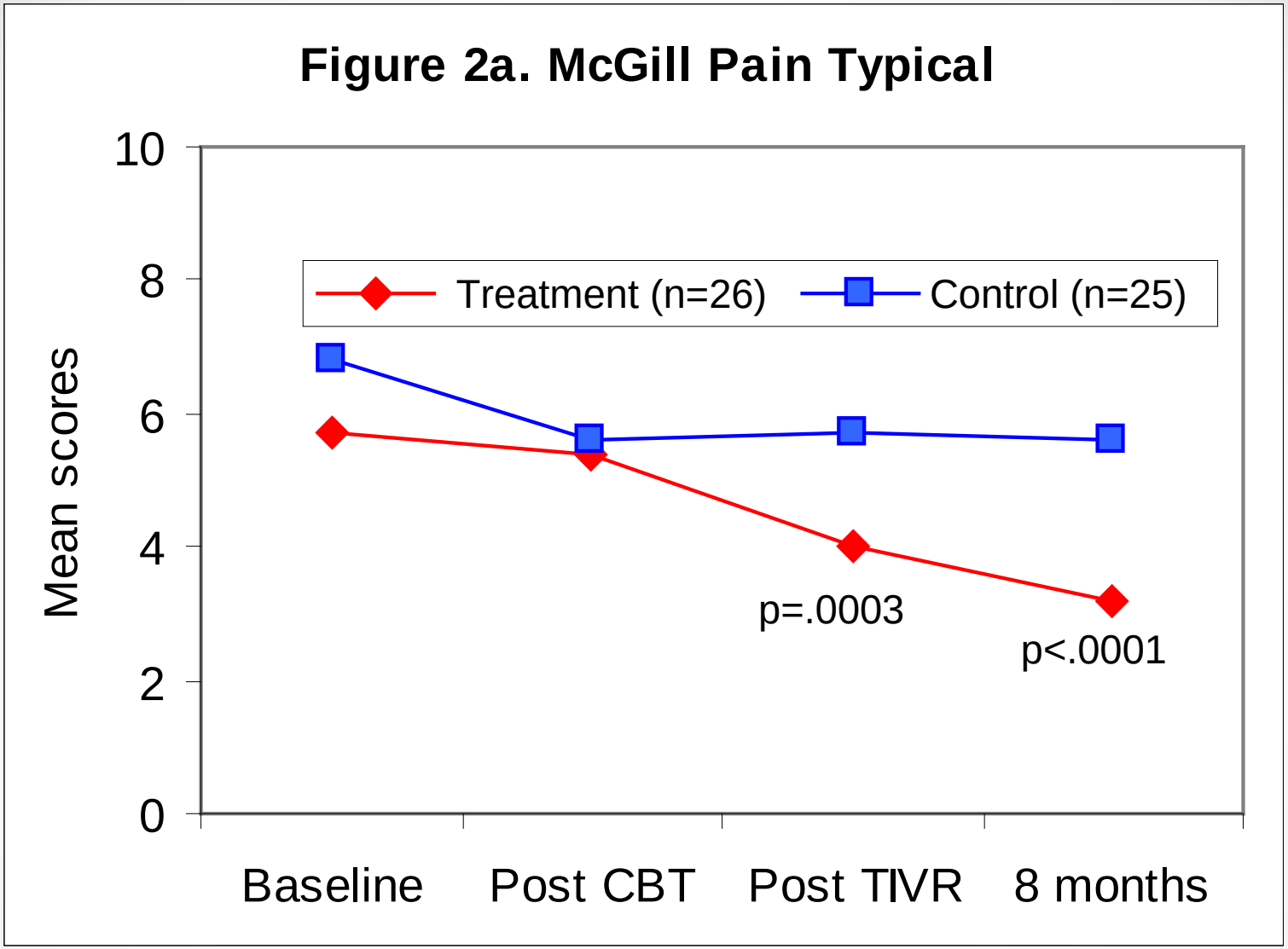


Table 1. Effectiveness of the group CST as an intervention for chronic pain

Test (N-50)	p-value Paired t-test	Mean difference (baseline – post CST)	Effect size
SF-36 Mental Composite	.003	-4.7 (±10.4)	.45
SF-36 Physical Composite	.06	-1.7 (±6.2)	.27
MPQ Pain Now	.01	1.0 (±2.6)	.38
MPQ Pain Typical	.02	.67(±2.1)	.32
CSQ Catastrophize	<.0001	7.0 (±7.6)	.92
CSQ Ability to Control Pain	<.0001	-1.0 (±1.3)	.77
CSQ Ability to Decrease Pain	.0004	-.6 (±1.1)	.55
TOPS Social Disability	.0006	7.1 (±13.7)	.52
TOPS Pain Symptom	.002	6.3 (±13.7)	.46
TOPS Total Pain Experience	<.0001	5.9 (±9.4)	.63
TOPS Life Control	<.0001	12.8(±17.6)	.58

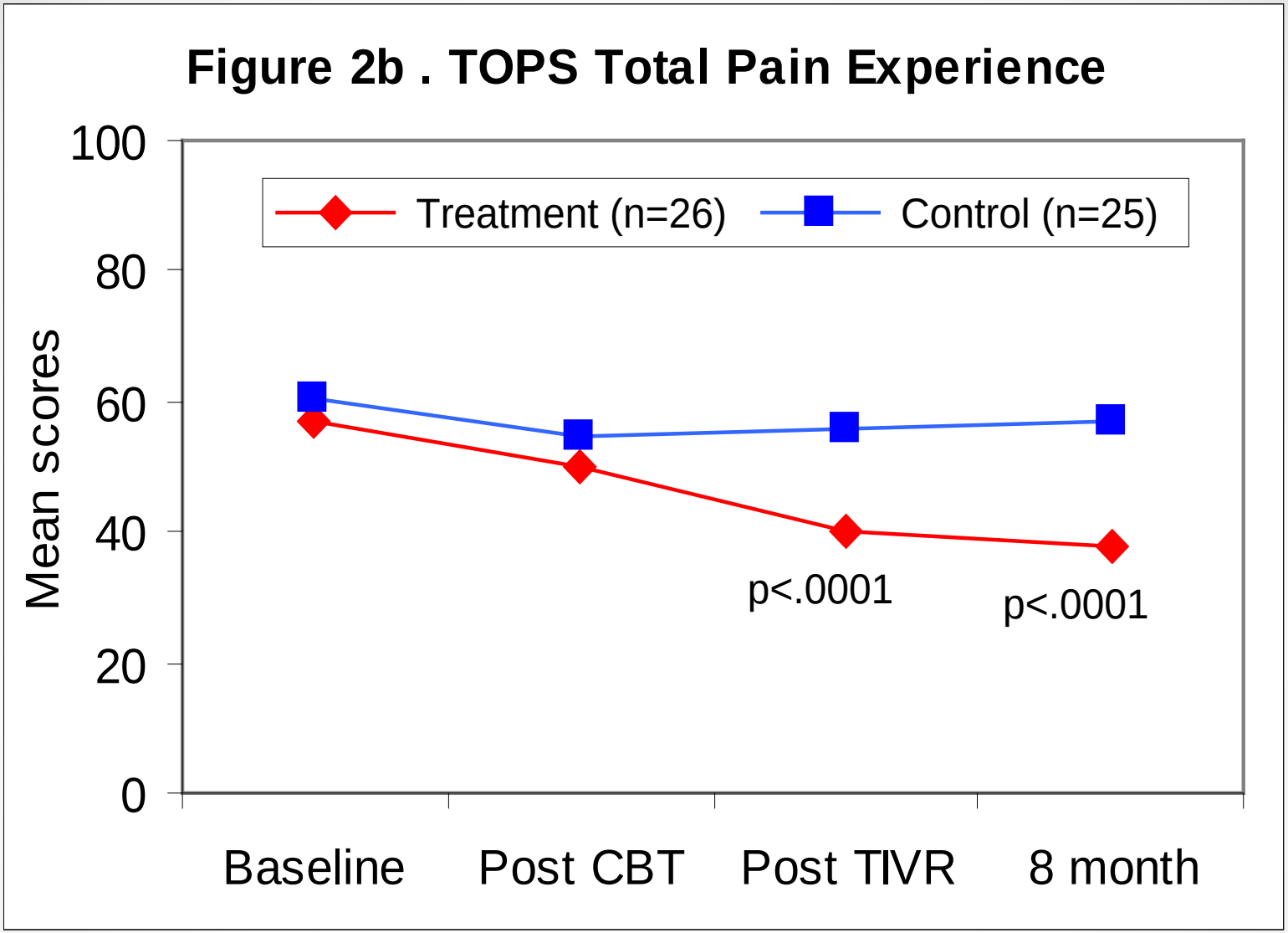
Was TIVR effective as a relapse prevention for chronic pain?



FIGURES 2a-d LEGEND

Figures 2a-d. Mean scores for the control and TIVR groups at four time points. The two groups' scores were similar at post-CBT but became significantly different by the end of the TIVR intervention and more so by the last follow-up since the TIVR group continued to improve. The p-values are reported for the between-group comparisons, adjusted for post-CBT differences (ANCOVA), at the last two assessments.

Naylor, MR, et al, Pain, 2008



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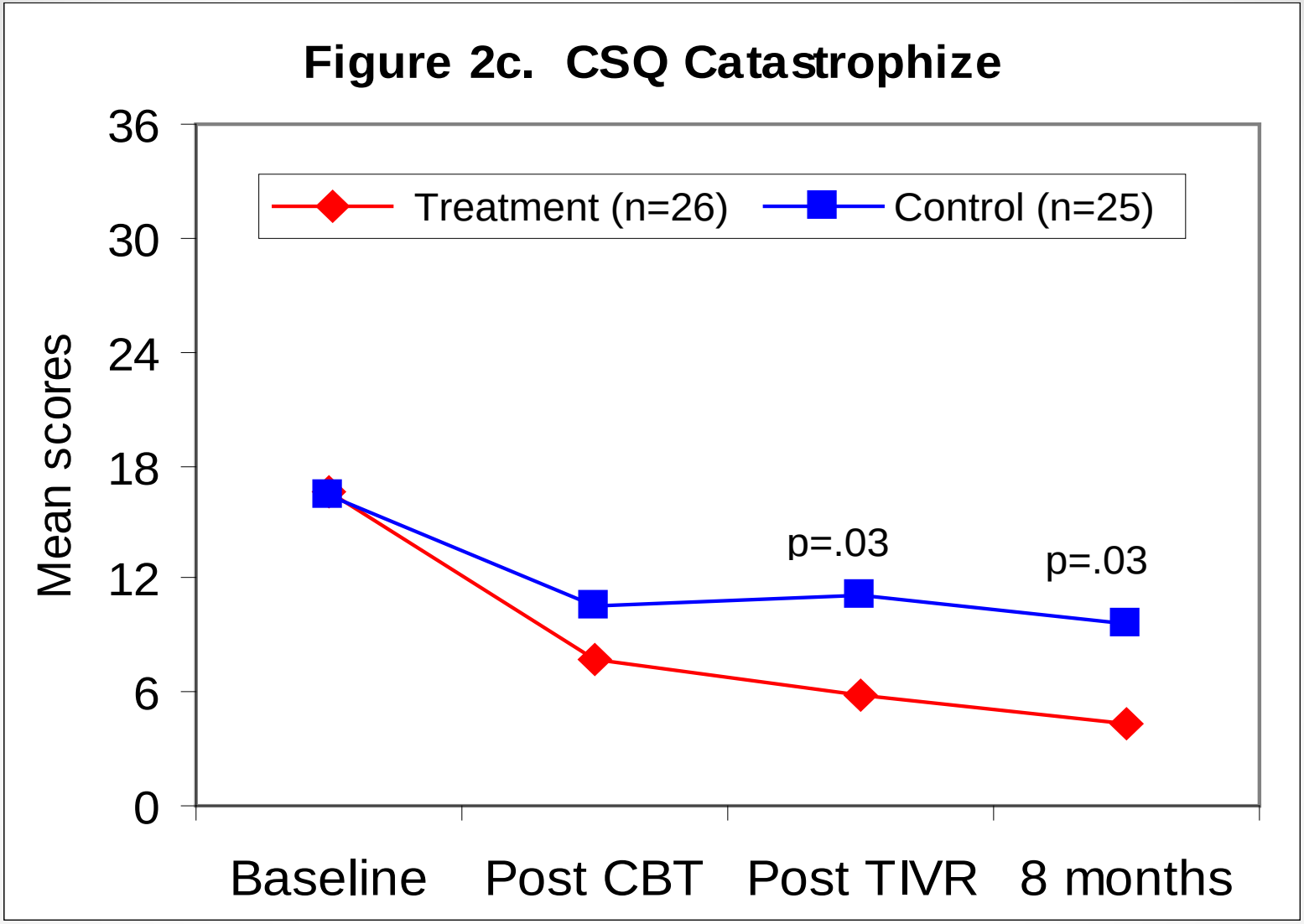

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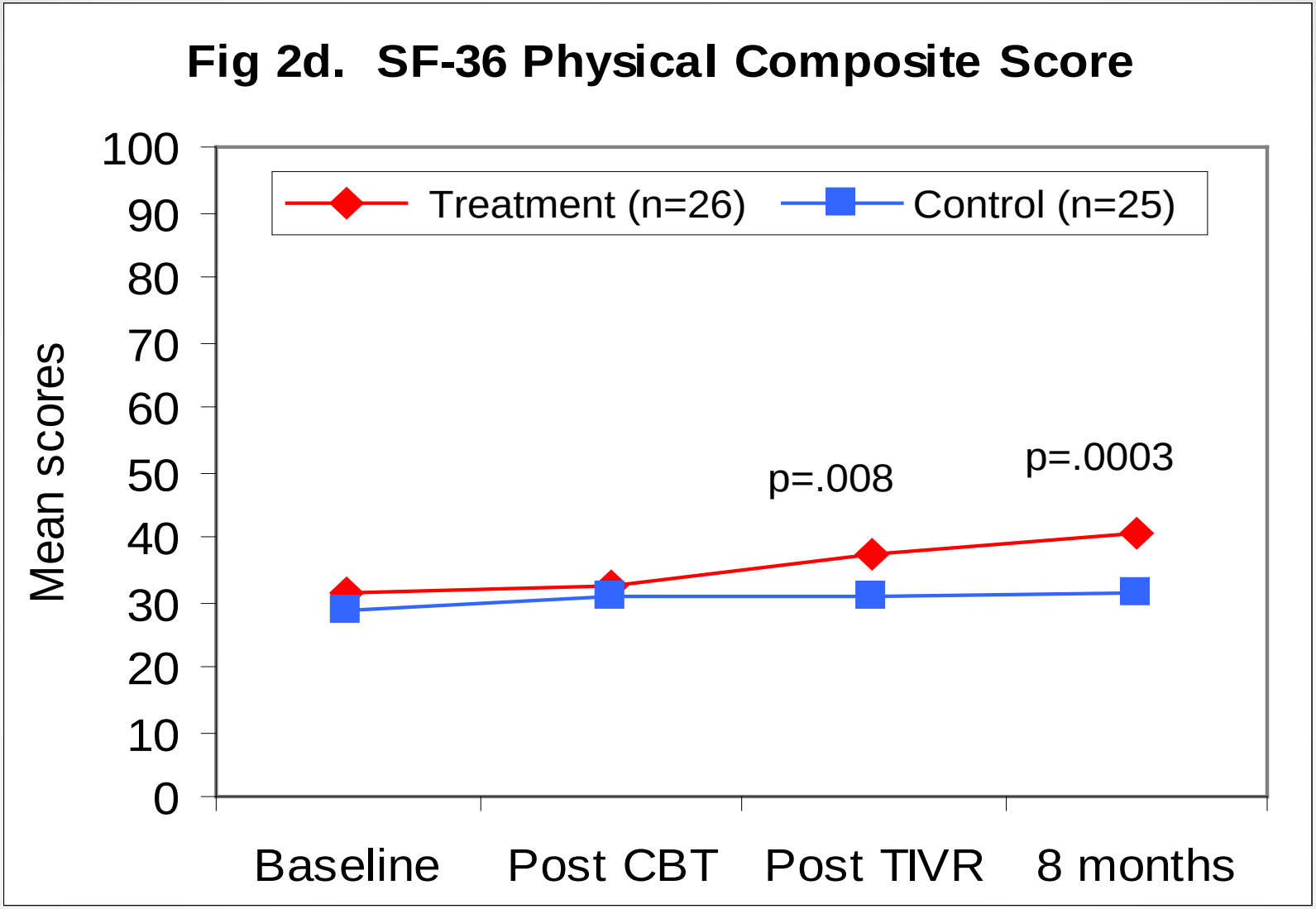

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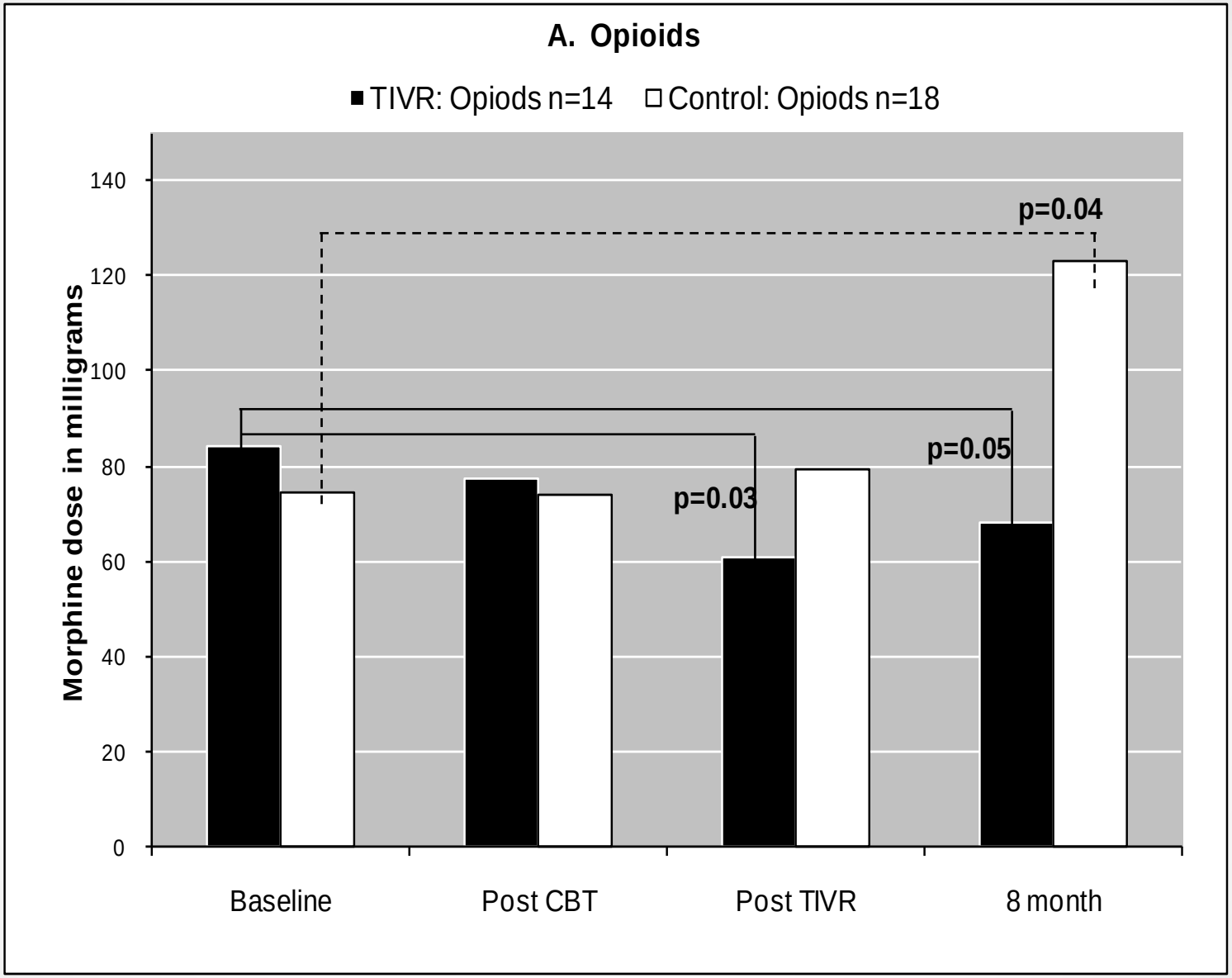
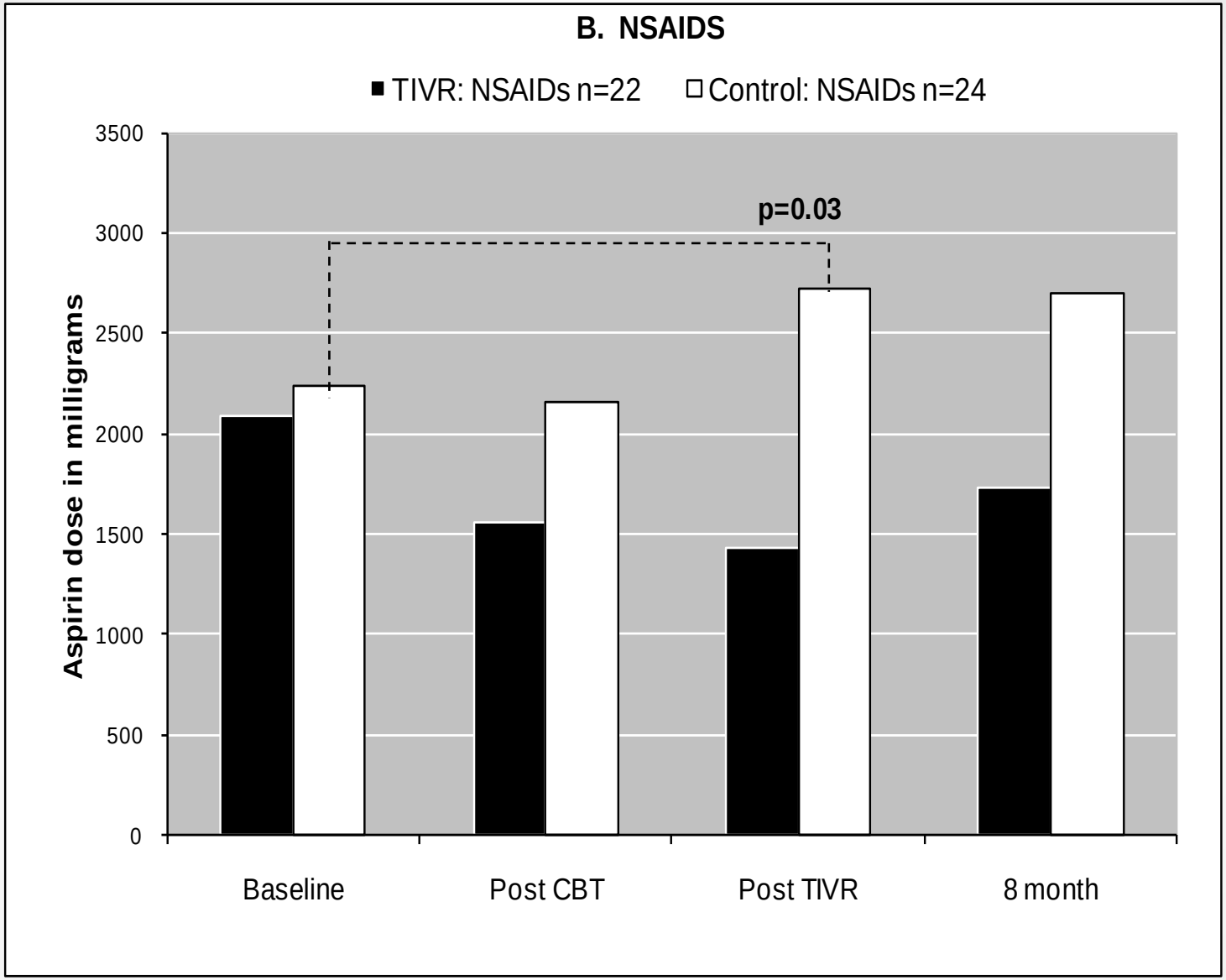
Naylor, MR, et al, Pain, 2008

Was TIVR helpful in concurrent decrease of opioid medication use?



Naylor, MR, et al, Journal of Pain, in print



Non Steroidal Anti-Inflammatory

Naylor, MR, et al, Journal of Pain, in print

Our recent NIH NIAMS sponsored study was designed to:

1. Replicate our pilot study results on a larger sample, and

2. To test a hypothesis that the TIVR with a "minimal" Monthly Message will be as effective relapse prevention intervention as the TIVR with a "full" Monthly Message (tested in a pilot study

Study design

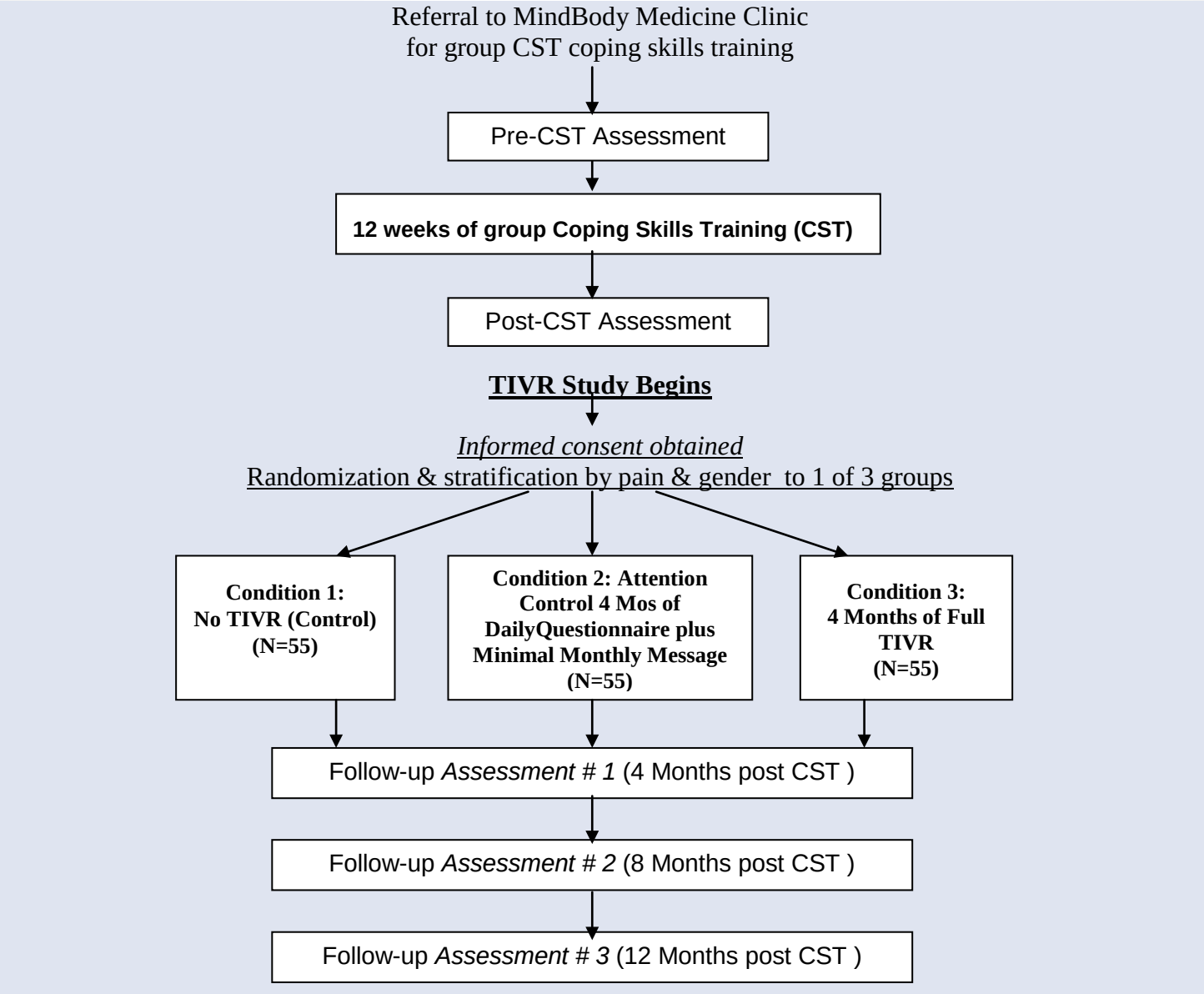


Table .
Demographics for each group and total sample

	Full TIVR N=49	Minimal TIVR N=50	Control Group N=52	Total Sample N=151
Age	$\bar{x}$ = 48 ± 10.94	$\bar{x}$ = 46 ± 11.36	$\bar{x}$ = 48 ± 10.05	$\bar{x}$ = 47 ± 10.77
Gender				
• Females	36 (73%)	39 (78%)	40 (77%)	115 (76%)
Race				
• White/Caucasian	46 (94%)	47 (94%)	49 (94%)	142 (94%)
Martial Status				
• Never Married	7 (14.9%)	6 (12%)	8 (15.38%)	21 (13.91%)
• Married/Living Together	29 (59.18%)	34 (68%)	34 (65.38%)	97 (64.24%)
• Divorced/Separated	12 (24.49%)	9 (18%)	9 (17.31%)	30 (19.87%)
Education in Years	$\bar{x}$ =14.39 ± 1.97	$\bar{x}$ =14.26 ± 1.82	$\bar{x}$ =13.98 ± 2.01	$\bar{x}$ =14.21 ± 1.93
• 9-12 years	12 (25%)	14 (28%)	20 (38.5%)	46 (30%)
• 13-16 years	28 (57%)	30 (60%)	25 (48%)	83 (55%)
• 17+ years	9 (18%)	6 (12%)	7 (13.5%)	22 (15%)
• Did not report education	0	0	0	0
Employment Status				
• full time employment	10 (20.41%)	13 (26%)	9 (17.31%)	22 (21.19%)
• part-time employment	7 (14.29%)	4 (8%)	2 (3.85%)	13 (8.61%)
• disability	18 (36.73%)	12 (24%)	20 (38.46%)	50 (33.11%)
• unemployed	5 (10.2%)	6 (12%)	4 (7.69%)	15 (9.93%)
• retired	1 (2.04%)	1 (2%)	4 (7.69%)	6 (3.97%)
Living Situation				
• 3+ person household	22 (44.9%)	18 (36%)	21 (40.38%)	61 (40.4%)
• 2 person household	18 (36.73%)	23 (46%)	21 (40.38%)	62 (41.06%)
• Living alone	9 (18.73%)	9 (18%)	10 (19.23%)	28 (18.54%)
Duration of Pain in Years	$\bar{x}$ =11.04 ± 10.74	$\bar{x}$ =11.3 ± 9.81	$\bar{x}$ =10.8 ± 10.24	$\bar{x}$ =11.04 ± 10.2
Diagnoses (primary)				
• back pain	17 (34.69%)	17 (34%)	22 (42.31%)	56 (37.09%)
• osteoarthritis	5 (10.20%)	5 (10%)	8 (15.38%)	18 (11.92%)
• fibromyalgia	9 (18.37%)	3 (6%)	10 (19.23%)	22 (14.57%)
• TMJ/jaw pain	1 (2.04%)	3 (6%)	2 (3.85%)	6 (3.97%)
• headaches	7 (14.29%)	6 (12%)	3 (5.77%)	16 (10.6%)
• post-trauma/post-surgical muscle pain	4 (8.16%)	10 (20%)	7 (13.46%)	21 (13.91%)
• other	6 (12.24%)	6 (12.00%)	0 (0%)	12 (7.95%)

Were we able to replicate our pilot study results that TIVR is an effective intervention as a relapse prevention?

Effect sizes for Full TIVR versus Control group differences in improvement.

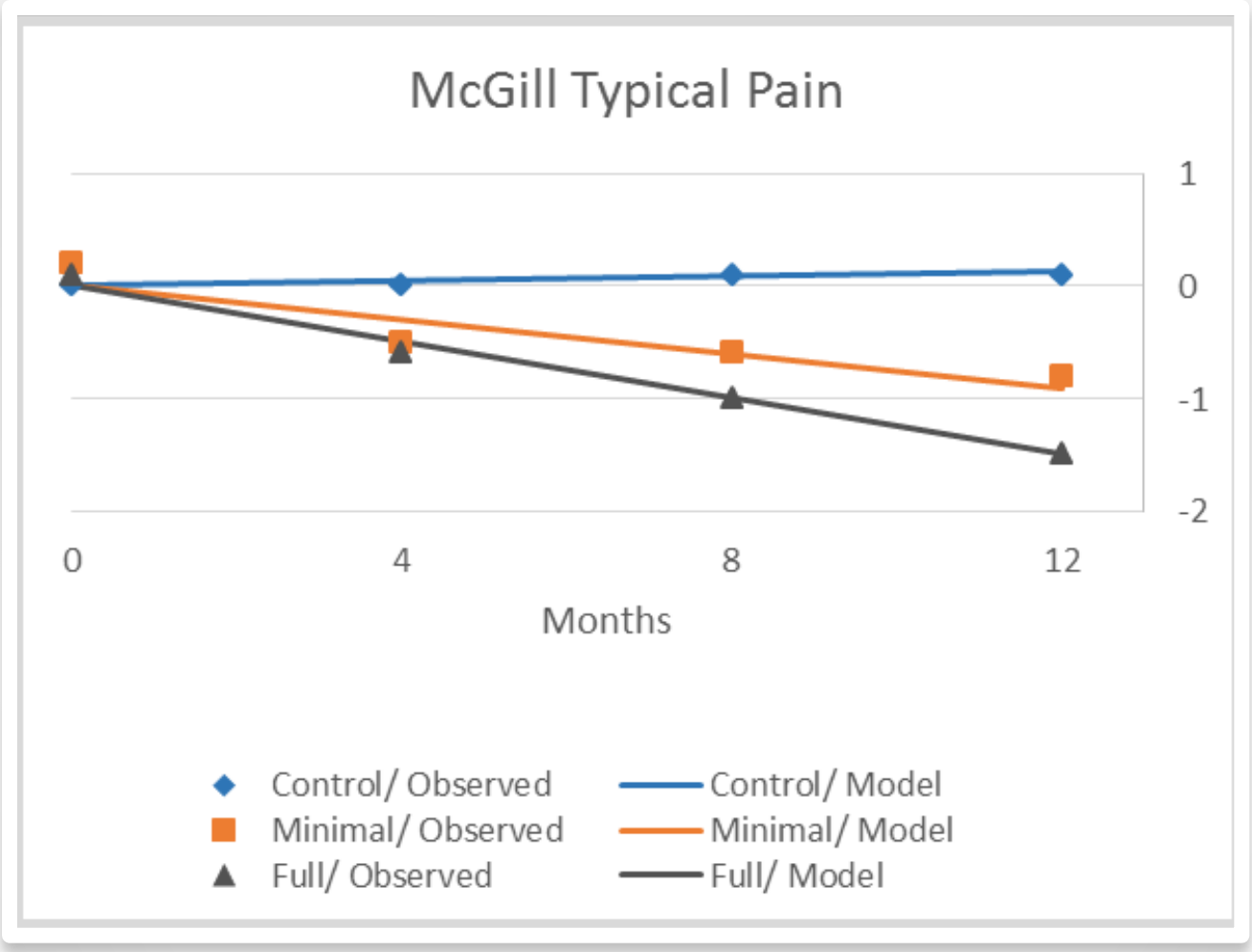
Effect sizes for Full TIVR versus Control group differences in improvement.			
Test	**Post CBT (1)**	**Fourth month follow-up (2)**	**One year follow-up (2)**
TOPS Total Pain Experience	0.2	0.4*	1.0 ***
SF-36 Mental Composite	0.1	0.3	0.9 ***
SF-36 Physical Composite	0.4 *	0	0.5 *
MPQ Typical Pain	0.1	0.5 *	1.2 ***
Self-efficacy for pain management	0.5 *	0.1	0.6 *
Self-efficacy for physical function	0.4	0.3	0.6 *
Self-efficacy for coping with symptoms	0.3	0.5 *	1.0 ***
CSQ Ability to Control Pain	0.1	0.5 *	1.0 ***
CSQ Catastrophize	0.4	0	0.4

(1) Post CBT group means were compared after adjusting for baseline scores. Group differences were not expected to be different.

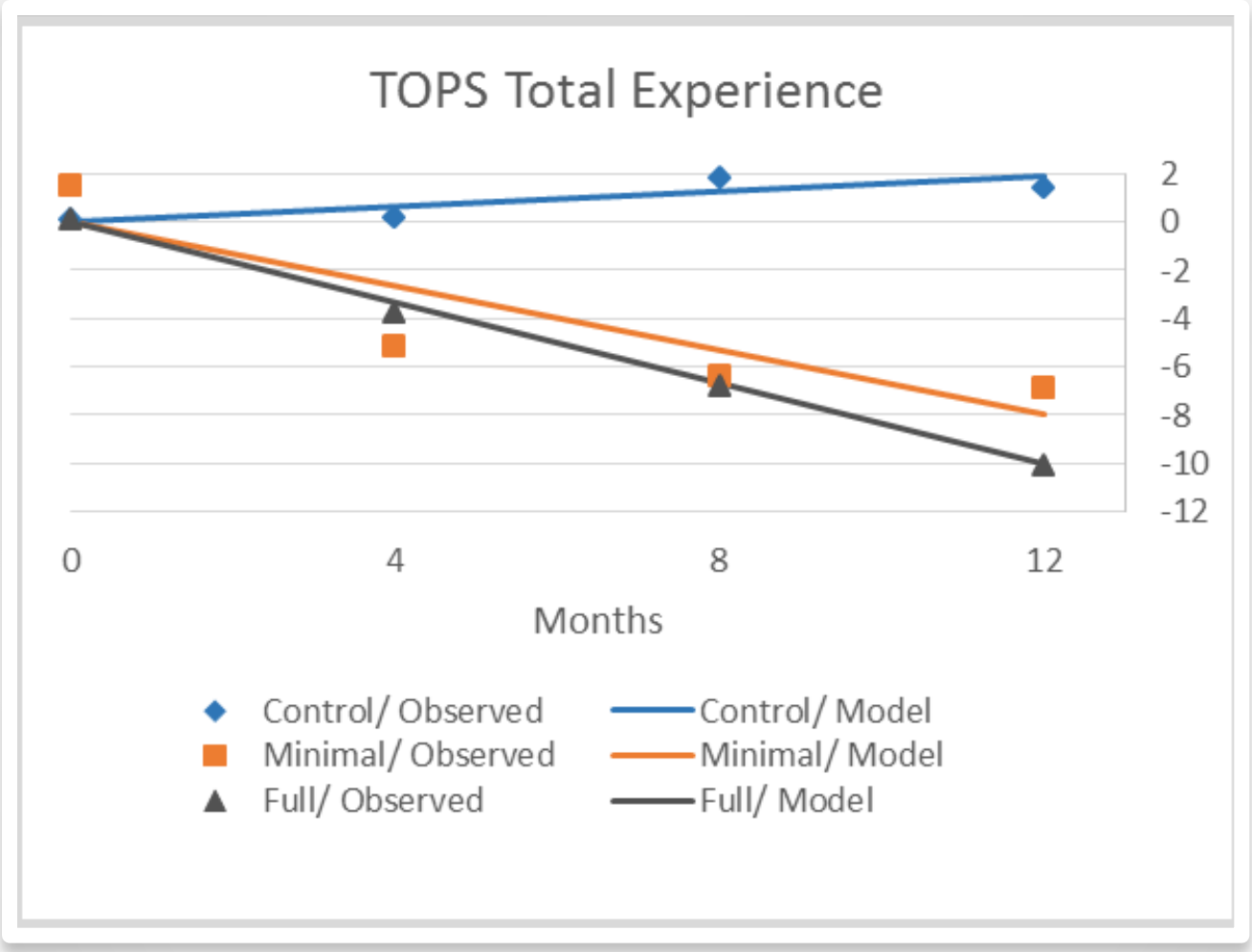
(2) Group means were compared after adjusting for post-CBT scores

Significance * p<.05, ** p<.001, *** p<.0001 Where significant, TIVR group showed more improvement

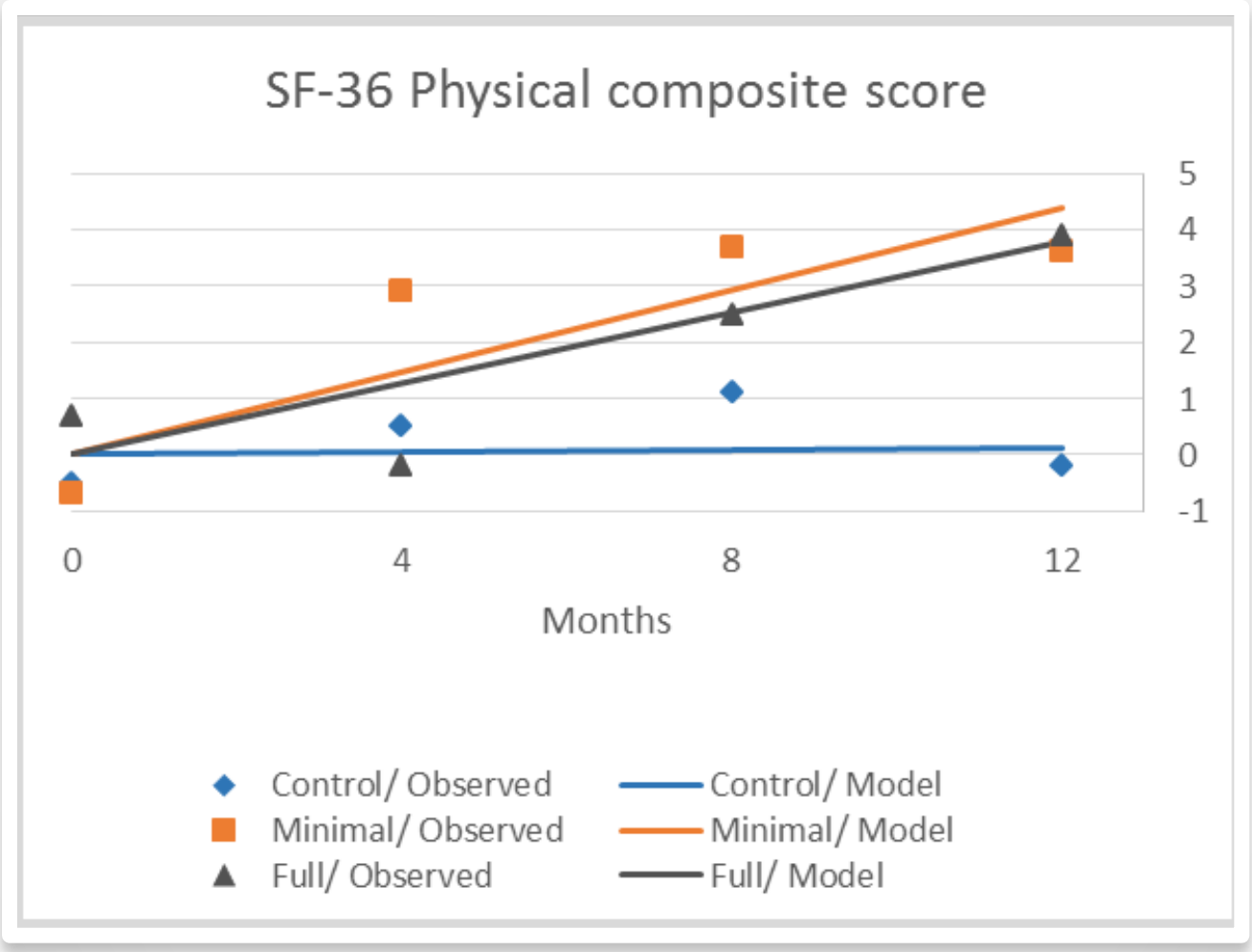
Outcome measures which improved as a result of both: Full and Minimal TIVR



Control minus Full Message: p<.0001
Control minus Minimal Message: p<.001
Minimal Message minus Full Message: NS

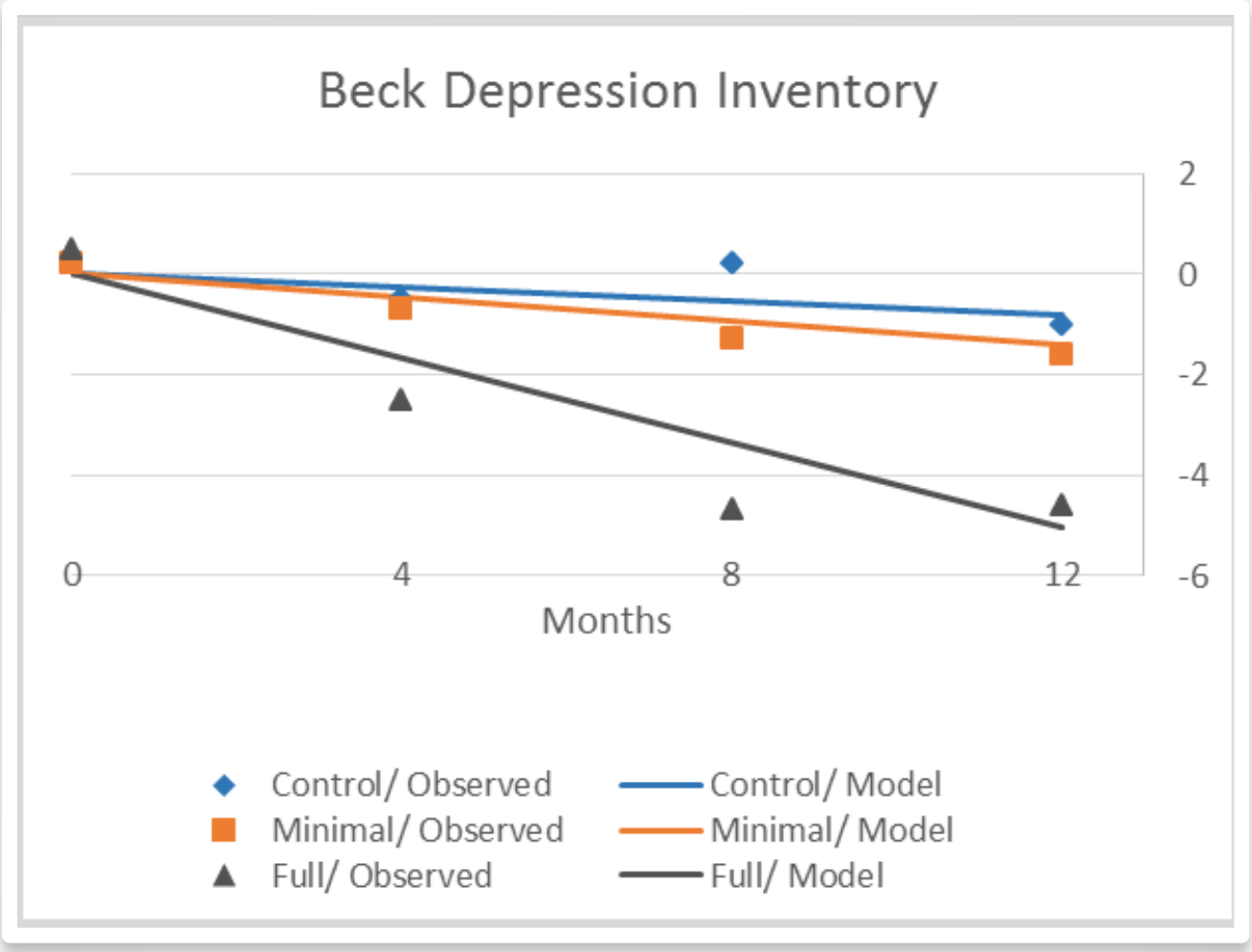


Control minus Full Message: p<.0001
Control minus Minimal Message: p<.0001
Minimal Message minus Full Message: NS

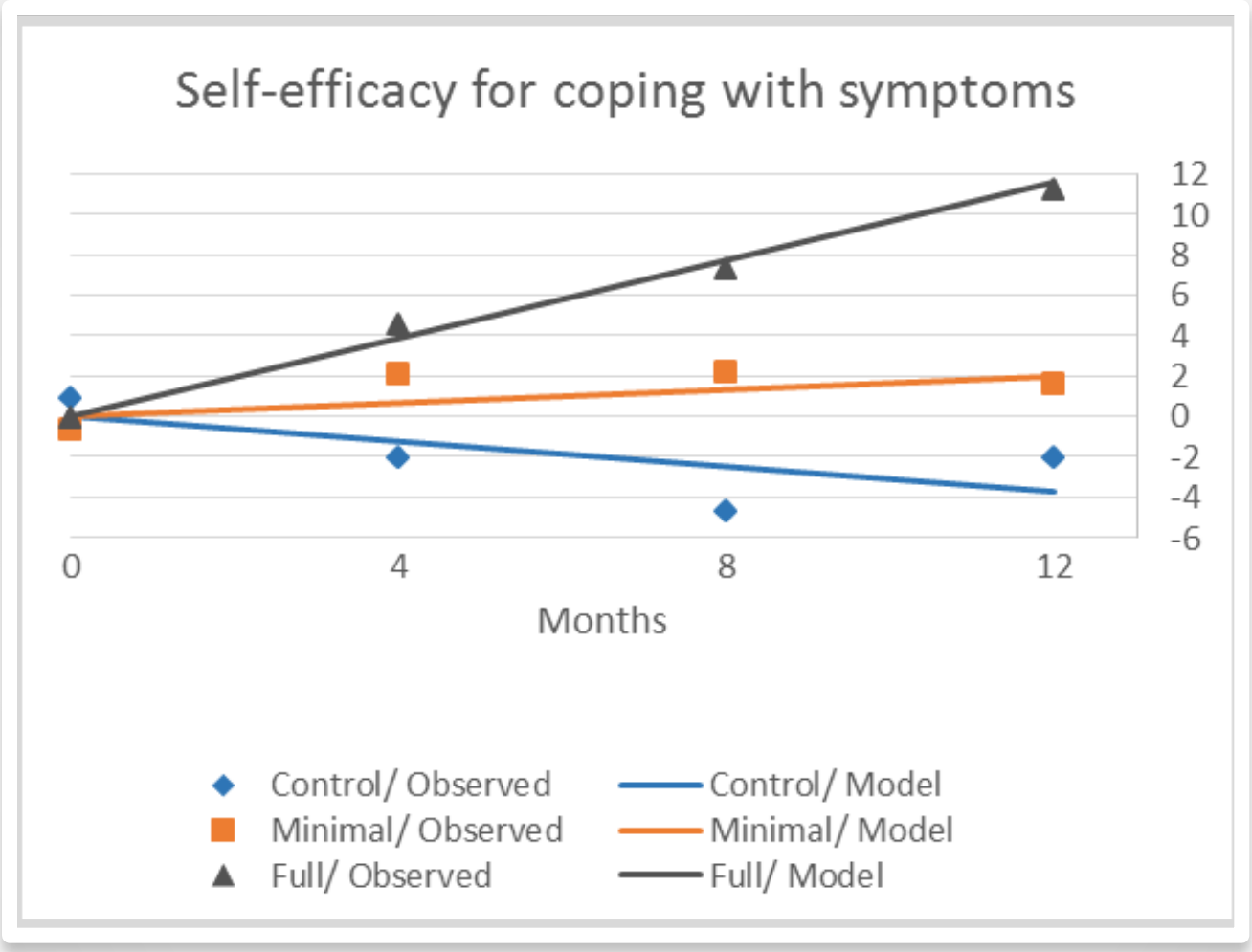


Control minus Full Message: p<.05
Control minus Minimal Message: p<.05
Minimal Message minus Full Message: NS

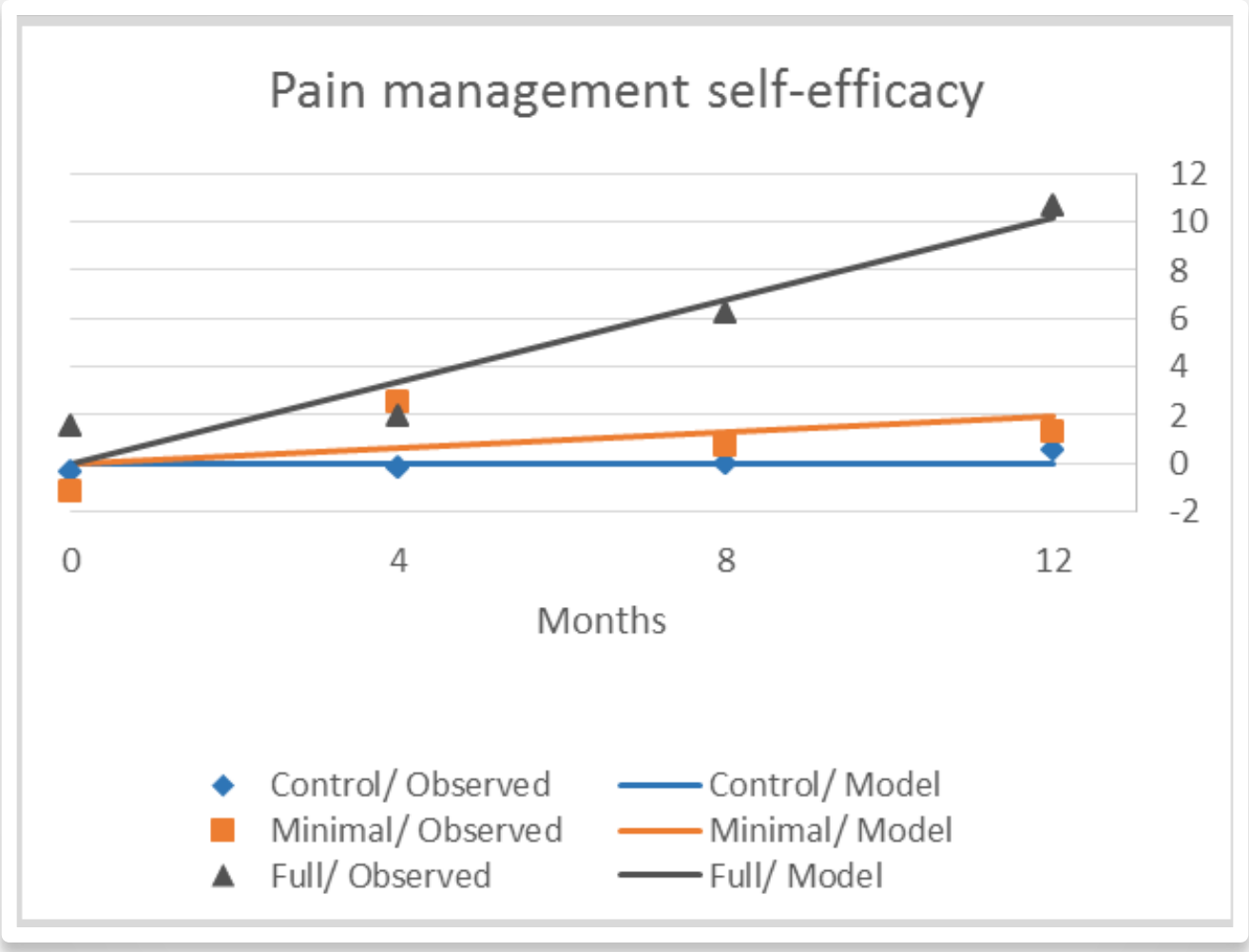
Were there any outcome measures which improved as an effect of Full TIVR but not Minimal TIVR?



Control minus Full Message: $p<.05$
Control minus Minimal Message: NS
Minimal Message minus Full Message: $p<.05$



Control minus Full Message: p<.0001
Control minus Minimal Message: NS
Minimal Message minus Full Message: p<.05



Control minus Full Message: $p<.05$
Control minus Minimal Message: NS
Minimal Message minus Full Message: $p<.05$

Conclusions, part 1:

1. 2009 Cochrane review of psychological therapies for the management of chronic pain revealed that CBT appears to have effects on pain and disability outcomes immediately post-treatment.

2. Our studies confirmed those results.

3. Interactive Voice Response (IVR) can be used as a therapeutic tool (TIVR) to enhance and extend the effect of coping skills patients learn in group CBT.

4. TIVR seems to reduce relapse into pain behaviors and concurrently decrease opioid medication use

5. TIVR can be cost effective therapeutic tool for relapse prevention

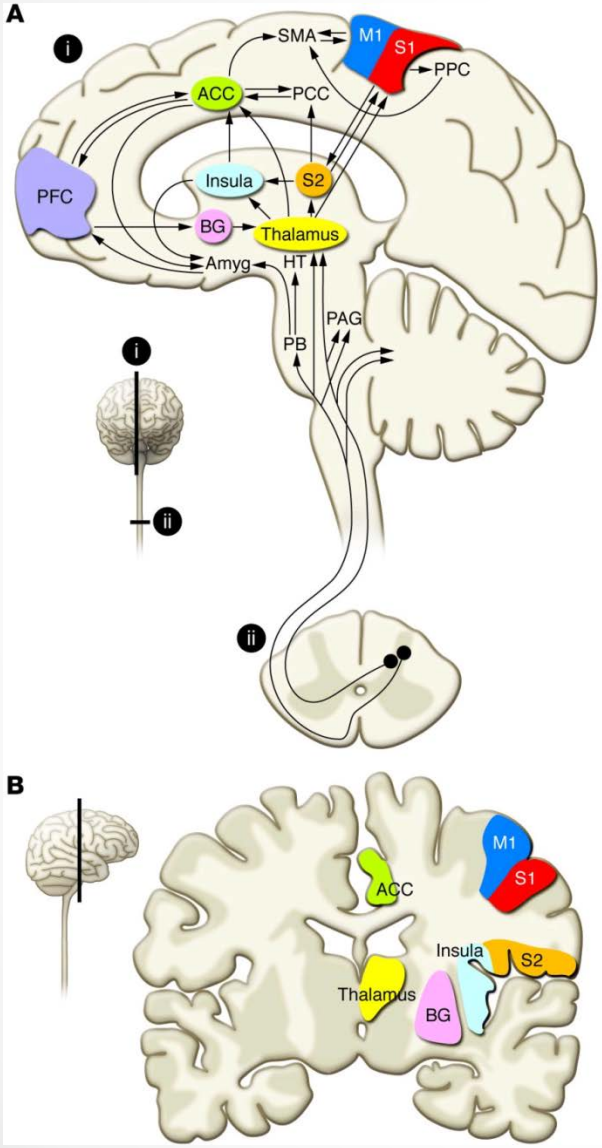
Neuroimaging (MRI) study

AIMs:

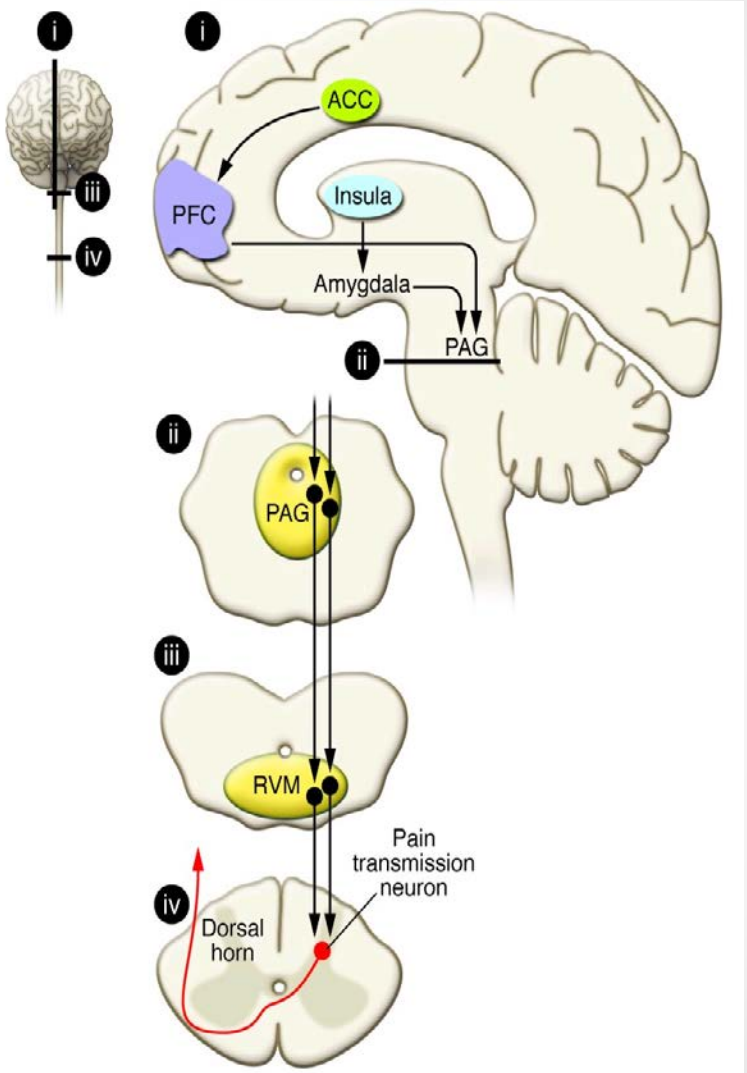
1. to investigate whether psychological interventions such as CBT modifies the dysfunctional neural circuitry associated with chronic pain
2. to investigate whether CBT can reverse gray matter changes in patients with chronic pain

Ascending (A) and descending (B) pain pathways in the human brain

(A)



(B)

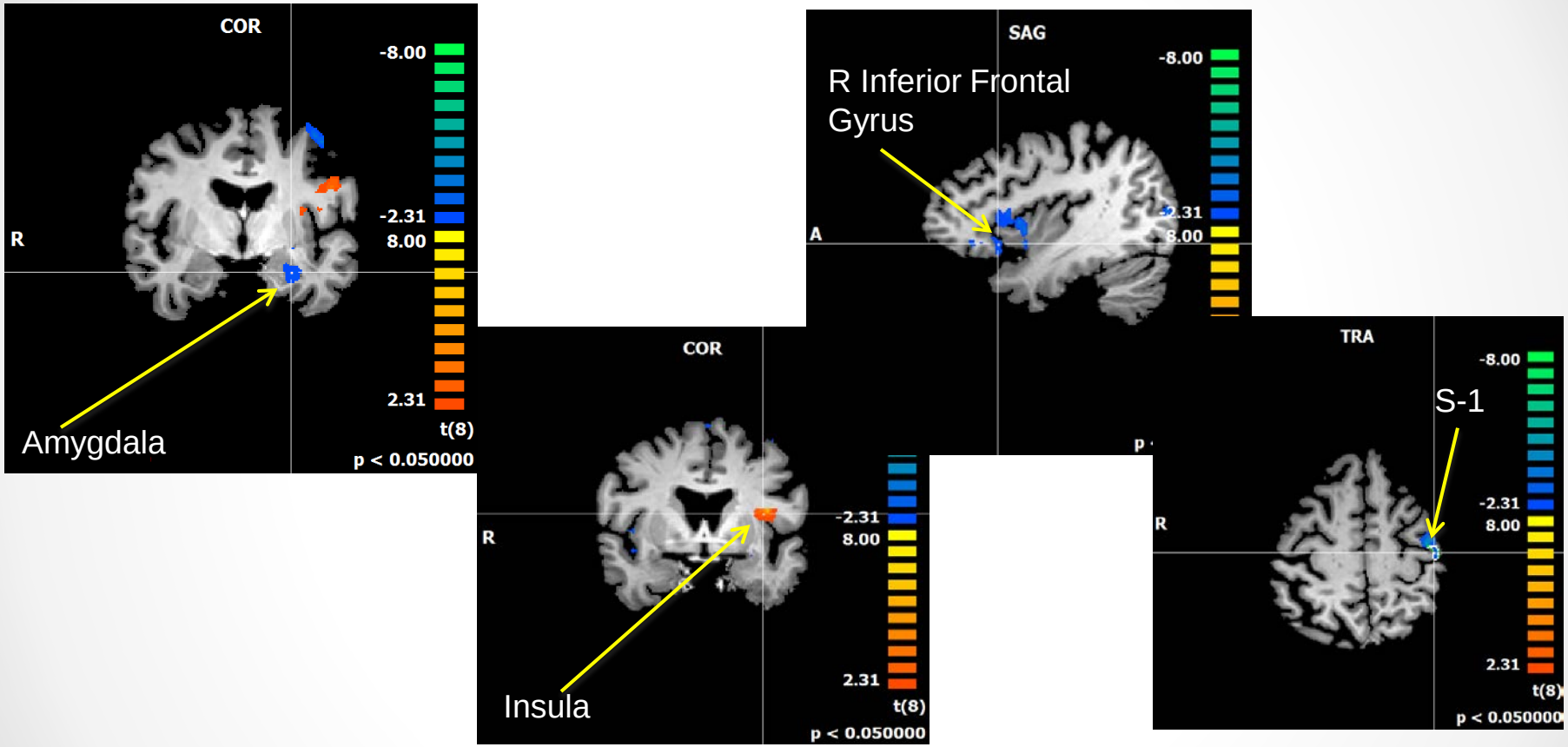


Petra Schweinhardt and M. Catherine Bushnell, J Clin Invest. 2010;120(11):3788–3797.

Can Cognitive-Behavioral Therapy (CBT) modify the dysfunctional neural circuitry associated with chronic pain?

1. Negative emotional stimulation task during fMRI scan consisted photos chosen from the International Affective Picture Set (IAPS) (block design)
2. Resting state analysis
   a) Functional Connectivity
   b) Intrinsic BOLD Fluctuations: fractional Amplitude of Low Frequency Fluctuations (fALFF)

Can Cognitive-Behavioral Therapy (CBT) modify the dysfunctional neural circuitry associated with chronic pain?



Post-11 week group-CBT chronic pain patients showed significantly decreased activation of left amygdala, right inferior frontal gyrus (rIFG) (BA 47), S-1 (Brodmann area 3), and increased activation of left Insula during the IAPS task as compared to baseline

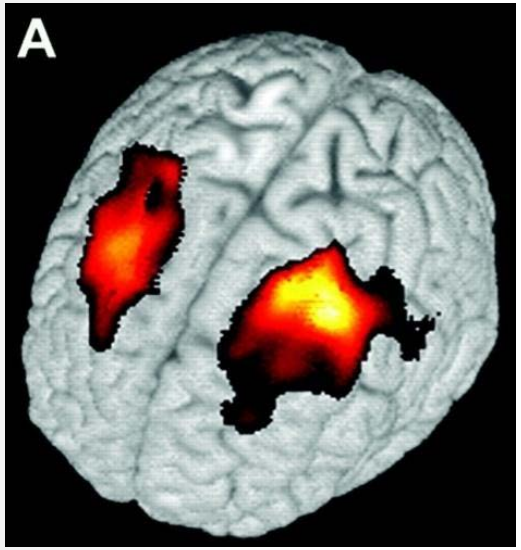
Correlations between BOLD changes and improvements in Clinical Outcomes:

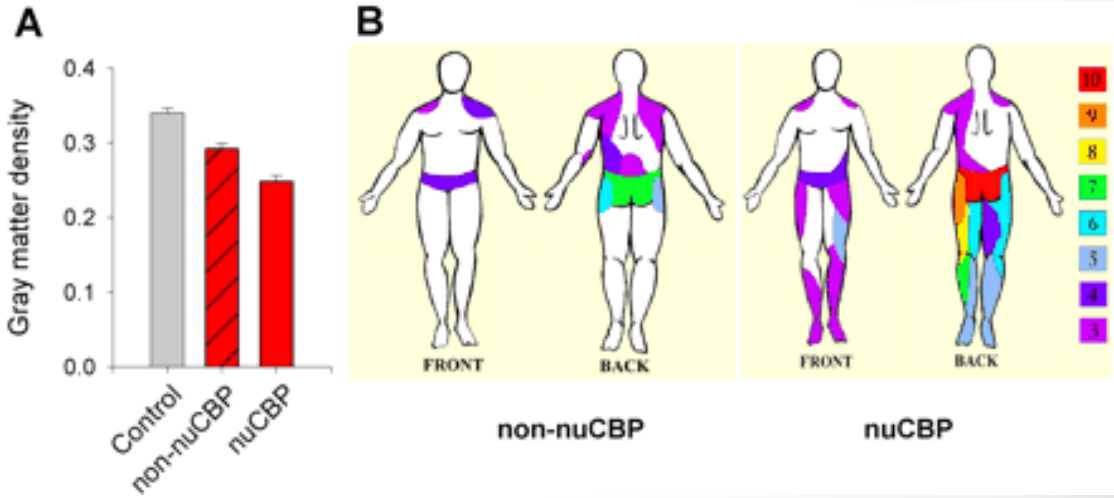
- CBT related improvements in CSQ catastrophizing scores were inversely correlated with decreased reactivity to negative stimuli in the R dorsolateral prefrontal cortex (”cognitive” DLPFC)(-0.656, $p<0.028$)

- CBT related improvements in Mental Health Function scores (SF-36) were inversely correlated with decrease in reactivity to negative stimuli in the R ventrolateral prefrontal cortex (“emotional” VLPFC)(r-IFG) (-0.722, $p< 0.014$)

Can gray matter changes be reversed in patients with chronic pain?

Gray matter volume decreased first shown by Apkarian in back pain patients





Apkarian AV, et al. J Neurosci. 2004;24:10410–10415.

Can CBT reverse gray matter changes in patients with chronic pain?

VBM results showing three regions where GM increased (right and left DLPFC) or decreased (Pre-SMA/SMA) in patients post-CBT compared to pre-CBT.

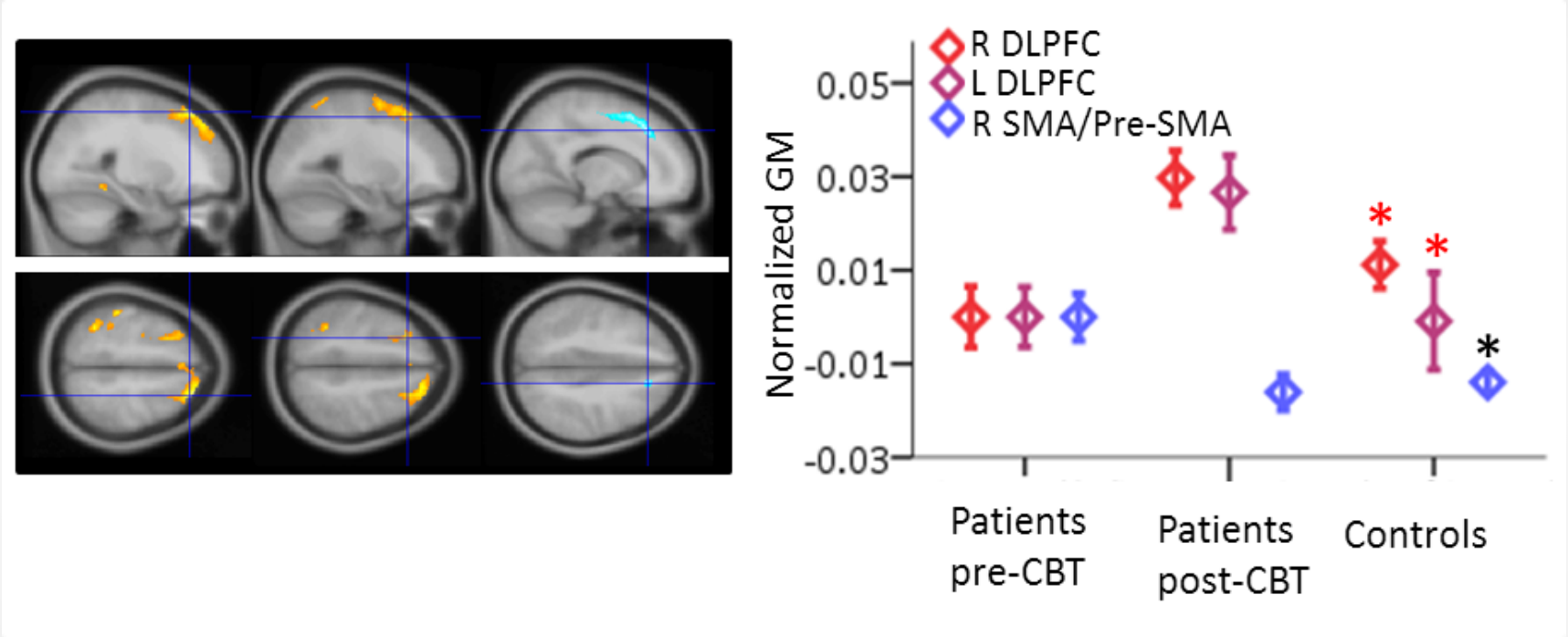
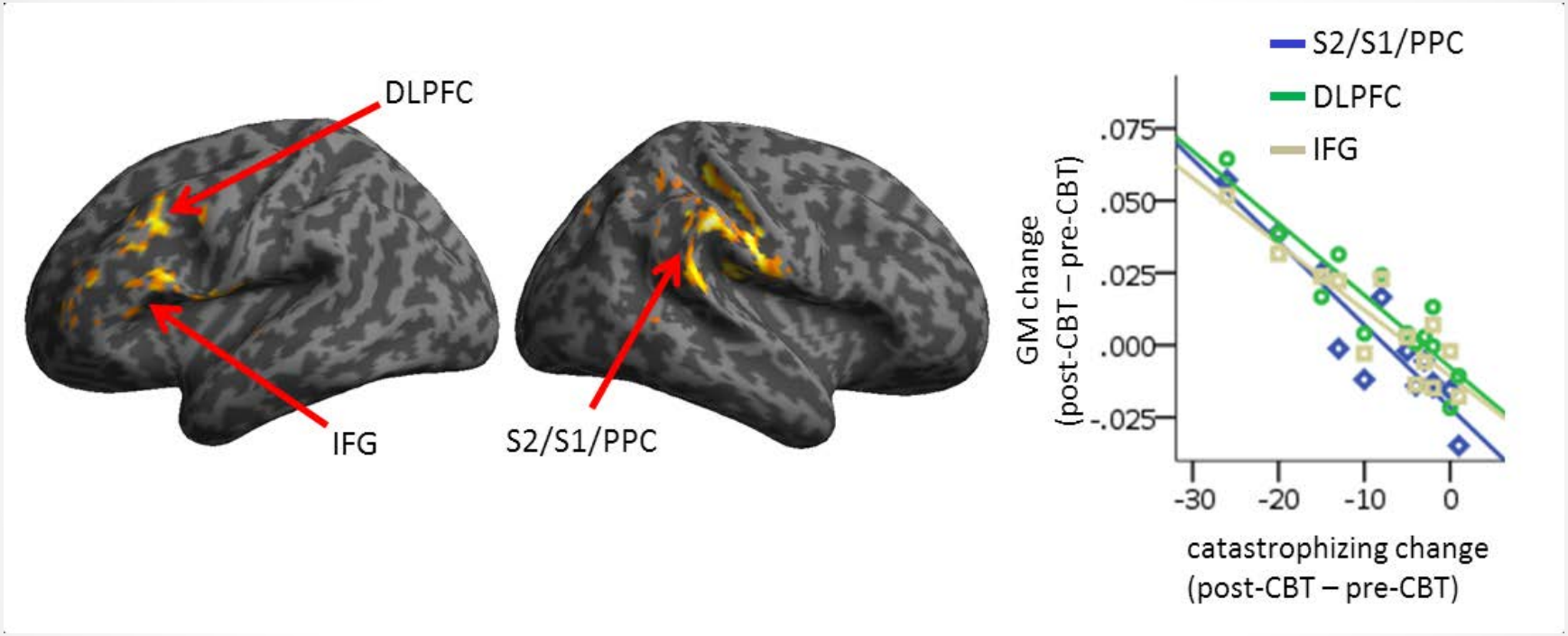


Figure 2. VBM results showing three regions where GM increased (right and left DLPFC) or decreased (Pre-SMA/SMA) in patients post-CBT compared to pre-CBT. The plot to the right shows the means and standard errors for each region shown in the panels to the left. Data for all three groups (patients pre- and post-CBT and controls) are normalized to patients pre-CBT. See Table 2 for details on the SPM statistics. Red asterisks indicate ROIs where controls had significantly less GM than patients post-CBT, and the black asterisk indicates the ROI where controls had less GM than patients pre-CBT, as determined by t-tests on mean values of the ROIs. DLPFC, dorsolateral prefrontal cortex; SMA, supplementary motor area

Seminowicz & Naylor, in revision, Journal of Pain

Increased gray matter volume after CBT correlated with decreased pain catastrophizing.



Three of the four clusters where increased gray matter volume after CBT correlated with decreased pain catastrophizing. The left DLPFC and IFG and the right S2/S1/PPC clusters are shown.

Scatterplot shows change in GM as a function of change in catastrophizing. DLPFC, dorsolateral prefrontal cortex; IFG, inferior frontal gyrus; PPC, posterior parietal cortex; S1, primary somatosensory cortex; S2, secondary somatosensory cortex.

Seminowicz & Naylor, in revision, Journal of Pain

Final conclusions:

1. Group Behavioral/Cognitive therapy improves coping skills and improves ability to control and decrease pain

2. IVR is a viable technology for patient self directed treatment and relapse prevention

3. Group CBT followed by TIVR can be used not only to decrease pain, improve coping, and diminish likelihood of relapse into pain behavior but also <u>concurrently decrease opioid medication use.</u>

4. CBT modifies the dysfunctional neural circuitry associated with chronic pain as examined with fMRI

5. Gray matter atrophy associated with chronic pain can be partially reversed by an 11-week group CBT.

6. These results add to mounting evidence that CBT can be a valuable treatment option for chronic musculoskeletal pain, and that treating pain can partially reverse abnormal brain function and structure associated with chronic pain.

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