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14. ABSTRACT

To briefly summarize, our work consisted of a.) developing a novel group psychotherapy for combat-related PTSD incorporating Mind-Body techniques / Mindfulness meditation as well as non-trauma related experiential exposure techniques; b.) comparing this novel therapy against an already developed and well-characterized credible active control group therapy, called "Present-Centered Group Therapy (PCGT)" in clinical outcome trial at the VA Ann Arbor PTSD clinic; and c.) conducting a translational neuroimaging mechanistic study with pre- and post fMRI and neurocognitive testing.

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INTRODUCTION:

Deployment-related posttraumatic stress disorder (PTSD) is a major clinical problem for the military and the Veterans Administration, and can lead to chronic disability and major human and economic costs to the warrior, their families, DoD / DVA, and society at large (Hoge et al., 2004; Kang, Natelson, Mahan, Lee, & Murphy, 2003; Kulka, 1990). With the increased incidence of PTSD among returning veterans of OEF and OIF, it is imperative to be better equipped for treatment of PTSD. Substantial barriers to seeking and providing treatment to returning veterans, including stigma, are being experienced - development of novel psychotherapies and treatments, including utilizing effective Complementary and Alternative treatments approaches may be an important way to improve access and quality of care to our veterans. Effective individual therapies exist for combat PTSD (e.g. prolonged exposure (Schnurr et al., 2007), eye-movement desensitization reprogramming (EMDR), cognitive processing therapy (CPT) (Monson et al., 2006), cognitive behavioral therapy (CBT)(Chard, Schumm, Owens, & Cottingham, 2010; McDonagh et al., 2005). However, there is much less evidence for effective group therapies for PTSD, even though groups are among the most widely used form of therapy at the VA. While recent developments in group CPT are encouraging (Chard, personal communication) there is as yet no published data of group CPT alone as a treatment for PTSD. In fact, existing studies of trauma-focused group therapy for PTSD suggested minimal improvement in PTSD symptoms (Schnurr et al., 2003), that furthermore is not different than “non-specific” present-centered group therapy. Designing more effective group therapies for PTSD is an important clinical goal, and we believe Mind-Body approaches including mindfulness and self-compassion exercises may be helpful in this pursuit. “Mindfulness meditation” is an ancient “Mind-Body” technique for cultivating present-focused, non-judgmental attention to one‟s body, emotions, and thoughts. It is proposed to lead to a greater sense of well-being and acceptance, greater cognitive flexibility, and better tolerance of painful and distressing sensations, emotions, and thoughts (Kabat-Zinn et al., 1992; Miller, Fletcher, & Kabat-Zinn, 1995; Shapiro, Oman, Thoresen, Plante, & Flinders, 2008), and mindfulness-based stress reduction (MBCT) prevents depression relapse (Teasdale et al., 2000). A recent open-label pilot study found an 8 week mindfulness-based stress reduction (MBSR) class led to significantly improved PTSD and depression symptoms in adult survivors of childhoods sexual abuse (Kimbrough, Magyari, Langenberg, Chesney, & Berman, 2010). Our pilot from the VA Ann Arbor also found an adaptation of MBCT was well tolerated in combat PTSD patients, and also lead to clinically meaningful improvements in PTSD symptoms (~15 point reduction in CAPS). “Self-compassion” and “cultivating kindness” meditations are also ancient techniques and there is some recent evidence this can help reduce chronic back pain. We are studying whether a new Mind-Body group therapy for PTSD that includes the practice of mindfulness meditation, which we think may help improve emotional regulation, and compassion meditation, which we think will increase positive emotions, is helpful for combat veterans suffering with PTSD. PTSD is also associated with deficits in positive emotions, so we think actively cultivating positive emotions may be helpful. Previously, stress reduction classes and therapies using mindfulness meditation and techniques like yoga have been found helpful for coping with chronic pain, fibromyalgia, and

distress, depression, and anxiety symptoms associated with major medical disorders, and for preventing depression relapse in people with recurrent depression. We also want to study specifically how these techniques might be helpful – both in terms of the psychological characteristics of change, and in terms of neural mechanisms in the brain. Mindfulness meditation may work by improving one"s ability to regulate distressing emotional reactions through allowing a non-judgmental awareness of one"s emotions. Our group has found a kind of emotional meta-cognition - i.e. noticing and rating the intensity of one"s emotional reactions - leads to decreased activity in parts of the brain associated with triggering emotional reactions, and increased activity in a part of the frontal lobe associated with regulating emotional responses.

We hypothesize mindfulness and self-compassion meditation will lead to:

1.) Improvement in PTSD symptoms and quality of life

2.) Improved emotional regulation, „mindfulness" and self-compassion, and

3.) Strengthening of mPFC circuits during emotional provocation.

BODY:

To briefly summarize, our work consisted of a.) developing a novel group psychotherapy for combat-related PTSD incorporating Mind-Body techniques / Mindfulness meditation as well as non-trauma related experiential exposure techniques; b.) comparing this novel therapy against an already developed and well-characterized credible active control group therapy, called "Present-Centered Group Therapy (PCGT)" in clinical outcome trial at the VA Ann Arbor PTSD clinic; and c.) conducting a translational neuroimaging mechanistic study with pre- and post fMRI and neurocognitive testing.

Our novel 16 week Mindfulness and Self-compassion group intervention, "Mindfulness-based Exposure therapy" (MBET), was developed at VA Ann Arbor by PTSD psychotherapists with consultation from Zindel Segal, PhD, original developer of MBCT. Treatment materials developed include a therapist manual, specific chart documentation, and audio recordings and a patient handbook for patient use. Our active control group therapy intervention for PTSD (Present Centered Group Therapy, PCGT, using a previously developed manual of Schnurr and Shea).

As described in detail below, we recruited and enrolled a total of 63 OEF/OIF veterans seeking treatment for PTSD at the VA Ann Arbor for this study over 4 years of recruitment; of these, 42 PTSD patients (67%) actually started group therapy in either MBET or PCGT. N=43 PTSD patients were assigned to the MBET Mindfulness intervention (with N=28 actually starting therapy), and N=20 were assigned to our active comparison group PCGT (with N=14 actually starting therapy). Our experiences with recruitment, initiation of therapy groups, and retention and completion of therapy by veterans in the two different kinds of groups are described in detail below. Therapy completers in the MBET groups showed clinically meaningful reductions in PTSD symptoms.

We have also performed neuroimaging with emotional regulation fMRI paradigms from N=39 PTSD patients at intake ("pre-therapy") in the newly opened VA Ann Arbor fMRI neuroimaging center, as well as a total of N=26 patients post-therapy; N=17 after MBET, and N=11 after PCGT. This neuroimaging data is currently being analyzed, and thus here we report available findings from data from this group, as well as comparison data from ongoing large fMRI studies also being conducted at VA Ann Arbor.

The work consisted of 9 "tasks" the completion of each are detailed below. Our initial plan was to run pilot groups of the experimental MBET and the active control PCGT, and then to conduct a randomized controlled trial (RCT) comparing MBET against PCGT. However, after running three groups of PCGT, it was determined by the clinical leadership of the VA Ann Arbor PTSD clinic that PCGT (the control intervention) did not show sufficient patient retention and thus would no longer be acceptable to offer to their PTSD patients. Therefore, it was necessary to alter our statement of work to reflect this development, and thus we will report clinical outcomes data for a total of 6 MBET groups and 3 PCGT groups.

A report of specific activities from our approved statement of work follows:

Task 1.) Start-up activities and regulatory approvals. IRB approvals were obtained from the VA Ann Arbor, University of Michigan IRB and the Human Research Protection Office (HRPO) for "Phase I" of this study in 2009. Phase I consisted of running two pilot groups of MBET (the Mindfulness/Self-compassion group), one without fMRI and one with fMRI, and one pilot group of our active control therapy PCGT (present-centered group therapy). A supplemental IRB application for "Phase II" of the study was obtained in 2011. Phase II involves conducting a randomized, controlled trial of Mindfulness/Self-compassion group intervention for PTSD in the VA Ann Arbor PTSD Clinic (compared to PCT), for randomizations with pre-post fMRI measurements. We further revised Phase II to discontinue PCGT in 2012.

Task 2.) Further adaptation of ad hoc manuals for the experimental Mindfulness/Compassion PTSD Therapy (MCPT) and the control Present-Centered Therapy (PCT). Both interventions will include present-centered cognitive-behavioral therapy, the experimental therapy will also include mindfulness and compassion meditations. A formal pilot manual for MCPT has been adapted from MBCT and components of PTSD therapy (e.g. *in vivo* exposure, cognitive processing) though a series of regular meetings among the clinical investigators (Giardino, King, Liberzon, Rauch), with additional input from discussion with consultant Dr. Zindel Segal. We are continuing to develop a therapist manual and patient materials (handbook and audio recordings with material for psychoeducation and specific mindfulness, self-compassion, and other cognitive-behavioral therapy exercises) of the intervention containing the following components / 4 week "modules":

1. Psycho-education / alliance, mindful stretching, and "mindful behavioral activation"
2. Mindfulness of body, body scan, and "mindful *in vivo* exposure"
3. Mindfulness of breath and emotion, Self-compassion exercises, and mindful coping and emotional processing
4. Mindful emotion regulation / coping, self-compassion, and cultivating positive emotion.

We also have obtained the manual for group "Present-centered therapy (PCGT)" from the authors Schnurr and Shea. This therapy was carefully designed as an active CBT group therapy for PTSD that includes as many of the "non-specific" salutary features of "good group therapy", including group support, weekly therapist contact (same number of hours) and alliance, normalization, and developing present-centered methods for coping with PTSD symptoms, but no specific trauma-focused exercises, and for this trial, no specific mindfulness or self-compassion exercises. In a previously published RCT trial, a 26-week PCT group compared favorably to trauma-focused therapy in terms of improvement of PTSD symptoms (Schnurr, et al., 2003). Our co-I Dr. Rauch has extensively used an individual version of the PCT treatment for PTSD in OEF / OIF PTSD patients in her career development award research at the VA Ann Arbor, and thus is now very proficient in delivery of this intervention. In her hands individual PCT also lead to significant improvement in PTSD symptoms (although less

than prolonged exposure); thus group PCT serves as a semi-validated active control therapy for PTSD; our main adaptation for this study will be to shorten the group to contain the same number of sessions as our Mindfulness/compassion group (16 weekly sessions, 2 hrs each).

Task 3.) Training of therapists and study personnel in the manuals and in recruitment and randomization protocols. Study staff including VA Ann Arbor staff psychologists Nicholas Giardino, PhD and Sheila Rauch, PhD, and co-PI Anthony King, PhD, attended a 5-day intensive residential training in Mindfulness-based Cognitive therapy led by Prof. Zindel Segal, PhD, an original author of MBCT. Dr. Giardino and King subsequently performed 8 week MBCT groups with VA Ann Arbor anxiety patients (mainly Vietnam veterans, not part of this study) to further strengthen skills. Our group has had further consultations with Dr Segal and continue to formally meet and discuss as a group. Study staff were trained in appropriate methods for subject recruitment, random assignment to group, contact, independent assessments and data management and security with advice from co-investigator Dr. Sheila Rauch, who has strong expertise in treatment studies.

Task 4.) Running the first pilot groups of each of the two intervention, and collecting pre- and post-therapy psychiatric assessment data and clinician impression.

We ran two Mindfulness-based Exposure Therapy (MBET) pilot groups to pilot methods and benefit from open-ended feedback from participants and clinicians to identify factors influencing acceptability, alliance, and symptom change, and make revisions to the manual. We have also ran a Present-centered Group Therapy (PCGT) group, optimized by Dr Sheila Rauch.

Recruitment and retention. For the first **MBET group** we recruited 7 returning combat veterans (7 deployed to OIF, 1 to OEF) who were seeking treatment for combat-related PTSD at the VA Ann Arbor PTSD clinic. All met criteria for PTSD, and the average clinician administered PTSD scale (CAPS) score of this group was in the moderate-severe range. (See Table 1A for demographic information and psychiatric symptom). Scheduling for group therapy for OEF/OIF veterans provides challenges, consistent with the experiences of others in the VA working with this population (Rauch et al., unpublished data). One patient never came to any sessions / never started the group. Two subjects dropped the group within the first three sessions, both attributed drop to irresolvable scheduling conflicts, due to unexpected changes in school or work schedules of themselves or wife. The five patients who completed the group (83% retention of those who started) missed an average 4 of the 16 sessions, by their report due to work shift rotations and other scheduling conflicts, National Guard trainings, childcare and family events, family vacations and other travel, etc. Given this level of missed sessions, we defined “completer” for any of the groups as attending 10 of the 16 sessions. However, patients reported a reasonably high level of engagement in home exercises (“homework”), and reported they engaged in the CDs and mindfulness exercises several times weekly.

The second MBET pilot group (with pre- and post fMRI scans) using our revised manual and patient handbook was completed in February 2011. Of the 8 PTSD patients

recruited, 2 were unable to start the group and did not attend any sessions (1 schedule conflict, 1 entered residential treatment). Of the 6 patients who started the group, 1 patient dropped and is lost to follow-up and 5 members completed (83% retention). Attendance in completers (average 13 sessions completed of 16 scheduled) and compliance as assessed by homework turn-in was consistent with the first group: patients report high levels of compliance with doing home exercises > 3 times a week.

We have also recruited and run a pilot group of the **Present-Centered Group Therapy**, our comparison condition. PCGT is a form of group therapy developed as a comparison condition for studies of trauma-focused group therapy (TFGT) in VA Cooperative Study 420 (CS420) (Schnurr et al., 2003) that contains the "non-specific" factors of group dynamic, social support, therapist contact and alliance, etc., but does not contain elements of exposure or mindfulness training. For these group we are using the manual used in CS420 (obtained from Schnurr and Shea and used with permission). The PCGT "pilot group" was administered by clinician who had previously administered >20 cases of PCT in an individual format. Of the five veterans who started the group (seven were recruited but two did not come to any sessions), only two veteran completed (attended a total of ten or more sessions of the sixteen sessions scheduled), i.e. 40% retention rate of those who started the group.

Table 1. Pilot groups of MBET and PCGT at VA Ann Arbor: Demographics and Psychiatric Symptoms at Intake

	Pilot					
	MBET pilot 1		**MBET pilot 2**		**PCGT pilot 1**	
Race	White, non-Hispanic (7)		White, non-Hispanic (7)		White, non-Hispanic (6) African American (1)	
Deployment	OIF (6) OEF (1)		OIF (8)		OIF (7)	
Age	31.2	10.3	32.3	11.5	29.4	7.9
N recruited	7		8		7	
N who started group	5		6		5	
N with post-group measure available	4		5		4	
Mean # sessions attended	11		13		9	
N Attended ≥ 10 session	4		5		1	

PTSD Symptoms:

	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
CAPS	91.6	16.4	83.6	15.5	90.8	12.5
Intrusive	24.9	5.8	23.5	8.8	23.6	7.6
Avoidant	35.4	7.6	32.5	7.6	37.1	6.8
Hyperarousal	31.3	5.5	27.6	4.7	30.7	2.9

PTSD: PCL-C	52	7	54	9	61	10

Other Symptoms:

DASS-21						
Depression	18.1	12.3	22.4	12.4	21.5	9.8
Anxiety	14.1	12.1	20.2	10.2	22.8	12.0
Stress	26.9	12.8	26.4	12.0	30.1	10.3

Clinical Outcomes: PTSD Symptoms Average PTSD symptoms, measured by both diagnostic interview (CAPS) and self-report (PCL-C) improved significantly in the 9 MBET "completers" from pre- to post-therapy. Total CAPS scores significantly decreased from pre- to post assessment (t[8] = 2.6, p = .03) in the nine completers, with an average CAPS scores was an average of 26 points, showing effect size of decrease ***Hedges g*** = 1.2. For reference, PTSD clinical trials have defined clinically significant reduction as a decrease of 12.5 points on total CAPS. Effect of MBET on self-report PTSD (PCL-C) was 12 point drop pre-post, Hedges g = 1.3. Effect size of PCGT on CAPS (10 point drop pre-post, ns) was Hedges g = 0.59, effect of PCL-C was on average increase of 2 points, g= -0.12 The figures below show the individual time courses pre-post therapy and mean change over pre-mid-post therapy for the n=9 MBET completers and n=4 PCGT completers for CAPS (top row) and PCL-C (bottom row).

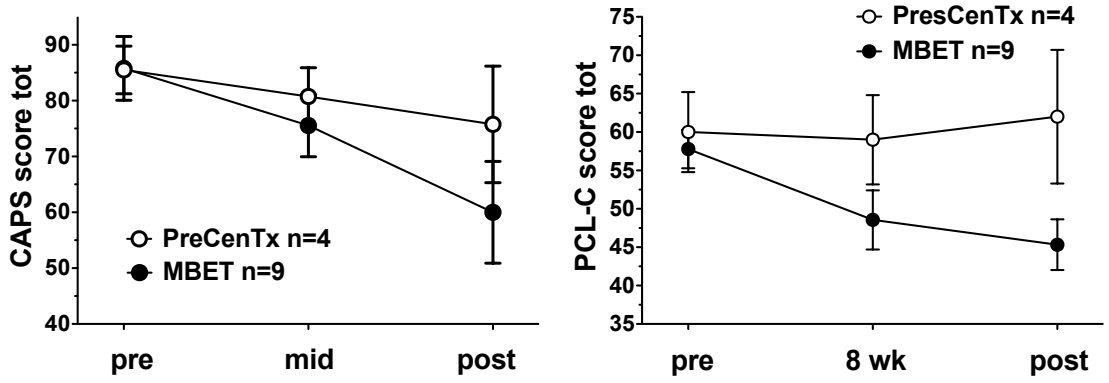


Figure 1: Change in PTSD symptoms in pilot groups of the 16 week Mindfulness based therapy in patients with post-therapy measures. Clinician rated PTSD symptoms (CAPS by independent clinical assessor) are shown in 1A & B: Individual (1A) and mean (1B) time course of before and after MBET (as well as pre- and mid-assessment of ongoing present centered therapy group (n=4). Self-reported PTSD symptoms (PCL-C) are shown in 1C & D: Individual (1C) and mean (1D) time course of PCL-C scores before and after MBET, as well as pre- and mid-assessment of the present centered therapy group (n=4).

One MBET patient had a very high response to treatment (at post assessment clinical interview endorsed a CAPS and PCL score of no PTSD symptoms; excluding this apparent outlier (post-CAPS > 2 standard deviations different than mean) found pre-post total CAPS (t[7] = 4.4, p = .003). A conservative intent-to-treat (ITT) analysis of all subjects who started the therapy (i.e. including the 4 patients who dropped treatment) carrying forward last available CAPS scores in patients who dropped also

found a significant reduction (t[12]=2.6, p=.03) in total CAPS (average 18 point decrease in ITT). While the N of the pilot groups is very small, in part due to the rate of drop associated with PTSD interventions, we still attempted an estimation of the between-groups effect of MBET vs PCGT in patients with post measures available, as we proposed in our SOW. The difference in CAPS scores at post was 15 points (60 ± 9 MBET, 75 ± 7 for PCGT), considered a clinically meaningful difference, and while the interaction of group*time in the RM-ANOVA was not significant, a Hedge‟s g of 0.57 for CAPS was calculated for between MBET and PCGT outcomes on CAPS. Interestingly, a RM-ANOVA of PCL-C scores did find a significant group*time interaction (F[1, 11] = 16.8, p=.002), with between group Hedges g = 1.3. Of course, care must be taken to not over-interpret results from pilot groups with small numbers of patient. In particular the post-PCGT group size is only N=4 from a single group. Furthermore, of those only PCGT, only two completed 10 or more sessions (our "completer" criteria); thus differences in response could also be attributed to "dose" of therapy obtained. However, the clinical improvements reported in our pilot groups are encouraging, and compare favorably with other kinds of group therapy alone for PTSD (i.e. group therapy alone without concurrent individual therapy). While generalizations cannot be made from initial pilot groups, we are working to continue to optimize measures to improve attendance in both the MBET and the control PCGT groups. Some measures include offering classes later (4 – 6 pm), and working with patients to improve contact with therapist / continue homework on days they must miss due to work or family obligations. Thus we are hopeful such further optimization measures will improve deliver and outcome of both interventions.

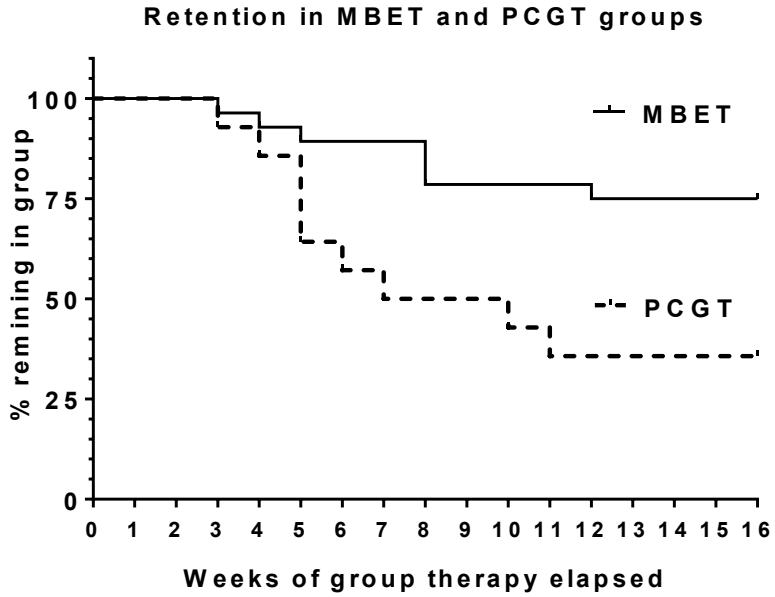
Task 5.) Revise treatment manuals, utilizing clinical experience and qualitative data. With both quantitative outcome data (e.g. symptom change) and qualitative data from both patients and therapists, study staff (PI, and Drs. Giardino, King, and Rauch) reviewed the manual, and input from and our expert consultant Professor Zindel Segal was also included to revise the treatment manuals to optimize acceptability and effectiveness. The treatment is now called "Mindfulness-based Exposure Therapy", and contains components of relaxation / breathing retraining, mindfulness exercises of body, breath, and emotions, mindful in vivo exposure and behavioral activation (noticing pleasant events), and loving-kindness / self-compassion meditations.

Task 6.) Recruit and randomly assign three separate cohorts of combat veterans seeking treatment for PTSD to either the Mindfulness/ Compassion or the control interventions. In addition to completing 2 pilot groups of MBET and 1 pilot group of PCGT, we have now recruited a total of three cohorts of PTSD for randomized assignment to either MBET or our active control group, PCGT, and a fourth cohort assigned to MBET. The first two cohorts were randomized to either MBET or PCGT (see table).

Several patients in each cohort never attended any therapy sessions, but dropped out of the study before the groups began due to scheduling or transportation difficulties, or because they changed their mind about engaging in therapy. The proportion of patients withdrawing before groups started (i.e. never attending any group therapy sessions) was not different between MBET (30%) and PCGT (25%), chisquared (1 df) = 0.3, p = .59. However, the number of patients who started therapy but then dropped out was significantly different between the therapy group conditions, with a total of 20% of PTSD patients who started MBET dropping out / not completing 10 sessions, compared to a total of 67% of PTSD patients who started PCGT dropping out / not completing 10 sessions (dropped vs completer chisquared (1 df) = 10.1, p = .001; never start vs dropped vs completer chi-squared (2 df) = 11.6, p < .005).

		total recruited	*never attend*	*% total*	Started therapy	Dropped therapy	% of starters'	Completed therapy	% of starters	*% total*
MBET	Pilot1	*7*	*2*	*29%*	5	1	20%	4	80%	*57%*
	Pilot2	*9*	*3*	*33%*	6	1	17%	5	83%	*56%*
	R1	*6*	*1*	*17%*	5	0	0%	5	100%	*83%*
	R2	*6*	*1*	*17%*	5	1	20%	4	80%	*67%*
	R3	*7*	*3*	*43%*	4	1	25%	3	75%	*43%*
	R4	*8*	*3*	*38%*	5	2	40%	3	60%	*25%*
MBET total		*43*	*13*	*30%*	*30*	*6*	20%	*24*	80%	*56%*
PCGT	Pilot1	*7*	*2*	*29%*	5	3	60%	2	40%	*29%*
	R1	*6*	*1*	*17%*	5	3	60%	2	40%	*33%*
	R2	*7*	*2*	*29%*	5	4	80%	1	20%	*14%*
PCGT total		*20*	*5*	*25%*	*15*	*10*	67%	*5*	33%	*25%*

A survival curve analysis of PTSD patients who started therapy found a significant difference in retention ("survival" in group) with Log-rank (Mantel-Cox) test Chisquare (1 df) = 7.1, p = 0.008



Thus, the MBET had a drop rate among PTSD patients who started therapy of 20%, and a "dropout rate" including patients who never started therapy of 44%, which while considerable and higher than published studies in Vietnam veterans, is consistent with other studies of PTSD interventions with OEF/OIF veterans (Rauch et al., personal communication / unpublished data) who have considerable barriers to engaging in therapy. Patients who were in MBET groups also showed compliance suggesting acceptability of the intervention, based upon attendance, performance of homework, patient report, and completion of the intervention. However, patients in the PCGT groups had considerably lower completion rate (using liberal "completion" criteria of attending 10 out of 16 sessions), drop-out rate of 67% of patients who started therapy, and 75% when including those who never started. This rate of drop-out was considerably higher than found in other interventions, and raised concerns in the VA Ann Arbor PTSD Clinic. The VA Ann Arbor PTSD Clinical Team and our study team clinicians concluded that the low retention rate of PCGT in OEF/OIF veterans in our study does not allow PTSD patients participating in the control condition to receive an adequate dose of therapy. Therefore, the VA Ann Arbor PCT has concluded that PCGT is not adequate intervention to be offered to returning veterans. They have further directed us that that will not accept for our study to assign patients to the control PCGT condition because they do not consider it a minimally effective intervention, because retention rate is so low.

We did not expect and in fact were surprised by the low retention rate of PCGT in our clinic. PCGT is a manualized group therapy developed by Paula Schnurr, PhD and Tracy Shea, PhD of the National Center for PTSD (Boston VA) as an active control therapy for an RCT with Trauma-focused Group Therapy for the VA multicenter Collaborative Study 420 (primary clinical outcomes results published in: Schnurr et al., 2002, Arch Gen Psychiatry, 60(5):481-9.). This 33 session group therapy has 3 initial

sessions of structured interactive psychoeducation, 26 weekly sessions of “open-ended” present centered group therapy, and 4 monthly “boosters”. PCGT was initially used with >150 Vietnam veterans in 10 VA PCTs. In the CS420 data, retention was greater in PCGT (8% drop-out) than TFGT (23% drop-out), and clinical outcomes were not different between the group. Therefore we expected good retention in PCGT in our study of OEF/OIF veterans, in which we retained the overall format and all of the content of the first 3 sessions, but shortened the total group time to 16 weeks. Furthermore, in this study, PCGT was led by experienced VA psychologists with appointments in the PTSD clinic, including one who has previously successfully delivered the individual version of Present Centered Therapy to OEF/OIF PTSD patients. It appears that differences in the clinical characteristics of OEF/OIF vs Vietnam veterans, including age and time from combat trauma, as well as socio-demographic / economic factors could explain the differences in drop rate. Most patients who dropped PCGT cited changes in work or family schedule or transportation problems. Our impression is that in addition, the PCGT format is not as structured (after week 4, essentially same format) and potentially not as engaging as the MBET, which was structured each week and also included more structured daily homework. We noted most drops in the PCGT group were after week 4.

As a result of the direction by the PTSD clinic to no longer conduct PCGT with VA Ann Arbor patients, and with IRB approval, we assigned the group of patients recruited for the third random assignment only the MBET group. Although patients were assigned to only one group, they were recruited with the understanding they had a 50% chance of being assigned to either PCGT or MBET, and thus patient preference did not play a role in assignment in this cohort. We revised our SOW to now no longer include the PCGT treatment, and instead to recruit and additional groups of the MBET treatment. Although it was our intention to conduct a randomized controlled trial immediately following our 2 “pilot” MBET groups (which were used for further treatment development) we feel that considerable and important information will be obtained from continued study of the MBET intervention. The three PCGT groups we performed have already given us important information about patient retention in this intervention within OEF/OIF population, and we will write our first publication about the low retention / low compliance of this intervention in this cohort, in contrast to the acceptability of the experimental MBET group. Furthermore the MBET treatment is a new intervention, not previously tested anywhere. Thus continued study of the novel MBET treatment will be important for estimation of its clinical efficacy and whether further trials with “mindfulness-based” group therapies should be considered in OEF/OIF PTSD patients.

Table 2. Randomized Groups: Demographics and Psychiatric Symptoms at Intake

	MBET 1		PCGT 1		MBET 2		PCGT 2		MBET 3	
Race	White, non-Hispanic (6)		White, non-Hispanic (5)		White, Non-Hispanic (4), Black (1)		White, Non-Hispanic (5),		White, Non-Hispanic (7)	
	Aug 2011 - Nov 2011				March 2012 - June 2012				Aug-Dec „12	
Deployment	OIF (6)		OIF (5), OEF (1)		OEF (2), OIF (4)		OEF (3), OIF (3)		OEF (2), OIF (3)	
Age	37.4	7.8	30.4	3	30.2	3	33.7	10.3	30.2	3
recruited	6		5		6		5		7	
started group	5		5		5		4		4	
post-group measures	5		4		4		3		3	
Average # sessions attended	12.7		6.6		11.8		8.2		12.1	
completed > 10 sessions	5		1		4		1		3	

PTSD Symptoms:

	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
CAPS	88.5	15.8	78.6	10.1	60	11.1	74.6	15.5	57.1	10.1
Intrusive	23.5	7.8	22	5.2	10.4	2.7	18.2	7.5	14.4	3.9
Avoidant	33.5	6.5	30.3	3.7	25.4	5	28.6	10.7	23.5	7.4
Hyperarousal	31.5	5.5	25.8	3	24.2	5.5	27.8	2.6	19.1	7.2
PCL-C	66.7	7.9	62.2	11.2	54.2	7.3	60.0	9.1	53.8	13.0

Other Symptoms:

DASS-21										
Depression	18.3	9.9	23	14.3	22.4	12.7	16.6	16.7	17.6	7.4
Anxiety	22.7	10.7	19.5	6.2	15.6	12.2	16.3	14.7	26.7	4.7
Stress	28	7.7	30.5	7.2	25.2	9.6	19.6	16.8	18.0	9.6

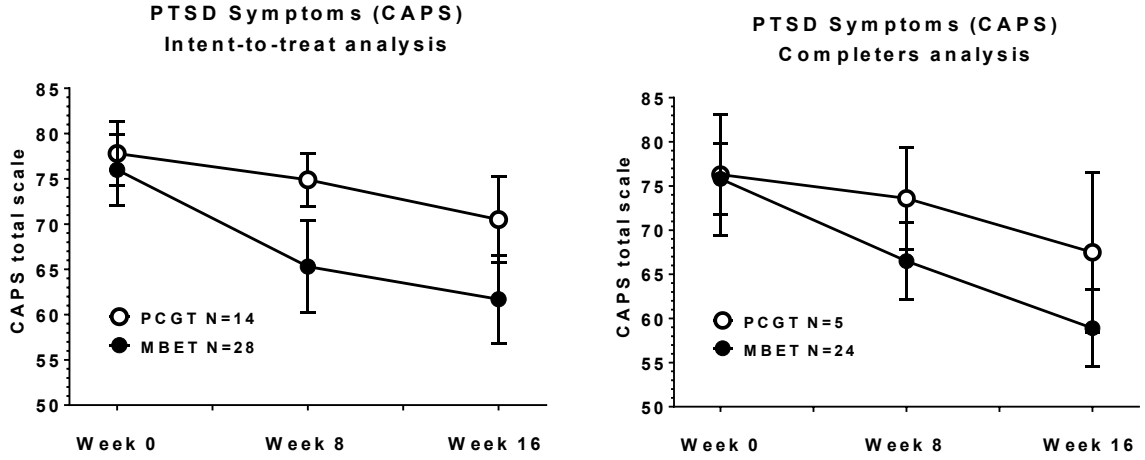
Clinical Outcome Data Collected:

We ran a total of 6 MBET groups and 3 PCGT groups. As we previously discussed, due to the difficulty in retaining PTSD patients in the PCGT (i.e. high rates of "drop-out", drop-out was 65% in veterans starting PCGT compared to 18% in veterans starting MBET) we discontinued PCGT at the instruction of VA Ann Arbor PTSD clinic. We are currently preparing a manuscript that describes the acceptability of the

experimental MBET group intervention in OEF/OIF veterans (18% dropout), in contrast to the very low retention / low compliance of the PCGT intervention (65% dropout)

Clinical outcomes analyses. We reported intention-to-treat (ITT) and completer analyses performed on PTSD clinical outcomes (CAPS scores). ITT analyses were performed with all PTSD patients who engaged in any therapy sessions, with last observation carried forward (LOCF) for patients for whom a "post-therapy" follow-up data was not available.

			Intake		mid therapy week 8		post-therapy week 16		pre-post	effect	95% CI	
		N	Mean	SD	Mean	SD	Mean	SD	delta	g	lower	upper
ITT	MBET	28	73.5	18.4	67.4	19.4	61.5	22.8	-12.0	**0.65***	0.06	1.22
	PCGT	14	77.8	13.4	74.9	11.1	70.5	17.7	-7.3	0.44	-0.30	1.20
Completers	MBET	24	74.6	16.9	66.5	19.9	58.9	22.8	-15.7	**0.75***	0.12	1.38
	PCGT	5	76.3	15.3	73.6	13.0	67.5	20.3	-8.8	0.44	-0.81	1.70

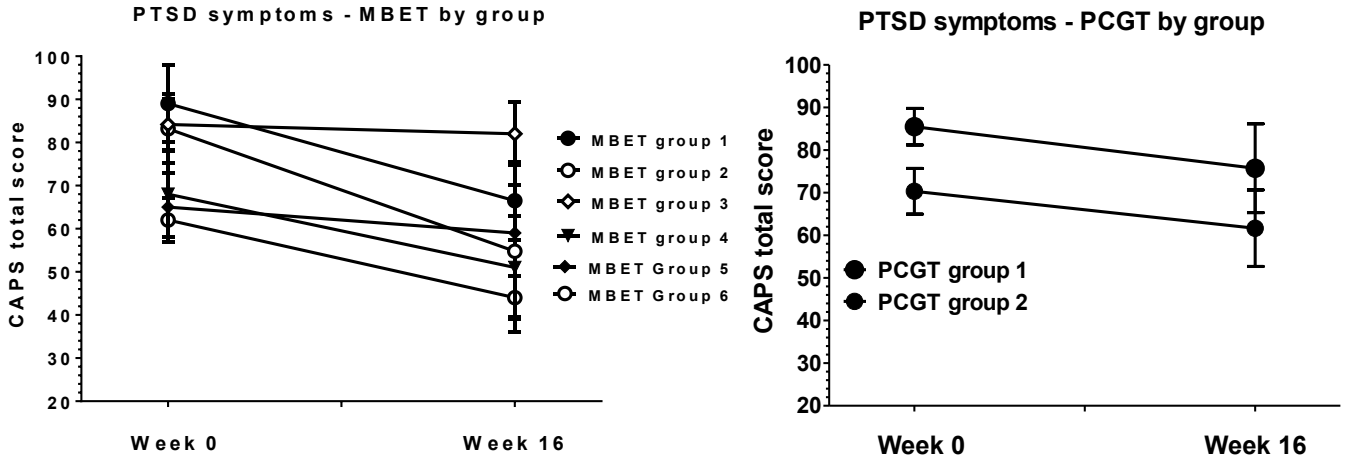


Intention to treat analyses found that MBET was associated with a significant decrease in PTSD symptoms (average pre-post therapy decrease of 12 points on the overall CAPS scores), with paired $t(27) = 3.1$, $p = .005$, and with a bias corrected effect size (Hedge‟s g) of 0.65. PCGT was associated with an average decrease of 7.3 points on the total CAPS score, a nonsignificant trend $t(13) = 2.0$, $p = .058$ and $g = 0.44$, with a 95% confidence interval that included zero (i.e. non-significant). Thus MBET was associated with a clinically meaningful (>10 points) and statistically significant decrease in symptoms while PCGT was not. The between condition effect size (Hedge‟s g of post-therapy CAPS scores) was 0.39 (95% CI -.27 - 1.06) which included zero, and thus not significant.

Completer‟s analyses were complicated by the small number of patients in the PCGT condition that completed the therapy. However completer analyses found MBET was associated with a significant decrease in PTSD symptoms (average pre-post therapy decrease of 15.7 points on the overall CAPS scores), with paired t(23) = 3.1, p = .007, and with a bias corrected effect size (Hedge‟s g) of 0.75.

PCGT was associated with an average decrease of 8.8 points on the total CAPS score, a nonsignificant trend t(4) = 1.8, p = .10 and g = 0.44, with a 95% confidence interval that included zero (i.e. non-significant). Thus MBET was associated with a clinically meaningful (>10 points) and statistically significant decrease in symptoms while PCGT was not. The between condition effect size (Hedge‟s g of post-therapy CAPS scores) was 0.34 (95% CI -0.64 - 1.32) which also included zero, and thus not significant. However, we did observe substantial differences in the pre-post changes in CAPS scores among the 4 groups of MBET we ran, as shown in the graph below

.



Task 8.) conduct a pilot fMRI neuroimaging paradigm with pre- and post brain scanning. Circumstances have allowed us to take advantage of opportunities Ann Arbor VA fMRI facility to scan all patients receiving group therapy (rather than a smaller subset), as was also recommended by our scientific reviewer. All scans were collected on a 3.0 T Phillips scanner, T1-weighted images (T1 overlay) are prescribed approximately parallel to the AC-PC line, in the same prescription as the functional acquisitions. A high resolution 3D structural scan is acquired to provide more precise anatomical localization. Briefly, ***Resting State connectivity***, as well as 3 kinds of emotional regulation paradigms were utilized 1.) ***Threat detection***: the “Emotional Faces Affective task” (EFAT) involved viewing emotional (fear) faces (activates amygdala), 2.) ***Implicit emotional regulation***: the “Shifted Emotional Appraisal Task” (SEAT), activates mPFC; and 3. ***Volitional emotional*** regulation: “re-appraisal” and cognitive-emotional „distancing“, activates dACC, IFG, dorsal striatum, and mPFC.

We have now collected pilot fMRI data from N=39 PTSD patients at intake ("pre-therapy"), as well as a total of N=26 patients post-therapy; N=17 after MBET, and N=11 after PCGT.

group	Pre-Therapy scanned pre-processed	POST-Therapy scanned/pre-processed
MBET	23	17
PCGT	16	11
total	39	26

We show in this report examples of results from analyses from each of the paradigms studied. However, it has been necessary to rerun the pre-processing and the level-1 scripts on all of our imaging data due to center-wide changes which have been implemented in our processing platform. In order that data from this project will be in a format in which we will be able to utilize the new Level 2 processing scripts, which include flexible ANOVA and a CONN (connectivity) toolbox that has been developed at Michigan over the past year, it has been necessary to completely re-process all of our data, which is currently ongoing. However, we show here preliminary analyses performed with the old scripts, and will submit a supplement to the current report when the analyses are completed.

Standard "resting state" (8 minutes) scans on which we perform connectivity analyses to examine default mode networks were performed, and we also are using a novel "Mindful resting" task, in which patients are given instructions similar to Mindfulness meditation during an 8 min resting. In Mindful resting, patients keep their eyes open and continue to look at the fixation plus, but are also given the instructions:

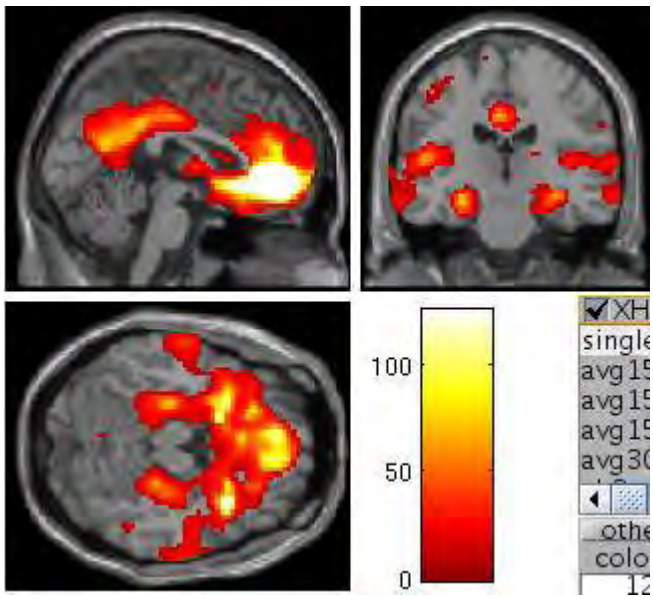
> *"For the next 8 minutes, please try to pay attention to the feelings, sounds, and physical sensations you are feeling right now. Please try to keep your attention in the present moment, noticing each sound and sensation as they arise. When you find your attention drifting off to thoughts other than the present moment, please try to return your attention to the feelings and physical sensations"*

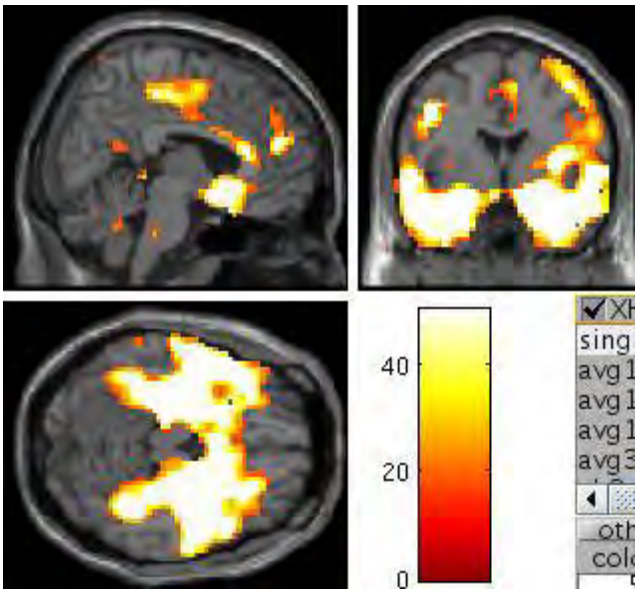
Thus these instructions will provide a somewhat novel condition at the pre-therapy time point. The patients in the MBET group (but not in the PCGT group) will have practiced mindfulness meditation for up to 12 weeks as part of their therapy, and thus we will use this condition to investigate specific training effects in the MBET patients.

We hypothesize that the "Mindful resting" state may show differences in functional connectivity compared to normal resting. Similar to what is thought to occur in Mindfulness meditation, due to continuous shifting of attention to somatic states (interoception) and checking attention / becoming aware of focus of attention and content of cognition (meta-awareness) we expect that these processes will alter normal "default mode" processing of self-referential material and thus may lead to specific alterations in functional connectivity of the amydgala, PCC, and/or vmPFC.

Here we report some preliminary outcomes of the Resting and “Mindful Resting” tasks functional connectivity.

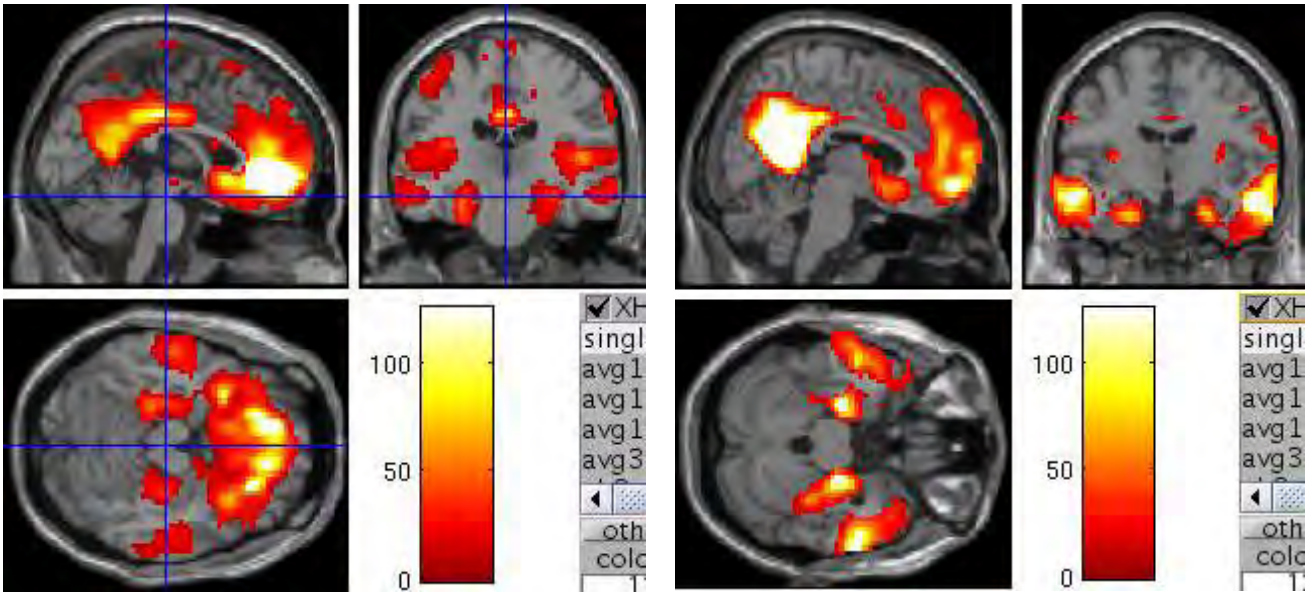
“Resting” state Functional Connectivity (during 8 min “normal” resting instructions)

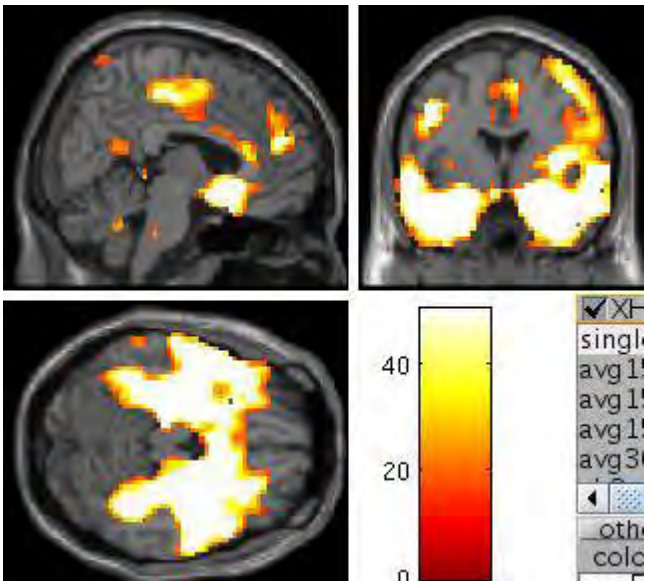




Default mode / resting state functional connectivity analyses during “regular resting”. Shown are areas of correlation with activity in A. vmPFC B. PCC, and C. right Amygdala “seeds”

“Mindful Resting State” Functional Connectivity (during 8 min “Mindfulness” resting instructions)

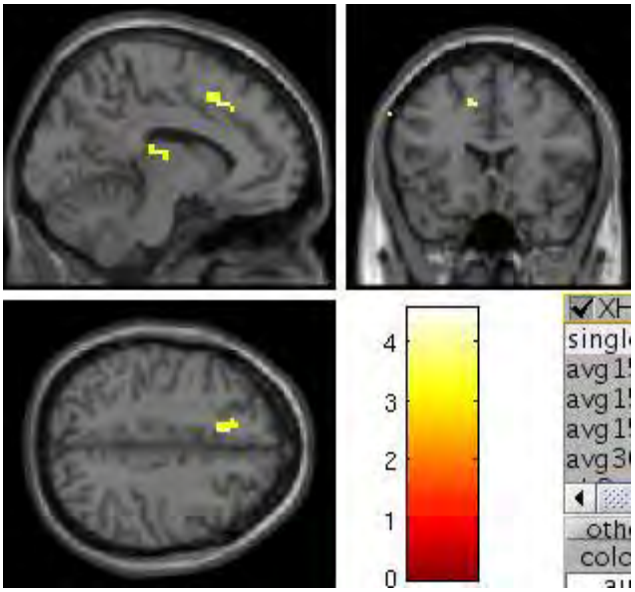




“Mindfulness Resting” mode / functional connectivity analyses during “mindfulness resting task”. Shown are areas of correlation with activity in A. vmPFC B. PCC, and C. right Amygdala “seeds”

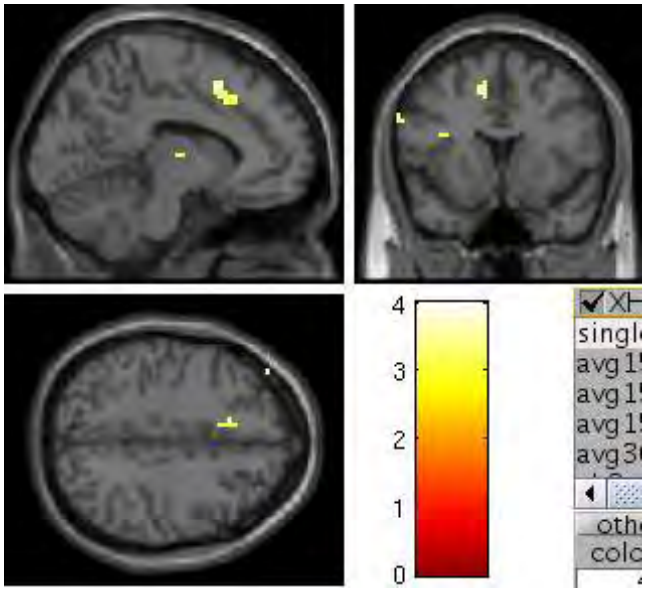
Right AMY connectivity

"Rest" > "Mindfulness" at intake



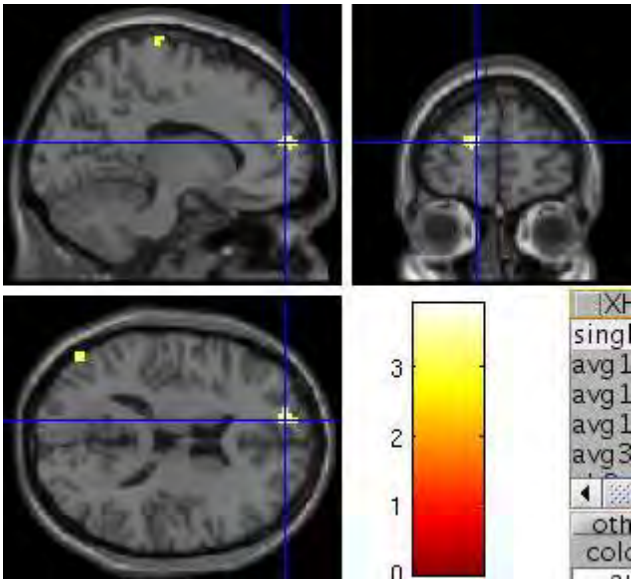
Left AMY connectivity

"Rest" > "Mindfulness" at intake



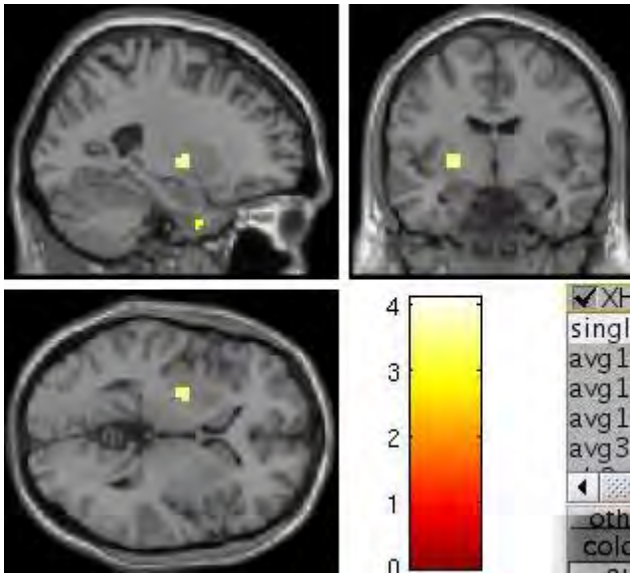
vmPFC seed connectivity

"Mindfulness" > "Rest" at intake

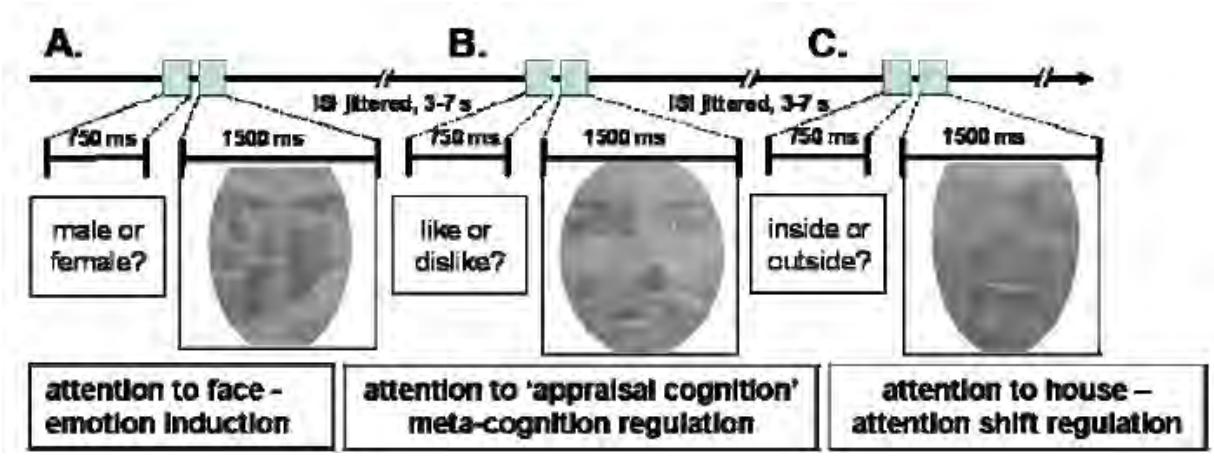


PCC seed connectivity

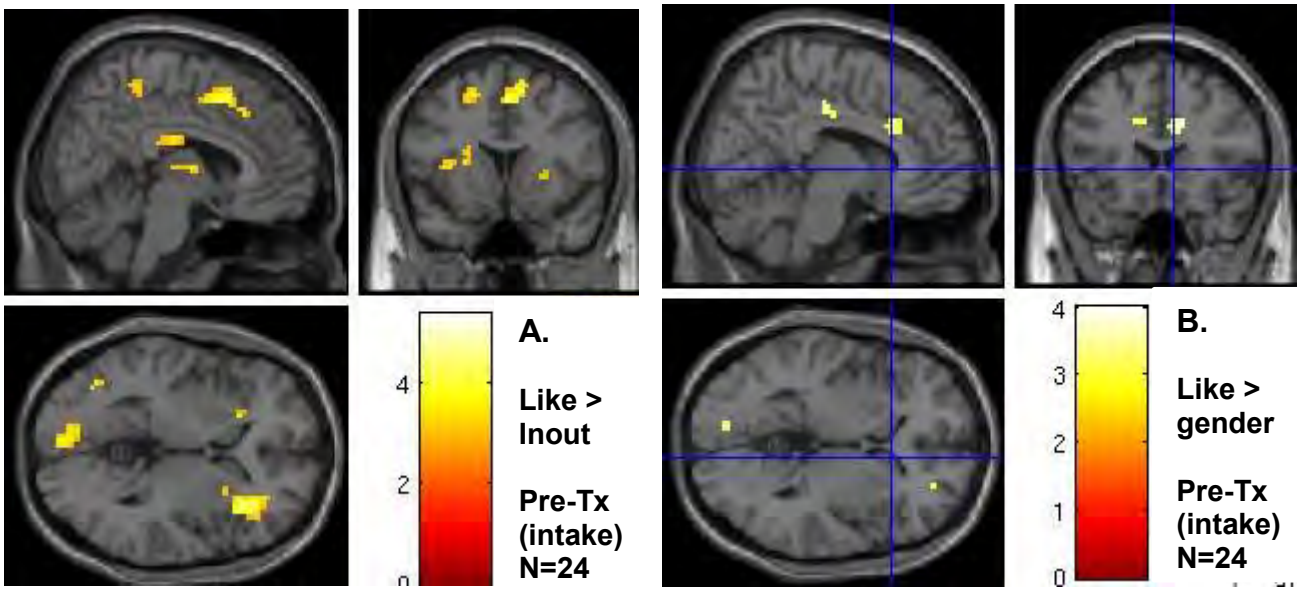
"Mindfulness" > "Rest" at intake



Shifted-attention Emotional Appraisal task interim analyses with available data.



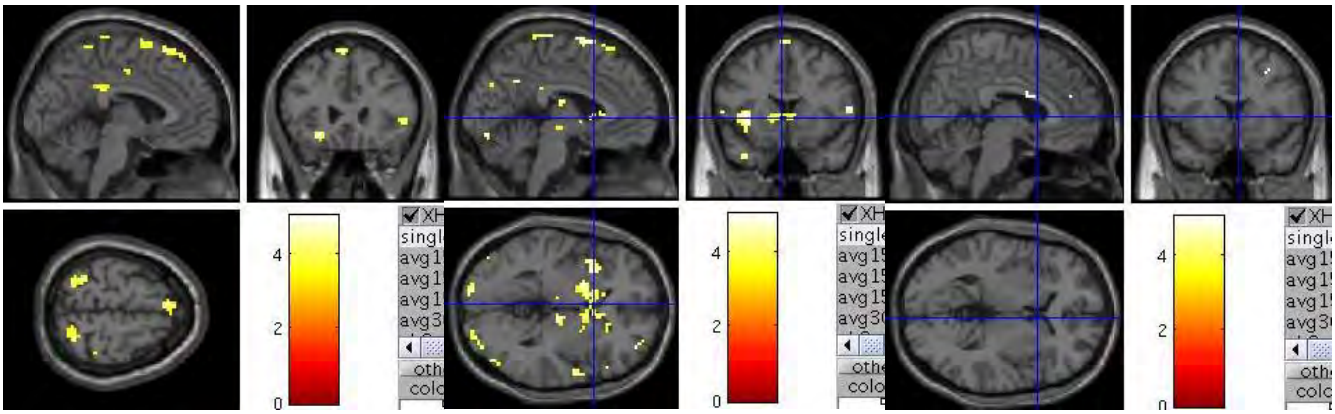
Schematic of the "Shifted-attention Emotional Appraisal Task" (SEAT),



Pre-Therapy (intake) time point, all patients (N=24). A. "Like" face (appraisal) > "In-out" place (attention shift) contrast, B. "Like" face (appraisal) vs "Gender" face (emotion induction)

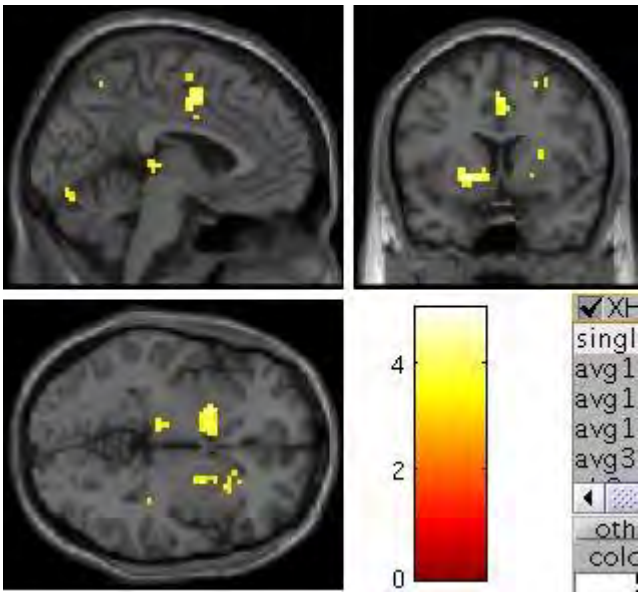
At the pre-therapy (intake) time-point, the "emotional appraisal" condition (i.e. viewing emotional faces with the instruction to appraise whether one "likes" the person) leads to greater activation of dorsal mPFC, dorsal ACC, and right inferior frontal gyrus / insula compared to the shifted attention condition (attention towards the landscape and not the face) and the covert emotional induction (attention toward the emotional face while discerning the gender).

All patients (N=14) **MBET treatment (N=8)** **PCGT treatment (N=6)**



Change in Brain activations to the the "Emotional Appraisal" task from pre- to post-therapy (Post-therapy > Pre-therapy contrast in paired t-tests), i.e. brain activations greater following therapy than before therapy in all available patients, N=14; MBET N=8, PCGT N=6).

Following 16 weeks of either group therapy, PTSD patients (N=14) showed greater activation in doral mPFC during the emotional appraisal condition. Those treated with MBET (N=8) showed increased activity in dmPFC, as well bilateral caudate-putamen and insula. These differences were not observed in the patients treated with PCGT (N=6), although of course with N=6 there is less power to observe differnces even in within subject repeated measures design.



The figure on the left shows group comparison of
brain activations during the emotional appraisal task ("Like" vs "Gender") at the "post-therapy" time-point, comparing patients treated with the MBET (N=8) to patients treated with PCGT (N=6) (i.e. MBET > PCGT independent samples t-test at post).

It can be seen that patients treated with MBET show greater activation of dorsal ACC and bilateral caudate / putamen during the emotional appraisal than patients treated with PCGT.

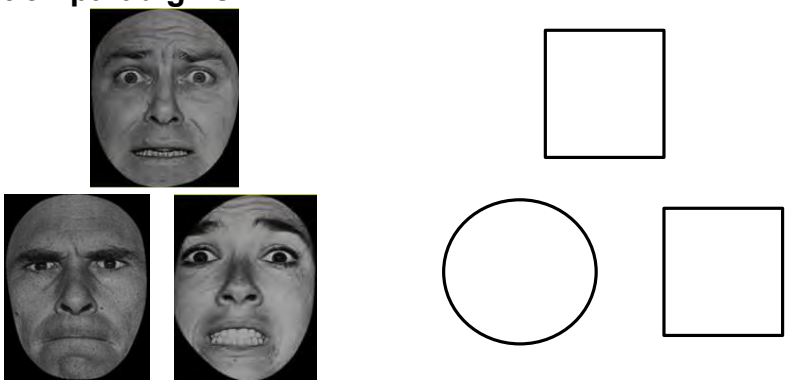
Thus these data provide intriguing initial evidence of potential brain activations associated with any group treatment, and specifically with group treatment involving mindfulness meditation. Greater numbers of subjects will be needed to provide appropriate power; these analyses are underway. We anticipate our total numbers of PTSD patients with both pre- and post-therapy scans at conclusion of the study will be MBET N=22 and PCGT N=11, which will be sufficient for overall effects of MBET alone (pre vs post MBET paired t-test), and we believe will be sufficient for observing differences in a repeated measures ANOVA design (i.e. group x time interaction term).

Threat detection (Emotional Faces):

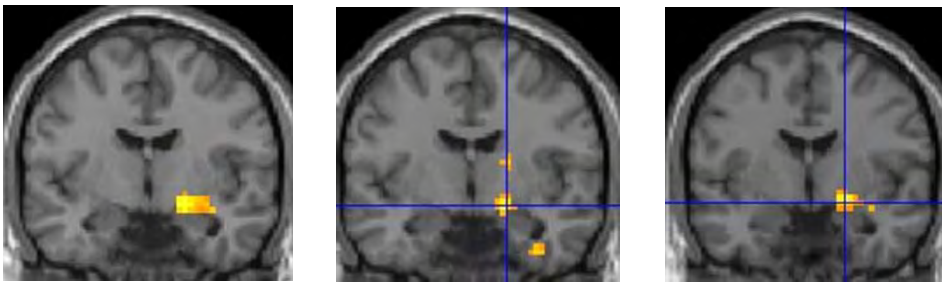
As we previously reported, our paradigm of threat detection involves viewing emotional (fear) faces, such paradigms have previously been shown to have greater activation of amygdala in PTSD patients (Rauch et al., 2002). The Figure shows preliminary data from our faces paradigm, adapted from Hariri et al., 2002. Figure 6, panel A shows a schematic of our stimuli, including fearful / angry faces (faces condition) and geometric shapes (shapes condition). Subjects are given the task of identifying the face on the bottom row that matches the expression of the face on the top (during the faces blocks), or identifying the shape on the bottom row that matches the expression of the shape on the top (during the faces blocks). Panels B and C. show activation of amygdala and deactivation of mPFC in pre-therapy scans (N=11) during the fearful > shape, neutral > shape, and fear > neutral conditons. Panel D shows a highly preliminary analysis of N=4 MBET patients Pre > Post therapy with MBET, indicating less amygdala and more mPFC BOLD activity following MBET.

Preliminary Neuroimaging data of **Emotional Faces / threat detection emotion induction paradigms:**

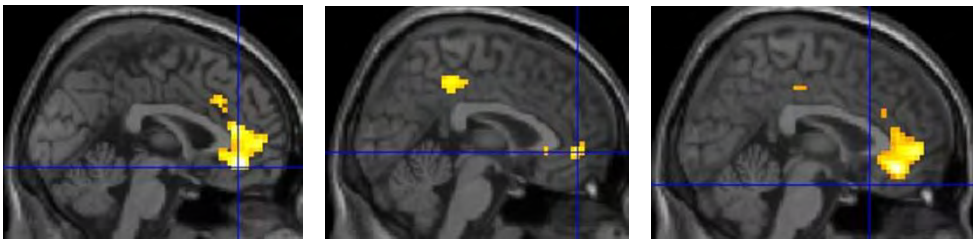
A.

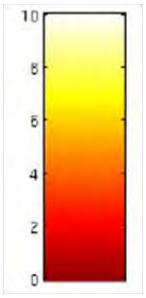


B. Fearful Face **Neutral Face** **Fearful > Neutral**

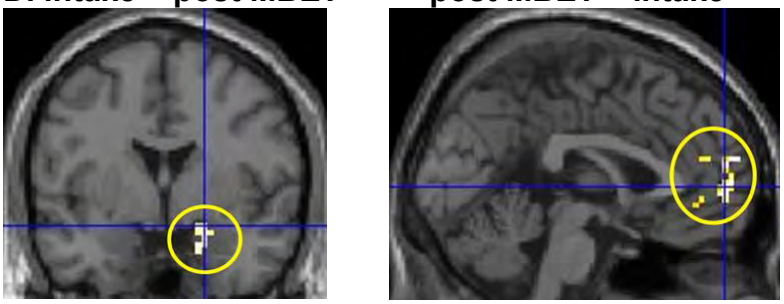


C. Fearful Face **Neutral Face** **Fearful > Neutral**





D. intake > post MBET **post MBET > intake**



Emotion induction from complex social scenes (IAPS) and volitional emotion regulation:

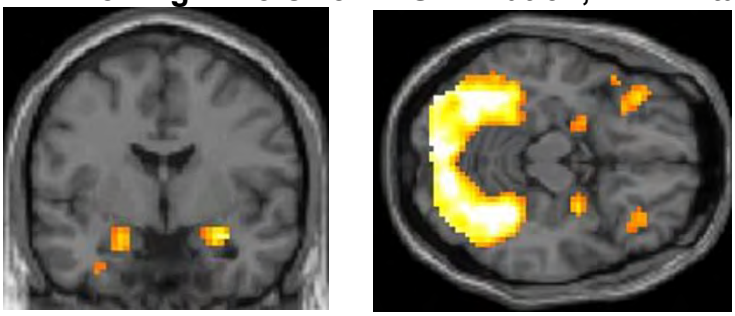
A metacognitive emotional task ("Rating" one"s emotional responses) and cognitive-emotional re-appraisal tasks have been adapted from Taylor et al. (2002) and Ochsner et al (2004) are used as emotional regulation probes of mPFC activity. These paradigm utilize highly aversive photos from the International Affective Picture System as aversive emotional induction probes, with emotionally "neutral" photos serving as controls.

Figure 5 shows preliminary data from our n=11 pilot group (pre-therapy "intake"), as well as reference data demonstrating PTSD-specific differences in mPFC revealed using these paradigms as probes. Subjects are instructed perform different tasks when viewing these photos: a.) to just "View" the photos, maintaining the evoked emotion, b.) to view and also to notice and "Rate" the intensity of their negative emotional response (implicit emotion regulation)

The Figure shows preliminary fMRI results for PTSD patients in their pre-therapy scans. Viewing Aversive pictures > fixation contrast in n=11 pre-therapy scans (activity associated with viewing pictures with negative emotional content) showing activation of amygdala and visual cortex and inferior frontal gyrus. "Rating your Emotional Response" > View contrast (which isolates activity associated with implicit / metacognitive regulation) which found greater activity in dorsal ACC and inferior frontal gyrus (IFG) during "Rating".

Preliminary Neuroimaging data of **Viewing Emotional IAPS and Emotional Regulation Paradigm (Rating ones Emotional Responses):**

A. "Viewing" Aversive IAPS > fixation, n=11 intake

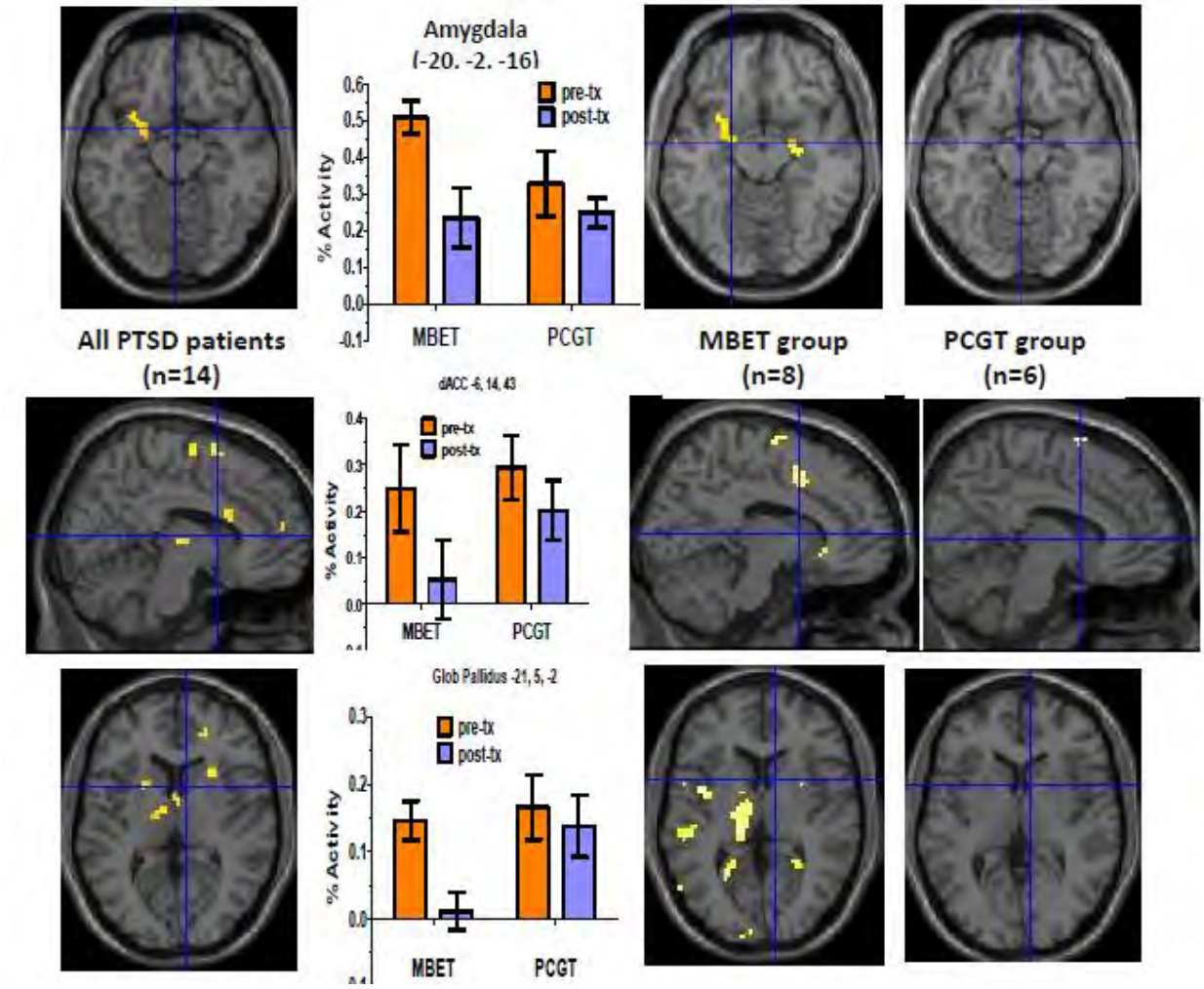


B. "Rating" emotional responses to IAPS > passive "Viewing" IAPS, n=11 intake

Taken together, these data provide data validating our choice of fMRI paradigms to isolate emotional regulation neurocircuitries that are relevant to PTSD symptoms; specifically to activate amygdala in paradigms of threat-detection (fearful faces), and dorsal and rostral ACC and medial PFC, in emotional regulation paradigms.

We also have data and preliminary results from N=14 patients from which we have both pre- and post-group therapy (MBET or PCGT) scans currently available of BOLD activity in the “meta awareness” Emotional Regulation task (i.e. viewing aversive, noting ones emotional response, and rating its negativity. In the group as a whole (n=14) whole brain (p<.005 uncorrected) voxelwise analyses found putative differences pre-post therapy, with decreased activity in **Amygdala**, **dmPFC / dACC**, and **striatum** (caudate, putamen, and ventral globus pallidus.

Preliminary fMRI data of Emotional Regulation Task: Rating Pretherapy > Posttherapy (N=14), MBET (N=8) and PCGT (N=6)



When the groups were examined separately (panels to the right), all of the observed changes (decreased activity) appear to be due to effects in the MBET group. The graphs show ROI analyses, showing % signal change (extracted from betas for 7 mm spheres around activation peaks)

Patients performed these fMRI tasks both before and after treatment with MBET or PCGT, allowing us to observe the apparent effects of the treatments on emotional

neurocircuitry. (Of course some effects might also be expected from simple habituation to the tasks, however a.) the scans are 4 months apart, b.) other studies in our group suggest minimal habituation effects (Luan Phan, MD personal communication), and we also compare effects of MBET to our active control group PCGT. (For ethical reasons, we will not have a PTSD waitlist no-treatment group to allow us to measure simple habituation).

KEY RESEARCH ACCOMPLISHMENTS:

2008 – 2009:

- Preparation and applications for Human Subjects protocols
- Training of study staff on recruitment and informed consent and human subjects procedures, including assessments and biological and neuroimaging protocols
- Training of study therapists in MBCT with Zindel Segal, PhD
- First experts meeting of Mindfulness and PTSD experts
- First draft of manual for 16-week treatment and treatment materials (patient handbook, audio CDs) available for pilot group

2009 – 2010:

- OHRP and IRB Approvals of "Phase 1" of the project Recruitment of first 2 cohorts of PTSD patients for Mindfulness- and Self-Compassion-based Therapy, and comprehensive pre-therapy psychiatric assessments, circadian cortisol, and neuropsychological / attention measures (Attention Network Task, "ANT")
- Additional training and preparation of logistic and human subject methodologies for the fMRI and cortisol sampling portions of the study.
- Running of MBET pilot Groups 1 and 2, and mid-, post-, and 3 mo follow-up psychiatric assessments, circadian cortisol specimens, and ANT).
- Pre- and post fMRI scanning of PTSD patients in MBET Group 2 subjects on emotional regulation paradigms, and ongoing processing and analyses
- Recruitment of Group 1 – active control (Present-centered Therapy) in VA Ann Arbor PTSD clinic
- Dr King attended and presented at 2010 "Basic and Clinical Studies of Mindfulness", small invitation-only meeting at University of Madison – Waisman Center, and consultation with Zindel Segal, PhD about MBET manual

2010 – 2011:

- Recruitment and administration of first randomized cohort, Completion of pre-post measures, and 3 mo FU.
- Acquire fMRI data on pilot groups and randomized groups.

2011 - 2012:

- Recruitment and administration of second and third randomized cohorts (third group was consented to be randomized but all were assigned to MBET) Completion of pre-post measures, and 3 mo FU.
- Acquire fMRI data on second and third randomized groups.

2012 - 2013:

- Recruitment and administration of the final MBET cohort. Completion of pre-post measures, and pre- and post fMRI scans.
- Processing and analyses of fMRI data (ongoing0 and preparation of manuscripts and final report

REPORTABLE OUTCOMES:

The following reportable outcomes that have resulted from this research include:

2008-2009:

Abstract, poster, and talk to the 2009 Military Health Research Forum, Kansas City, MO (September 2, 2009):

- King, A.P., Rauch, S., Giardino, N, Liberzon, I, Mindfulness and Self-Compassion Meditation for Combat Posttraumatic Stress Disorder (PTSD)

  (Abstract text is attached as an Appendix to this report)

2009-2010:

Abstract and talk accepted for slide talk at Anxiety Disorders Association of America (ADAA) Scientific Sessions: (March, 2011):

- King, A.P., Giardino, N, Sripada, R, Rauch, S., Liberzon, I, Mindfulness and Self-Compassion Meditation for Combat Posttraumatic Stress Disorder (PTSD)

  (Abstract text is attached as an Appendix to this report)

2010 - 2011

Abstract and talk accepted for slide talk at Anxiety Disorders Association of America (ADAA) Scientific Sessions: (March, 2011):

2011- 2012

Abstract and poster accepted for slide talk at American College of Neuropsychopharmacology (ACNP) Scientific Sessions: (December, 2011):

2013

Article published of pilot MBCT study (part of training in MBCT by Giardino and King) in ***Depression and Anxiety*** 2013 *A Pilot Study of Group Mindfulness-Based Cognitive Therapy (MBCT) for Combat Veterans with Posttraumatic Stress Disorder (PTSD).*

Manuscripts describing PTSD patient retention / engagement; clinical PTSD outcomes; and resting state and emotional regulation fMRI paradigms are in preparation.

CONCLUSIONS:

This study demonstrates that group therapy for PTSD utilizing fairly intensive training in Mindfulness meditation was acceptable to returning OEF/OIF veterans, and actually showed higher levels of engagement and significantly better retention in therapy than an already developed "active control" form of group therapy. We believe combat veterans with symptoms of PTSD will directly benefit from this research. The potential applications of this study lie in developing improved group treatments for PTSD that are accessible and effective, and better understanding the psychological and brain mechanisms that underlie the symptoms of PTSD and their effective treatment. Group therapy is a widely utilized modality at VA facilities, yet surprisingly little efficacy data on symptom reduction is available.

Our data suggests that while not every veteran was interested in Mindfulness-based approaches, those who continued in the group showed good compliance and acceptability, many said they enjoyed the exercises and believed they found benefit. Many patients in the MBET group also showed significantly reduced PTSD symptoms. On average in a pre-post therapy contrast (paired t-tests), patients in the MBET group showed a clinically meaningful 15 point reduction in CAPS score ($p = .007$), whereas an active control group PCGT showed an 8 point drop which was not significant; however, the group x time interaction in repeated measures ANOVA was not significant overall.

Analyses of fMRI neuroimaging identify possible neurocircuitry associated with pre to post therapy in the MBET group, including decreased amygdala activation, dorsal ACC, and globus pallidus / putamen activation during an emotional processing task. Thus we believe this study is likely to advance research into understanding the mechanisms of emotional regulation in PTSD, and how training in mindfulness meditation and specific forms of emotional regulation and positive mood induction may be helpful for coping with or improving symptoms of PTSD. This research examines efficacy of a novel treatment for PTSD, and the neural mechanisms of emotional regulation that may mediate effects. It may thus lead to improved treatment and understanding of therapeutic mechanisms involving emotional regulation.

REFERENCES:

Britton JC, Phan KL, Taylor SF, Fig LM, Liberzon I. Corticolimbic blood flow in posttraumatic stress disorder during script-driven imagery. Biol Psychiatry 2005;57(8):832-40.

Baer RA, Smith GT, Lykins E, Button D, Krietemeyer J, Sauer S, Walsh E, Duggan D, Williams JM. Construct validity of the five facet mindfulness questionnaire in meditating and nonmeditating samples. Assessment. 2008; 15(3):329-42

Foa EB, Rauch SA. Cognitive changes during prolonged exposure versus prolonged exposure plus cognitive restructuring in female assault survivors with posttraumatic stress disorder. J Consult Clin Psychol 2004;72(5):879-84.

Gordon JS, Staples JK, Blyta A, Bytyqi M. Treatment of posttraumatic stress disorder in postwar Kosovo high school students using mind-body skills groups: a pilot study. J Trauma Stress 2004;17(2):143-7.

Gross JJ, John, O.P.Gross, J.J., Richards, J.M., John, O.P., . Individual differences in two emotion regulation processes: implications for affect, relationships, and well-being. Journal of EmotionPersonality and Social Psychology 2003;85:348-62.

Grossman P, Niemann L, Schmidt S, Walach H. Mindfulness-based stress reduction and health benefits. A meta-analysis. J Psychosom Res 2004;57(1):35-43.

Hickling EJ, Sison GF, Jr., Vanderploeg RD. Treatment of posttraumatic stress disorder with relaxation and biofeedback training. Biofeedback Self Regul 1986;11(2):125-34.

Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. N Engl J Med 2004;351(1):13-22.

Kang HK, Natelson BH, Mahan CM, Lee KY, Murphy FM. Post-traumatic stress disorder and chronic fatigue syndrome-like illness among Gulf War veterans: a population-based survey of 30,000 veterans. Am J Epidemiol 2003;157(2):141-8.

Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. Arch Gen Psychiatry 1995;52(12):1048-60.

Kingston T, Dooley B, Bates A, Lawlor E, Malone K. Mindfulness-based cognitive therapy for residual depressive symptoms. Psychology and psychotherapy 2007;80(Pt 2):193-203.

Kulka RA, Schlenger, W. E., Fairbanks, J. A., Hough, R. L., Jordan, B. K., Marmar, C. R., Weiss, D. S. Trauma and the Vietnam War generation : report of findings from the National Vietnam veterans readjustment study. 1990;book.

Lanius RA, Williamson PC, Hopper J, et al. Recall of emotional states in posttraumatic stress disorder: an fMRI investigation. Biol Psychiatry 2003;53(3):204-10.

Lazar SW, Bush G, Gollub RL, Fricchione GL, Khalsa G, Benson H. Functional brain mapping of the relaxation response and meditation. Neuroreport 2000;11(7):1581-5.

Liberzon I, Abelson JL, Flagel SB, Raz J, Young EA. Neuroendocrine and psychophysiologic responses in PTSD: a symptom provocation study. Neuropsychopharmacology 1999;21(1):40-50.

Liberzon I, Britton JC, Phan KL. Neural correlates of traumatic recall in posttraumatic stress disorder. Stress 2003;6(3):151-6.

Liberzon I, King AP, Britton JC, Phan KL, Abelson JL, Taylor SF. Paralimbic and medial prefrontal cortical involvement in neuroendocrine responses to traumatic stimuli. Am J Psychiatry 2007;164(8):1250-8.

Liberzon I, Martis B. Neuroimaging studies of emotional responses in PTSD. Annals of the New York Academy of Sciences 2006;1071:87-109.

Liberzon I, Phan KL. Brain-imaging studies of posttraumatic stress disorder. CNS Spectr 2003;8(9):641-50.

Liberzon I, Taylor SF, Amdur R, et al. Brain activation in PTSD in response to trauma-related stimuli. Biol Psychiatry 1999;45(7):817-26.

Linehan MM, Schmidt H, 3rd, Dimeff LA, Craft JC, Kanter J, Comtois KA. Dialectical behavior therapy for patients with borderline personality disorder and drug-dependence. The American journal on addictions / American Academy of Psychiatrists in Alcoholism and Addictions 1999;8(4):279-92.

Miller JJ, Fletcher K, Kabat-Zinn J. Three-year follow-up and clinical implications of a mindfulness meditation-based stress reduction intervention in the treatment of anxiety disorders. Gen Hosp Psychiatry 1995;17(3):192-200.

Neff KD, Vonk R. Self-compassion versus global self-esteem: two different ways of relating to oneself. Journal of personality 2009;77:23-50.

Nolen-Hoeksema S, Morrow, J., & Fredrickson, B. L. Response styles and the duration of episodes of depressed mood. . Journal of Abnormal Psychology 1993;102:20-8. Orsillo SM, Batten SV. Acceptance and commitment therapy in the treatment of posttraumatic stress disorder. Behav Modif 2005;29(1):95-129.

Phan KL, Wager T, Taylor SF, Liberzon I. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. Neuroimage 2002;16(2):331-48.

Ramel W GP, Carmona PE, McQuaid JR. The Effects of Mindfulness Meditation on Cognitive Processes and Affect in Patients With Past Depression. Cognitive Therapy and Research 2004;28(4):433-55.

Rauch SL, Whalen PJ, Shin LM, et al. Exaggerated amygdala response to masked facial stimuli in posttraumatic stress disorder: a functional MRI study [In Process Citation]. Biol Psychiatry 2000;47(9):769-76.

Schnurr PP, Friedman MJ, Engel CC, et al. Cognitive behavioral therapy for posttraumatic stress disorder in women: a randomized controlled trial. Jama 2007;297(8):820-30.

Schnurr PP, Friedman MJ, Engel CC, et al. Issues in the design of multisite clinical trials of psychotherapy: VA Cooperative Study No. 494 as an example. Contemporary clinical trials 2005;26(6):626-36.

Schnurr PP, Friedman MJ, Foy DW, et al. Randomized trial of trauma-focused group therapy for posttraumatic stress disorder: results from a department of veterans affairs cooperative study. Arch Gen Psychiatry 2003;60(5):481-9.

Seagal Z, Williams, Mark, Teasdale, John, . Mindfulness-based Cognitive Therapy for Depression: A New Approach for Preventing Relapse. New York: Guilford Press; 2002.

Segal ZV, Williams, J. M. G., & Teasdale, J. D. . Mindfulness-based cognitive therapy for depression: A new approach to preventing relapse. . New York: : Guilford Press.; 2002.

Shapiro SL, Carlson LE, Astin JA, Freedman B. Mechanisms of mindfulness. J Clin Psychol 2006;62(3):373-86.

Shin LM, Orr SP, Carson MA, et al. Regional cerebral blood flow in the amygdala and medial prefrontal cortex during traumatic imagery in male and female Vietnam veterans with PTSD. Arch Gen Psychiatry 2004;61(2):168-76.

Shin LM, Rauch SL, Pitman RK. Amygdala, medial prefrontal cortex, and hippocampal function in PTSD. Annals of the New York Academy of Sciences 2006;1071:67-79.

Taylor SF, Phan KL, Decker LR, Liberzon I. Subjective rating of emotionally salient stimuli modulates neural activity. Neuroimage 2003;18(3):650-9.

Teasdale JD, Segal ZV, Williams JM, Ridgeway VA, Soulsby JM, Lau MA. Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. J Consult Clin Psychol 2000;68(4):615-23.

Thompson BL, Waltz J. Self-compassion and PTSD symptom severity. Journal of traumatic stress 2008;21:556-8.Wallace BA, Shapiro SL. Mental balance and well-being: building bridges between Buddhism and Western psychology. The American psychologist 2006;61(7):690-701.

Wells A, Sembi S. Metacognitive therapy for PTSD: a preliminary investigation of a new brief treatment. J Behav Ther Exp Psychiatry 2004;35(4):307-18.

APPENDIX

Presentations 2009:

1. Abstract presented at Military Health Research Forum, Kansas City, MO (September 2009)

Title: Mindfulness and Self-Compassion Meditation for Combat Posttraumatic Stress Disorder (PTSD)

Authors: King, A.P., Rauch, S., Giardino, N, Liberzon, I,

(a) Background and objectives: "Mindfulness meditation" cultivates present-focused, non-judgmental attention to interoceptive, emotional, and cognitive processes. It is proposed to lead to a greater sense of well-being and acceptance, cognitive flexibility, and tolerance of distress. "Compassion meditation" induces and stabilizes pro-social, empathic, kind/loving and compassionate regard to one"s self and others. Mindfulness-based Stress Reduction (MBSR) is helpful for coping with chronic pain, and distress and anxiety of medical disorders, and Mindfulness-based Cognitive Therapy (MBCT) for preventing depression relapse in patients, whereas a trial loving-kindness meditation improved chronic lower back pain. Our group has found emotional meta-awareness leads to decreased amygdala and increased medial prefrontal cortex (mPFC) activation. Neuroimaging studies of compassion have found effects on emotional neurocircuitry. Mindfulness and compassion meditation may be useful for distress to trauma memories, guilt and self-blame, and emotional dysregulation found in combat PTSD. We hypothesize mindfulness and self-compassion meditation will lead to 1.) improvement in PTSD and quality of life 2.) improved emotional regulation, „mindfulness" and self-compassion, and 3.) strengthening of mPFC circuits during emotional provocation.
(b) Brief description of methodologies: We are currently developing a manual for a 16-week group therapy including mindfulness and self-compassion, using input from patients and an expert advisory board of meditation and PTSD experts, and are validating emotional and social cognition neuroimaging paradigms to study mPFC and cortico-limbic neurocircuitry in PTSD. We will use present-centered therapy as a control, controlling for hours of therapist contact and daily homework, but no meditation or mindfulness exercises. We will randomly assign a total of n=96 patients to meditation and control groups, with pre- post, and 3 mo followup assessments with validated measures of PTSD symptoms, quality of life, "mindfulness", emotional regulation, and trauma-related cognitions. We will also perform a "nested" study of fMRI neuroimaging to examine neurocircuitry underlying emotional regulation that may mediate therapeutic effects.
(c) Results to date: A pilot study at the Ann Arbor VA of an 8 week group using mindfulness meditation, mindful movement (e.g. yoga), and self-compassion meditation found these techniques generally acceptable to combat PTSD patients, with high levels of compliance in completers. We also found significant reductions in „avoidant" PTSD symptoms and self-blame cognitions compared to a treatment-as-usual group. Importantly, we have gained greater insight and experience into how to acceptably and effectively deliver meditation programs to combat veterans seeking treatment for PTSD.
(d) Conclusions: Mindfulness and self-compassion exercises appear to be acceptable to combat veterans with PTSD and also appear to lead to reductions in PTSD symptoms.
(e) Impact statement. This research will examine efficacy of a novel treatment for PTSD, and the neural mechanisms of emotional regulation that may mediate effects. This will advance understanding of mechanisms of emotional regulation in PTSD, and how training in emotional regulation and positive mood induction may be helpful PTSD. It may thus lead to improved treatment and understanding of therapeutic mechanisms involving emotional regulation.

Title: Mindfulness and Self-Compassion Meditation for Combat Posttraumatic Stress Disorder (PTSD)

Authors: King, A.P., Giardino, N., Sripada, R., Rauch, S., Liberzon, I,

Presentations 2010:

1. Abstract accepted for presentation at Anxiety Disorders Association of America (ADAA), New Orleans, LA March 2011

Mindfulness-based "Mind-Body" interventions can be effective for stress-reduction in general medical disorders, and for prevention of depression relapse, and may also have promise for anxiety disorders including posttraumatic stress disorder (PTSD). In particular, the efficient group format and the level of engagement found in Mind-Body approaches make them attractive as potential treatments or adjunctive therapies for combat PTSD. We conducted several open-label pilot groups adapting the 8 week Mindfulness-based Cognitive Therapy manual for use with combat PTSD, with Vietnam and Gulf War veterans (n=25), and found significant reduction in PTSD symptoms (CAPS) and trauma-related cognitions (PTCI). These data suggested that Mindfulness-based groups were acceptable to a VA PTSD population and may have potential efficacy. We are currently engaged in a 4-year treatment development and RCT of a new 16-week Mindfulness-based group therapy for combat PTSD with veterans returning from combat deployments to Afghanistan (OEF) and Iraq (OIF). We are furthering manual development with open label pilot groups, which will be followed by an RCT comparing our 16 week Mind-Body group to an active 16 week control ("present-centered") group therapy. Our new group intervention uses in-session and daily home Mindfulness training and other Mind-Body components of MBCT (yoga- and Chi gung-like stretches and movement), as well as PTSD psychoeducation, mindful coping techniques for PTSD symptoms, "mindful engagement" (practices similar to behavioral activation and in vivo exposure), and "self-compassion" exercises working with guilt. We have run the first pilot of the new 16 week MBCT intervention, which showed significant reductions in CAPS and PCL scores. A second group is currently underway, which also includes pre-post fMRI neuroimaging. The specific components of the group intervention and study design, as well as treatment outcome data (PTSD symptoms and related cognitions) of our first 2 groups will be discussed. We will also discuss preliminary analyses of measures of "Mindfulness" and self-compassion, emotional regulation, cognitive neuroscience (attention measures), potential roles for our neuroendocrine and neuroimaging data in this multi-modal translational research with combat PTSD patients. We will also discuss potential efficacy and mechanisms of Mind-Body approaches in the context of existing well empirically supported approaches (e.g. exposure- and cognitive processing-based therapies).

Presentations 2011:

American College of Neuropsychopharmacology (ACNP) Scientific Sessions:

Pilot Study of Mindfulness-based Exposure Therapy for PTSD in OEF/OIF Veterans: Preliminary Clinical Outcomes and Pre-post fMRI Neuroimaging

Anthony King1,2, Nicholas Giardino1,2, Sheila Rauch1,2, Sripada Rebecca1, Jiun-Yiing Hu1, Israel Liberzon1,2. 1University of Michigan, Ann Arbor, MI, United States; 2VA Ann Arbor, Ann Arbor, MI, United States

Background.

Combat PTSD is a seriously debilitating disorder affecting up to 20% of returning veterans. Trauma-focused therapies such as prolonged exposure (PE) show substantial efficacy, but additional approaches are important for patients who will not engage or do not benefit from this approach. Mindfulness-based Cognitive Therapy (MBCT) shows substantial efficacy for prevention of depression relapse, and an uncontrolled pilot study of Mindfulness-based Stress Reduction (MBSR) found acceptability and decreased PTSD symptoms in adult survivors of childhood sexual abuse. We conducted a pilot study of MBCT adapted for PTSD in combat veterans with PTSD, and found acceptability and a significant (~25%) reduction in PTSD symptoms. We have subsequently developed a manualized 16-week group mindfulness-based intervention specific for PTSD combining mindfulness training, self-compassion exercises, and in vivo exposure, which we call "Mindfulness-based Exposure therapy" (MBET), and which we are currently testing in an RCT and neuroimaging study.

Methods.

A total of n=22 combat veterans of OEF (Afghanistan) and/or OIF (Iraq) seeking treatment for PTSD at the VA Ann Arbor were sequentially recruited for pilot groups: two MBET (n=15) and one PCGT (n=7) group. Psychiatric interviews with an independent assessor blind to treatment assessed PTSD (CAPS) and psychiatric co-morbidity (MINI) at intake (pre), 8 weeks (mid), 16 weeks (post-therapy), and 28 weeks (3 mo FU), and self-report measures were obtained. Emotional regulation fMRI neuroimaging paradigms were conducted in a 3T environment, using passive viewing of aversive IAPS pictures as an emotional probe and compared two volitional emotional regulation conditions (re-appraisal and meta-cognitive "rating" tasks). Scans were performed before the start of therapy, and post-therapy following assessment.

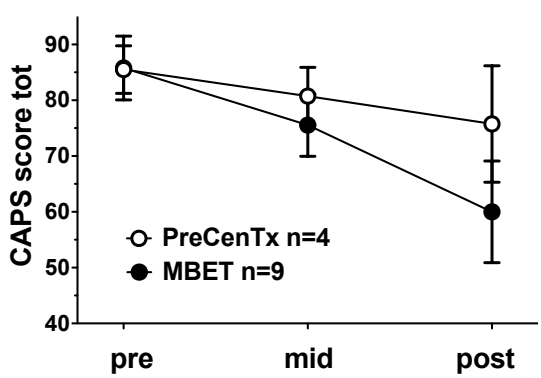
Results.

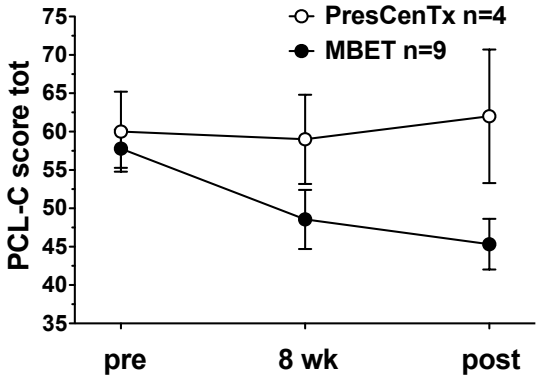
Drop rate was high in both groups, consistent with previous PTSD intervention studies. Six patients dropped before starting therapy (most citing changes in schedules). In the two MBET pilot groups, 3 patients dropped after 1-8 sessions (25%), and 9 patients completed, in one PCGT pilot group, 1 patient dropped after a single session (25%), and 4 completed. However, in MBET completers, acceptability and compliance both in session and homework appeared good. Age, combat exposures, and PTSD symptoms were not different at intake in completers of the two kinds of groups (MBET (n=9) CAPS 85 ± 6, PCGT (n=4) CAPS 85 ± 4). CAPS scores improved significantly in MBET completers (mean decrease 25.7 ± 10.1, $t[8] = 2.6$, $p = .03$, Hedges $g = 1.2$) but not in the PCGT completers (mean decrease 9.7 ± 7.8, $t[3] = 1.2$, $p = .38$). Intent-to-treat (ITT) analysis of the n=12 subjects who began MBET also found a significant

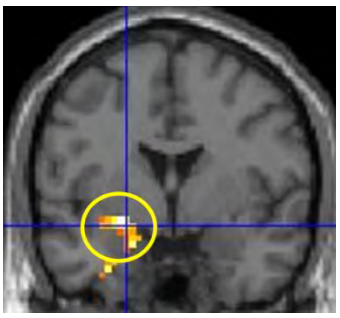
reduction in total CAPS (average decrease 19.7 ± 8.1, t[11]=2.1, p=.03). MBET also showed Improvement in self report measures of PTSD (PCL-C mean decrease 12.1 ± 1.5, t[8] = 8.0, p < .001), and rumination (RSQ), anxiety and depression (DASS-21), and "non-reactivity" facet of mindfulness (FFMQ), all p<.05. fMRI data are currently available from n=11 patients pre-therapy, and n=8 post-therapy. Pre-therapy, patients showed activation of bilateral amygdala, visual cortex, and IFG when viewing aversive IAPS, and greater activation of dorsal ACC (10, 48, 20, Z=3.0) and right IFG (33, 27, -6, Z=3.2) when "rating" ones emotional responses to IAPS. Preliminary analyses of pre-post scans (MBET n=4, PCGT n=4) found reduced activation of amygdala (-18, -6, -15, Z=3.5) post-MBET while viewing aversive IAPS, and a factorial Group x Time interaction in peri-amygdala (-27, -3, -21, Z=3.2) and dorsal ACC (18, 30, 27, Z=4.4).

Discussion.

This pilot study suggests a group therapy for PTSD containing mindfulness training and self-compassion exercises appears well-tolerated by OEF/OIF combat veterans seeking treatment for PTSD, and may lead to clinically meaningful improvement in PTSD symptoms. While the improvement in PTSD symptoms in MBET was not as large as reported for individual trauma=focused therapy (e.g. PE), it compares favorably with other published reports of group therapy for PTSD. This small pilot study suggests mindfulness-based modalities may be a reasonable alternative for PTSD patients who will not tolerate trauma-focused approaches. fMRI neuroimaging results are highly preliminary, but suggest possible changes in emotional neurocircuitry that may accompany clinical change. A randomized controlled trial of MBET compared to PCGT, with pre-post fMRI, is being conducted at VA Ann Arbor.







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Presentations 2012:

Symposium at Anxiety and Depression Association of America (Chair Elizabeth Hoge, MD)

Pilot Study of Mindfulness-Based Exposure Therapy (MBET) for Combat PTSD in Returning Veterans: Preliminary Clinical Outcomes and fMRI Neuroimaging

Anthony King, PhD University of Michigan

Background.
PTSD affects ~20% of combat veterans returning from Afghanistan (OEF) and Iraq (OIF). Mindfulness-based Cognitive Therapy (MBCT) is effective for depression relapse, and pilot studies suggested acceptability in sexual assault survivors and combat veterans. Here we report initial findings of a novel 16-week PTSD-specific intervention combining mindfulness, self-compassion, and in-vivo exposure; "Mindfulness-based Exposure Therapy" (MBET).

Methods.
OEF/OIF combat veterans with PTSD were sequentially recruited for two MBET (n=15) groups and one comparison "Present-Centered Group Therapy" (PCGT, n=7). Psychiatric interviews and self-report measures were obtained intake, post, 3mo FU. 3T fMRI neuroimaging scans were performed pre- and post-therapy, using emotional probe (IAPS) and regulation tasks (re-appraisal and meta-cognitive "rating").

Results.
Age, combat exposures, and PTSD symptoms were not different at intake. PTSD improved in MBET completers (mean CAPS decrease 25.7±10.1, $p=.03$, Hedges $g=1.2$) and intent-to-treat analysis (19.7±8.1, $p=.03$), but not in PCGT completers (decrease 9.7±7.8, $p=.38$). MBET also showed improvement in self-report PTSD ($p<.01$), rumination ($p=.01$), depression ($p<.05$), and "non-reactivity" mindfulness facet ($p<.05$). Pre-therapy fMRI (n=11) found activation of amygdala, visual cortex, and inferior frontal gyrus (IFG) viewing aversive IAPS, and greater activation of dorsal anterior cingulate (ACC) and right IFG while "rating". Preliminary analyses of available pre-post scans (MBET n=4, PCGT n=4) found reduced activation of amygdala to IAPS post-MBET, and GroupxTime interaction in amygdala and dACC.

Conclusions.
MBET for PTSD appears well-tolerated by OEF/OIF veterans with PTSD, and may lead to clinically meaningful improvement in PTSD symptoms. Preliminary fMRI neuroimaging results suggest possible changes in emotional neurocircuitry that may accompany clinical change.

Research Article

A PILOT STUDY OF GROUP MINDFULNESS-BASED COGNITIVE THERAPY (MBCT) FOR COMBAT VETERANS WITH POSTTRAUMATIC STRESS DISORDER (PTSD)

Anthony P. King, Ph.D.,[1,2]* Thane M. Erickson, Ph.D.,[3] Nicholas D. Giardino, Ph.D.,[1,2,4] Todd Favorite, Ph.D.,[1,2,5] Sheila A.M. Rauch, Ph.D., ABPP,[1,2,4] Elizabeth Robinson, Ph.D., MSW,[1] Madhur Kulkarni, Ph.D.,[6] and Israel Liberzon, M.D.[1,2,4]

Background: *"Mindfulness-based" interventions show promise for stress reduction in general medical conditions, and initial evidence suggests that they are accepted in trauma-exposed individuals. Mindfulness-based cognitive therapy (MBCT) shows substantial efficacy for prevention of depression relapse, but it has been less studied in anxiety disorders. This study investigated the feasibility, acceptability, and clinical outcomes of an MBCT group intervention adapted for combat posttraumatic stress disorder (PTSD).* **Methods:** *Consecutive patients seeking treatment for chronic PTSD at a VA outpatient clinic were enrolled in 8-week MBCT groups, modified for PTSD (four groups, n = 20) or brief treatment-as-usual (TAU) comparison group interventions (three groups, n = 17). Pre and posttherapy psychological assessments with clinician administered PTSD scale (CAPS) were performed with all patients, and self-report measures (PTSD diagnostic scale, PDS, and posttraumatic cognitions inventory, PTCI) were administered in the MBCT group.* **Results:** *Intent to treat analyses showed significant improvement in PTSD (CAPS ($t(19) = 4.8$, $P < .001$)) in the MBCT condition but not the TAU conditions, and a significant Condition × Time interaction ($F[1,35] = 16.4$, $P < .005$). MBCT completers (n = 15, 75%) showed good compliance with assigned homework exercises, and significant and clinically meaningful improvement in PTSD symptom severity on posttreatment assessment in CAPS and PDS (particularly in avoidance/numbing symptoms), and reduced PTSD-relevant cognitions in PTCI (self blame).* **Conclusions:** *These data suggest group MBCT as an acceptable brief intervention/adjunctive therapy for combat PTSD, with potential for reducing avoidance symptom cluster and PTSD cognitions. Further studies are needed to examine efficacy in a randomized controlled design and to identify factors influencing acceptability and efficacy. Depression and Anxiety 30:638–645, 2013.*

Key words: *clinical trials; life events; meditation; mindfulness; posttraumatic stress disorder (PTSD); stress; treatment*

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INTRODUCTION

Stress-reduction groups involving mindfulness meditation techniques delivered as classes in healthcare settings (e.g. mindfulness-based stress reduction, MBSR) and psychotherapies incorporating mindfulness techniques (e.g. mindfulness-based cognitive therapy, MBCT) have shown promise for reducing emotional distress and symptom severity across a number of psychiatric conditions with anxious and depressive symptomatology. MBSR has demonstrated durable, albeit moderate sized, effects on mental health measures of depression, anxiety, and stress when performed in "health-related" class settings.[1] MBCT was designed to prevent the recurrence of depressive episodes in patients with chronic recurrent depression, and is associated with substantial reduction in depression recurrence over 2 years of followup.[2–4] A subsequent version of the MBCT group-based intervention adapted for generalized anxiety disorder (GAD) has also shown significant symptom improvement,[5] as have individual interventions for GAD integrating mindfulness meditation techniques.[6,7]

There are theoretical reasons to expect that mindfulness-based interventions may be similarly useful in treatment of posttraumatic stress disorder (PTSD),[8,9] and combat-related PTSD in particular.[10] Mindfulness-based interventions strive to entrain sustained mindful attention to and acknowledgment of even unpleasant emotions or memories in a nonjudgmental manner.[11] As previously suggested,[9] such techniques stand diametrically opposed to the psychological processes of avoidance and suppression of painful emotions and memories, which are thought to contribute to symptom maintenance in PTSD.[12] Accordingly, mindfulness practice in patients with anxiety disorders was conceptualized as providing a form of exposure to experience of feared thoughts and bodily states.[6] Interestingly, in contrast to "refuting" or changing the content of negative cognitions that is typical of traditional cognitive-behavioral therapies, MBCT appears to alter one's relationship to negative cognitions.[13] Additionally, from a purely behavioral perspective, MBCT involves techniques similar to relaxation, and non-MBCT relaxation therapies have been commonly studied in PTSD, albeit usually as an "active control" therapy delivered individually. Most studies have found these relaxation techniques having small effect sizes (~0.5) when compared to individual exposure-based PTSD therapies (often with effect sizes >1.5).[14,15] However, as reported in a recent meta-analysis[16] published studies of group therapies for combat PTSD, including exposure-based group therapy,[17] have shown much smaller effect sizes (~0.3) than individual exposure-based therapies.

Preliminary studies among trauma-exposed persons support the notion that mindfulness-based therapies may be useful in PTSD treatment. Preliminary evidence suggests that Mind–Body group interventions with civilians with war-related trauma reduced PTSD symptoms.[18] A case study of acceptance and commitment therapy (ACT), which includes some mindfulness exercises, also suggested potential efficacy for combat PTSD.[19] An adaptation of MBSR for adults with a history of childhood sexual abuse, was well accepted and led to decreased symptoms of self-reported depression and PTSD.[20] A recent study at a VA hospital offered MBSR classes to interested veterans (about a third of whom had a history of PTSD on their computerized charts) as an adjunct to their current treatment, and also found a significant decrease in self-reported PTSD and depression symptoms.[21] Another recent study from the same research group randomly assigned patients with charted diagnoses of PTSD to either "standard" MBSR groups (i.e. with majority patients in the group without PTSD), or no additional treatment/treatment-as-usual (TAU).[22] MBSR was associated with improvement in self-report measures of PTSD (PCL-C), depression, quality of life, and mindfulness skills, although improvement in PCL-C was not different between the MBSR and control TAU condition. Taken together, these studies suggest that mindfulness techniques found in MBSR might be acceptable to persons with PTSD and/or trauma history, and may lead to meaningful improvements in mental health functioning. However, to our knowledge the use of mindfulness-based therapies such as MBCT, targeted to treat chronic combat-related PTSD, has not been reported.

Exposure-based therapies have been highly effective in the treatment of PTSD,[15] and do not show higher rates of adverse events or premature dropout than other forms of PTSD therapy.[23] Nonetheless, a significant minority of combat PTSD patients still decline this form of therapy (Liberzon et al., unpublished data). In light of this, the development of additional effective therapeutic approaches will be highly useful, and initial reports of treatment benefits of MBSR with trauma-exposed individuals[20–22] warrant further testing of mindfulness-based interventions tailored for the treatment of PTSD. Mindfulness-based interventions may serve as an adjunctive preparation for exposure (e.g. by increasing ability to tolerate experiencing emotions), an aid to cognitive therapies (e.g. by increasing engagement and developing cognitive skills), or possibly a stand-alone intervention to modulate emotional reactivity. The present pilot study examined the acceptability and effectiveness of a brief mindfulness-based group intervention (MBCT) adapted for treatment of combat-related PTSD.

METHODS

PARTICIPANTS

Participants were consecutive patients recruited from the PTSD Outpatient Clinic of the Ann Arbor VA Health Care System based upon referral by treating clinician. Patients were recruited for a total of seven groups (four MBCT, one PTSD psychoeducation and skills group (psychoed), and two Imagery Rehearsal Therapy groups (IRT)) over a 4-year period. Assignment to groups was not randomized, but

only a single group was recruited for at a time. Inclusion criteria were long-term (>10 years) PTSD (as assessed by Clinician Administered PTSD Scale (CAPS),[24] or PTSD in partial remission. Exclusion criteria included diagnoses of psychosis (e.g. schizophrenia, bipolar, and schizoaffective disorders) and current substance dependence, or active suicidal intent, as assessed using the Mini International Neuropsychiatric Interview (MINI).[25] All participants endorsed combat-related traumas (DSM-IV A criteria) from military service in conflicts including World War II, Korea, Vietnam, and Operation Desert Storm (Iraq and Kuwait). We report pre and posttherapy interview data for all subjects; complete self-report measures were not available for four patients completing MBCT. Psychiatric medication regimens were unchanged over the course of the study for veterans completing the study except for one patient with comorbid MDD in the MBCT condition, who received a new prescription of citalopram during the study. No patient in any treatment group started new psychotherapy during the study. Three patients in MBCT and four patients in TAU continued ongoing group therapy in long-term process groups during the study.

PROCEDURE

Therapists and Raters. Clinical team members included five doctoral or masters level clinicians. MBCT sessions were audio taped, and a doctoral-level clinical psychologist provided weekly supervision to promote treatment integrity and fidelity; the fidelity for each of the manualized groups was also supported using therapist "checklists" used in the session. Each of the four MBCT groups had at least one clinician with formal training in MBCT and/or MBSR and previous experience with facilitating mindfulness group interventions; and at least one clinician in each group also had training in psychotherapies for treatment of PTSD. The Psychoed and IRT groups were each coled by a doctoral-level and a masters level clinical psychologist. Pre and posttreatment PTSD interview assessments (CAPS) were performed by PTSD clinic clinicians trained on CAPS not involved in the treatment delivery and not informed of the treatment status of patients.

Treatments. The MBCT treatment protocol was adapted for combat-related PTSD from MBCT for the prevention of depression relapse.[26] The main adaptation was substitution of psychoeducation about depression with psychoeducation geared toward PTSD and stress physiology, discussion of patients PTSD symptoms in session, and encouraging patients to use a formal mindfulness exercise (the "3-Minute Breathing Space") as well as informal mindfulness when distressing situations arose during the week. We also shortened the length of the mindfulness meditation in session and at home from 45 min to 15–20 min, and increased attention to distress from trauma memories during in-session and at-home exercises. The adapted MBCT consisted of eight, weekly 8-hr group sessions, which included skills training and in-class practice in: (1) mindfulness techniques; (2) psychoeducation regarding PTSD and stress responses; and (3) feedback and supportive group discussion of exercises. Specific in-class mindfulness exercises included: (a) "mindful eating" (the "raisin exercise"), (b) the "body-scan" exercise, (c) "mindful stretching," (d) sitting "mindfulness" meditation exercises with various objects (breath, body, sounds, emotional states, thoughts), and (e) the "3-Minute Breathing Space" (a brief mindfulness of breath exercise). The program incorporated daily assignments of "formal" home practice of mindfulness techniques (using 15–20 min audio-recordings) as well as "informal" exercises to integrate mindfulness into everyday experiences (e.g. eating, walking, and showering), and use of the MBCT "3-Minute Breathing Space" at pre-ordained times and also when confronted with upsetting situations, including trauma memories, anxiety, and other PTSD symptoms throughout the day. Participants were instructed to practice mindfulness exercises aided by audio recordings at least 5 days a week, and the 3-Minute Breathing Exercise daily after week 4, as well as practicing mindfulness thoughout the day (e.g. while walking, eating, showering, etc.), for an additional 10–15 min a day, for a total of 25–40 min of total practice per day. Patients recorded daily practice times in homework logs that were collected weekly, in which they checked which audio recording(s) they had listened to that day, and how much time they had spent doing other mindfulness practice throughout the day.

The comparison interventions were intended as brief, plausible "treatment-as-usual" (TAU) group interventions for PTSD to control for nonspecific effects of group therapy (social support, normalization, expectancy, therapist contact), but did not exactly match contact hours or forms of homework. PTSD psychoeducation and skills (psychoed) was developed at VA Ann Arbor and consisted of eight weekly 1-hr sessions with psychoeducation about PTSD symptoms, anger, emotions, sleep, forms of coping with symptoms, PTSD psychotherapy, medications, and other services. Imagery rehearsal therapy group (IRT) was based on previous work with Vietnam veterans,[27,28] and consisted of six weekly 1.5-hr group sessions as previously described. The rationale of imagery rehearsal was explained as using alterations to the content of a recurrent nightmare that promote mastery or control nightmare (e.g. changing a violent scene to a alternate nonviolent version) as a method to decrease distress to nightmares. Potential changes to each patients nightmares were discussed in group, and each patient selected alternate forms of their own nightmare, rewrote a script that was discussed by the group, and rehearsed this script in imagination each night prior to sleep.

Measures. Treatment responses were assessed at intake and posttreatment in all patients using a semistructured clinician-administered interview (CAPS),[24] Patients in the MBCT condition also completed the self-report PTSD diagnostic scale (PDS)[29] and the posttraumatic cognitions inventory (PTCI),[30] which measures negative posttraumatic cognitions including negative (incompetent) self, negative (dangerous) world, and self blame.

Statistical Analyses. Both intention-to-treat and completer analyses were performed. Within-group effects on PTSD symptoms in the MBCT and TAU groups were examined with two-tailed paired samples *t*-tests of pre and posttherapy total CAPS scores (and intrusive, avoidant, and hyperarousal subscales), and within group effect sizes (Hedge's g) were calculated. Between group effects were examined using repeated-measures analyses of variance (RM-ANOVA), and between group effect sizes calculated from the posttherapy CAPS scores. Independent sample *t*-tests and chi-squared analyses were used to examine differences between demographics, previous treatment, and symptom measures at intake.

RESULTS

At the time of recruitment, patients enrolled in the MBCT or TAU groups (Psychoed and IRT) did not differ in terms of PTSD symptom severity (CAPS), comorbidity, age, marital, or employment status, time from combat trauma, or psychistaric service-connected disability. Table 1 shows patient demographic and clinical characteristics. All of the patients had long-term PTSD (>10 years) associated with military deployment traumas, and the majority reported experience of symptoms of PTSD for >30 years. Most of the patients enrolled in this study had extensive previous psychiatric treatments, including medications and individual and group psychotherapies. There was a considerable range in patient retrospective report of psychiatric treatment history, with two patients reporting no previous treatment. Given the problems of patient retrospective report, we examined history of previous psychiatric treatment at

TABLE 1. Demographics and clinical characteristics of PTSD patients at intake

	MBCT		TAU		t or χ^2	P
Total N	20		17			
Age	60.1	9.7	58.3	8.3	0.9	.33
Years from trauma	37.3	11.3	35.7	8.7	0.5	.61
Completed therapy	15	75%	13	77%	0.0	.97
Military deployment						
Korea or WWII	3	15%	1	6%	0.8	.67
Vietnam	15	75%	14	82%		
Desert Storm (Iraq)	2	10%	2	12%		
Married	14	70%	14	82%	0.7	.38
Employed	8	40%	6	35%	0.1	.79
Service-connect psychiatric disability $\geq$ 50%	14	70%	9	53%	1.1	.29
Comorbidity						
Current MDD	13	65%	13	76%	0.6	.44
Alcohol depend in remission	12	60%	9	62%	0.2	.76
# patients with previous weekly psychotherapy > 1 year	14	70%	10	59%	0.5	.47
Years in Psychiatric Treatment at VA Ann Arbor	4.9	5.1	3.5	3.3	0.9	.36
Current Medications						
Antidepressant	13	65%	11	65%	0.0	.99
Benzodiazepine	5	25%	4	24%	0.5	.50
Trazadone	7	35%	2	12%	2.7	.11
Antipsychotic	3	15%	4	24%	0.4	.51
Prazocin	2	10%	0	0%	1.8	.18
None	4	20%	3	18%	0.0	.93

this VA. The overall years of any form of treatment (e.g. medication, group and individual psychotherapy, inpatient and high-intensity outpatient program) were not different between the treatment groups. In terms of previous psychotherapy, the majority of patients had long-term group (and/or individual) psychotherapy, and others fewer than eight previous mental health encounters, (not different between treatment groups). Patients did not start new individual or group therapy during the study period. Three patients in MBCT and four patients in the IRT group were also in concurrent group therapies (remained in their long-term process groups). The majority of patients were taking psychiatric medications for PTSD, depression, and/or pain, there were no differences in medications between treatment groups.

COMPLIANCE AND RETENTION

We report behavioral evidence of acceptability as reflected in session attendance and homework completion. Treatment "completion" was defined as attending at least five sessions of MBCT or Psychoed, and at least four sessions of IRT. Five (25%) patients enrolled in MBCT groups and four (29%) patients enrolled in TAU groups discontinued treatment within the first three sessions. MBCT noncompleters endorsed several reasons for their decision not to continue with treatment: two cited low expectations/interest, three cited scheduling/transportation difficulties, and two endorsed increased anxiety during mindfulness exercises involving attending to bodily states; one, a survivor of sexual trauma, reported that the "body scan" exercise triggered traumatic memories of his assault. Reasons for drop out in the TAU groups were not specified.

Of the seven homework sheets, MBCT treatment completers turned in an average of 4.6 (SD = 1.4) sheets, in which they reported listening to at least one 15–20 min audio recording on average 5.5 (SD = 1.3) days per/week, amounting to an average self-report of 102.3 (SD = 20.4) min/week of audio-guided mindfulness practice. There was wide variation of self-report of mindfulness throughout the day (i.e. while eating, walking, showering, etc.), which was further skewed by three older retired veterans who each reported >60 min of informal practice per day, 7 days a week in which they included time spent doing daily physical therapy exercises or other routines "mindfully." Exclusion of these three participants found self-report of an average of 12.2 (SD = 6.6) additional minutes of "informal" mindfulness practice on days practice is reported.

TREATMENT RESPONSE

Intent-to-treat analyses found that patients who were enrolled in MBCT showed a significant reduction in total CAPS score (pre versus post MBCT $t(19) = 4.8$, $P < 0.001$, average 11-point decrease in total CAPS, effect size Hedges $g = 0.54$). In contrast, patients enrolled in the TAU did not show a significant reduction in CAPS ($t(16) = 0.2$, $P = .83$, $g = -0.04$)). In between condition analyses, RM-ANOVA found a significant Condition × Time interaction ($F[1,34] = 11.4$, $P = 0.002$) in total CAPS scores, with between condition posttherapy CAPS scores Hedges $g = 0.67$.

Differences in demographics, symptoms severity, and treatment history were not detected at intake between treatment completers ($N = 32$) and noncompleters ($N = 9$). Patients who completed MBCT ($N = 15$) showed significant improvement in PTSD symptoms (Table 2 and Figure 1), with effect size $g = 0.67$ for pre-post CAPS total score. The improvement in the MBCT condition appeared to be explained by a significant reduction in the CAPS-avoidant subscale. A single patient in the MBCT condition received a new prescription of citalopram during the group. This patient had among the highest intake CAPS, and also showed the least improvement at posttherapy assessment. Exclusion of this subject from the MBCT completer analysis did not affect reduction in total CAPS score findings ($t(13) = 5.6$, $P < 0.001$); nor did exclusion of the three older veterans with reports of very high home practice ($t(11) = 5.7$, $P < 0.001$). In contrast, patients who completed the TAU interventions (Psychoed and IRT) did not show reduction in total CAPS ($t(12) = 0.5$, $P = 0.622$) or any CAPS subscale (Table 2, Figure 1). Between treatment condition comparisons in completers also found a significant condition × time interaction in total CAPS scores and

TABLE 2. PTSD symptoms (CAPS) prepost and condition effects

Intention-to-treat analysis (MBCT N = 20, TAU N = 17)													
		Pre-therapy		Post therapy						Prepost	Btw group	Group* × Time	
Outcome		Mean	SD	Mean	SD	Delta	*t*	*df*	*P*	*g*	*g*	*F[1,35]*	*P*
CAPS Total	MBCT	74.5	19.3	62.6	23.1	−11.8	4.8	19	<0.001	0.55	0.77	14.7	0.001
	TAU	76.8	15.1	78.4	15.5	1.6	0.7	16	0.518	− 0.10			
Intrusive	MBCT	20.5	7.2	18.8	9.2	−1.7	1.4	19	0.183	0.20	0.77	1.2	0.290
	TAU	24.5	5.5	24.9	5.7	0.4	0.3	16	0.786	− 0.07			
Avoidance	MBCT	29.2	10.3	20.9	11.2	−8.3	4.6	19	<0.001	0.76	0.67	11.9	0.001
	TAU	27.0	8.6	27.8	9.6	0.8	0.4	16	0.673	− 0.09			
Hyperarousal	MBCT	24.7	6.9	22.9	7.9	−1.7	1.7	19	0.100	0.24	0.37	0.6	0.461
	TAU	26.3	5.1	25.6	5.9	−0.6	0.6	16	0.554	0.12			
Completer analysis (MBCT N = 15, TAU N = 13)													
		Pre therapy		Post therapy						Prepost	Btw group	Group × Time	
Outcome		Mean	SD	Mean	SD	Delta	*t*	*df*	*P*	*g*	*g*	*F[1,26]*	*P*
CAPS total	MBCT	73.5	21.7	57.7	24.3	−15.7	6.2	14	<0.001	0.67	1.01	16.2	0.001
	TAU	77.2	16.3	79.4	16.7	0.8	−0.2	12	0.838	− 0.05			
Intrusive	MBCT	19.3	6.9	17.1	9.4	−2.2	1.3	14	0.621	0.26	0.86	1.2	0.290
	TAU	24.4	9.1	24.9	6.4	0.5	−0.3	12	0.780	− 0.06			
Avoidance	MBCT	30.5	10.1	19.5	11.1	−11.0	5.6	14	<0.001	1.01	0.76	14.7	0.001
	TAU	27.1	9.9	28.2	11.1	1.1	−0.4	12	0.680	− 0.10			
Hyperarousal	MBCT	23.7	7.8	21.3	8.5	−2.5	1.9	14	0.151	0.29	0.67	0.7	0.407
	TAU	27.2	4.0	26.3	5.3	−0.8	0.6	12	0.560	0.19			

CAPS, clinician administered PTSD scale; MBCT, mindfulness-based cognitive therapy; TAU, treatment as usual; SD, standard deviation; g, Hedge's g (bias corrected effect size).

the CAPS-avoidant subscale. The number of treatment completers with "clinically meaningful" improvements in PTSD symptoms (reduction of 10 points on the total CAPS scale) was significantly greater in the MBCT completers (11 of 15, 73%) compared to TAU completers (4 of 13, 33%), chi squared = 4.2, Fisher's exact $P < 0.05$. Decrease in PTSD intrusive symptoms (CAPS intrusive subscale) in MBCT completers was correlated with reported average time per week spent on mindfulness practice using audiorecordings ($r(15) = 0.53$, $P = 0.03$).

Additional self-report measures were available for MBCT completers only (Table 3). Similar to CAPS, self-report of PTSD symptoms (PDS) were significantly reduced following MBCT, and appeared to be due to decrease in PDS "numbing" subscale. Negative cognitions (PTCI) also improved significantly following MBCT, with significant reductions in total PTCI score and self-blame cognitions, as well as marginally significant decreases in negative self and world cognitions.

DISCUSSION

The results of this pilot trial of a brief mindfulness-based group therapy suggest that an MBCT group therapy targeted for combat-related PTSD is acceptable and a potentially effective novel therapeutic approach for PTSD symptoms and trauma-related negative cognitions. The majority of veterans enrolled in the mindfulness group showed good engagement in the "in session" exercises, and were also compliant with daily

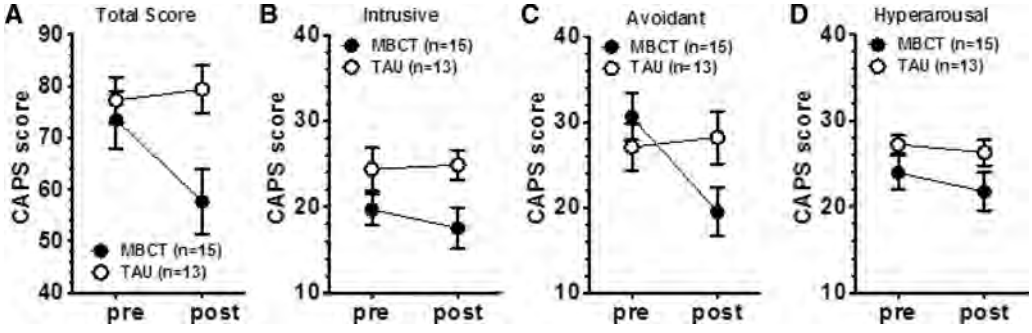

Figure 1. PTSD symptom severity before and after the 8-week mindfulness training group. Shown are plots of changes in PTSD symptoms (Clinician-Administered PTSD Scale) total and intrusive, avoidant, and hyperarousal subscales.

TABLE 3. Self-report measures (MBCT group only)

Outcome	Pre therapy		Post therapy		Delta	*t*	*df*	*P*	Prepost *g*
	Mean	SD	Mean	SD					
PDS									
PDS total	34.8	9.6	29.7	12.6	−5.1	2.3	12	0.014	0.59
Re-experiencing	9.1	4.1	7.8	3.7	−1.3	2.6	12	0.119	0.30
Numbing	13.6	4.5	11.0	5.3	−2.6	1.0	12	0.029	0.69
Hyperarousal	12.1	3.1	10.8	5.2	−1.2	2.6	12	0.267	0.25
PTCI									
Negative self	4.0	1.3	3.4	1.5	−0.6	1.94	10	0.081	0.48
Negative world	5.3	1.0	4.4	1.9	−0.9	2.07	10	0.065	0.61
Self blame	3.6	1.3	2.3	1.3	−1.3	2.86	10	0.017	1.04

MBCT, mindfulness-based cognitive therapy; PDS, PTSD diagnostic scale; PTCI, posttraumatic cognitions inventory; SD, standard deviation; g, Hedge's g (bias corrected effect size).

mindfulness practice; several reported an unexpectedly high level of engagement and compliance with home mindfulness practice. There was a 25% dropout rate of veterans discontinuing MBCT (all within the first three weeks), a dropout rate that was not different from the TAU groups and similar with typical dropout rates in outpatient treatment studies of PTSD.[27] However, it is important to note that two patients who dropped reported increased anxiety during the mindfulness exercises as a factor contributing to dropping the group. This suggests that great attention should be paid to "body-focused" exercises such as the body scan, which may be especially challenging for veterans with a history of sexual assault. Delivering such interventions in modified form and/or only after establishment of appropriate rapport and safety, might be useful for these patients.

The MBCT group showed significant reduction in PTSD symptoms pre- versus post MBCT as assessed by clinician-administered interview (CAPS) in both intent-to-treat and completer analyses. MBCT also showed significantly greater reduction in CAPS than a comparison "TAU" group therapy condition. While the improvement in PTSD symptoms in the brief 8-week MBCT intervention was moderate (averaging ~16 points on the total CAPS, effect size Hedge's g ~0.7), this level of CAPS reduction has been interpreted as representing a clinically meaningful improvement in PTSD (e.g. 10 points or more),[33] and 73% of patients in MBCT (compared to 33% in TAU groups) showed clinically meaningful improvement. While the effects of MBCT on PTSD symptoms were smaller than treatment effects reported with individual, 12–15 week, prolonged exposure therapy,[31,32] group PTSD treatments have shown smaller effects sizes; and the present data compare favorably to effects reported in other group therapies for combat PTSD, including a 30-week trauma-focused exposure based group therapy.[17] The outcomes seen in MBCT (adapted for PTSD) on both self-reported and clinician-rated PTSD symptoms found in this study were similar to effects of MBSR on self-reported PTSD symptoms in recent studies.[20–22]

These findings are particularly noteworthy in light of the short duration of MBCT-based intervention in this trial on one hand, and the chronicity of PTSD symptoms reported by our veterans (15–50 years) on the other. Interestingly, the mindfulness group appeared to reduce mainly the avoidant cluster symptoms, on CAPS, suggesting potential specificity of action here, which is consistent with the emphasis on reduced avoidance of unwanted emotions, and experiences in mindfulness training.[6,8,11] Given that one might expect avoidance symptoms to change first, a longer intervention or follow-up assessments may show greater impact on intrusive and hyperarousal symptoms, although such speculation requires further study. Additionally, consonant with an emphasis on mindful attention to positive experiences and nonjudgmental acceptance, the intervention led to a significant decrease in cognitions of self-blame and a trend toward decreased perception of the world as a dangerous place.

Several limitations of this pilot study should be noted. Our patients were recruited based upon availability and included veterans of a range of ages, conflicts, and deployments (e.g. WWII, Korea, Vietnam, Desert Storm), but were primarily older veterans with long-term PTSD. While we are reporting results of a "treatment as usual" group intervention for comparison, with a well-matched long-term combat PTSD patient sample, it is important to note that patients were not randomly assigned to different treatments. Thus, the reported results must be considered as preliminary, and these finding have to be replicated in random assignment design (currently underway). Nevertheless, groups were recruited one at a time with consecutive patients, and patients were not selected based upon clinical characteristics or preferences. Furthermore, although the TAU groups were both brief weekly group interventions for PTSD, they had lower contact time than MBCT and did not match amount of daily homework. It should be noted that the lack of significant decrease in PTSD symptoms in the IRT intervention was inconsistent with our initial expectations, but is consistent with subsequent findings of only small improvements in PTSD symptoms in group

IRT in Vietnam veterans with PTSD.[28] The study included a relatively small sample and several patients did not complete posttreatment measures. MBCT and IRT treatment fidelity was assessed by therapist checklist, but not by independent assessment of recorded sessions.

Nonetheless, despite the small sample, patients who completed the MBCT group showed meaningful improvements in both PTSD symptoms and cognitions. Future studies with larger samples and random assignment will be needed to determine whether mindfulness-based interventions also significantly reduce PTSD symptoms beyond the avoidance cluster. Additionally, the lack of follow-up assessment in this study limits ability to determine additional symptom changes subsequent to treatment. Given the long-term protection from depression relapse afforded by MBCT,[2–4] future studies of this type of intervention should assess PTSD outcomes at later follow-ups.

The purpose of the present pilot study was to provide initial data on the feasibility and acceptability, as well as estimates of effect sizes, of a mindfulness-based group intervention (MBCT) targeted for treatment of combat PTSD. The brief 8-week group-based intervention appeared acceptable to veterans in a VA PTSD clinic, who demonstrated high levels of engagement, and was associated with a statistically significant and clinically meaningful improvement in PTSD symptoms. Thus, despite limitations, the preliminary results of this pilot study are encouraging and support further investigation of mindfulness-based interventions for combat-related PTSD, particularly with larger samples and treatment randomization. Mindfulness-based therapies provide a strategy that encourages active engagement without explicit cognitive restructuring or exposure to trauma memories, are relatively easy to learn, and can be administered in an efficient group format. Increased ability to actively attend to, and generate nonjudgmental acceptance of, traumatic memories and physiological responses may help prepare individuals for trauma-focused therapies, such as prolonged exposure. Further research is needed to determine whether mindfulness training is more aptly considered an adjunct to the gold-standard treatment of prolonged exposure, or whether PTSD interventions including mindfulness can function as interventions for treating avoidant and other symptoms of combat PTSD in their own right.

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REFERENCES

1. Grossman, P, Niemann L, Schmidt S, Walach H. Mindfulness-based stress reduction and health benefits. a meta-analysis. J Psychosom Res 2004;57:35–43.
2. Ma SH, Teasdale JD. Mindfulness-based cognitive therapy for depression: replication and exploration of differential relapse prevention effects. J Consult Clin Psychol 2004;72:31–40.
3. Teasdale JD, Segal ZV, Williams JM, Ridgeway VA, Soulsby JM, Lau MA. Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. J Consult Clin Psychol 2000;68:615–621.
4. Segal ZV, Bieling P, Young T, et al. Antidepressant monotherapy vs sequential pharmacotherapy and mindfulness-based cognitive therapy, or placebo, for relapse prophylaxis in recurrent depression. Arch Gen Psychiatry 2011;67(12):1256–1264.
5. Evans S, Ferrando S, Findler M, Stowell C, Smart C, Haglin D. Mindfulness-based cognitive therapy for generalized anxiety disorder. J Anxiety Disord 2008;22:716–721.
6. Roemer L, Orsillo SM. Expanding our conceptualization of and treatment for generalized anxiety disorder: integrating mindfulness/acceptance-based approaches with existing cognitive-behavioral models. Clin Psychol 2002;9:54–68.
7. Roemer L Orsillo SM, Salters-Pedneault K. Efficacy of an acceptance-based behavior therapy for generalized anxiety disorder: evaluation in a randomized controlled trial. J Consult Clin Psychol, 2008;76(6):1083–1089.
8. Follette V, Palm KM, Pearson AN. Mindfulness and trauma: Implications for treatment. J Ration Emot Cogn Behav Ther 2006; 24:45–61.
9. Follette V, Palm KM, Rasmussen-Hall ML Acceptance, mindfulness, and trauma. In: Hayes SC, Follette VM Linehan MM, editors. Mindfulness and Acceptance: Expanding the Cognitive-Behavioral Tradition. Gilford Press, New York, 2004; pp. 192–208.
10. Vujanovic AA, Niles B, Pietrefesa A, Schmertz SK, Potter CM. Mindfulness in the treatment of posttraumatic stress disorder among military veterans. Prof Psychol 2011;42: 24–31.
11. Bishop SR, Lau M, Shapiro S, et al. Mindfulness: a proposed operational definition. Clin Psychol 2004;11:230–241.
12. Hembree EA, Foa EB. Posttraumatic stress disorder: psychological factors and psychosocial interventions. J Clin Psychiatry2000;61:33–39.
13. Teasdale JD, Moore RG, Hayhurst H, Pope M, Williams S, Segal ZV. Metacognitive awareness and prevention of relapse in depression: empirical evidence. J Consult Clin Psychol 2002;70: 275–287.
14. Bradley R, Greene J, Russ E, Dutra L, Westen D. A multidimensional meta-analysis of psychotherapy for PTSD. Am J Psychiatry 2005;162:214–227.
15. Powers MB, Halpern JM, Ferenschak MP, Gillihan SJ, Foa EB. A meta-analytic review of prolonged exposure for posttraumatic stress disorder. Clin Psychol Rev 2010;30(6): 635–641.
16. Sloan DM, Feinstein BA, Gallagher MW, Beck JG, Keane TM. Efficacy of group treatment for posttraumatic stress disorder symptoms: a meta-analysis. Psychological Trauma: Theory, Research, Practice, and Policy 2013;5(2):176–183.
17. Schnurr PP, Friedman MJ, Foy DW, et al. Randomized trial of trauma-focused group therapy for posttraumatic stress disorder: results from a department of veterans affairs cooperative study. Arch Gen Psychiatry 2003;60:481–489.
18. Gordon JS, Staples JK, Blyta A, Bytyqi M, Wilson AT. Treatment of posttraumatic stress disorder in postwar Kosovar adolescents using mind-body skills groups: a randomized controlled trial. J Clin Psychiatry 2008;69:1469–1476.
19. Orsillo SM, Batten SV. Acceptance and commitment therapy in the treatment of posttraumatic stress disorder. Behav Modif 2005;29:95–129.

20. Kimbrough E, Magyari T, Langenberg P, Chesney M, Berman B. Mindfulness intervention for child abuse survivors. J Clin Psychol 2010;66:17–33.
21. Kearney DJ, McDermott K, Malte C, Martinez M, Simpson TL. Association of participation in a mindfulness program with measures of PTSD, depression and quality of life in a veteran sample. J Clin Psychol 2012;68:101–116.
22. Kearney DJ, McDermott K, Malte C, Martinez M, Simpson TL. Effects of participation in a mindfulness program for veterans with posttraumatic stress disorder: a randomized controlled pilot study. J Clin Psychol 2013;69(1):14–27.
23. Hembree EA, Foa EB, Dorfan NM, Street GP, Kowalski J, Tu X. Do patients drop out prematurely from exposure therapy for PTSD? J Trauma Stress 2003;16(6):555–562.
24. Blake DD, Weathers FW, Nagy LM, et al. The development of the Clinician-Administered PTSD Scale. J Trauma Stress 1995;8:75–90.
25. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59:22–33.
26. Segal ZV, Williams JM, Teasdale JD. Mindfulness-based cognitive therapy for depression: a new approach to preventing relapse. Guilford Press, New York; 2004.
27. Forbes D Phelps A, McHugh T. Treatment of combat-related nightmares using imagery rehearsal: a pilot study, J Trauma Stress 2001;14, 433–442.
28. Cook JM, Harb GC, Gehrman PR, Cary MS, Gamble GM, Forbes D, et al. Imagery rehearsal for posttraumatic nightmares: a randomized controlled trial. J. Trauma Stress 2010;23, 553–563.
29. Foa EB, Cashman L, Jaycox LH, Perry K The validation of a self-report measures of PTSD: the PTSD diagnostic scale (PDS). Psychological Assessment 1997;9:445–451.
30. Foa EB, Ehlers A, Clark DM, Tolin DF, Orsillo SM. The posttraumatic cognitions Inventory (PTCI): development and validation. Psychological Assessment 1999b;11:303–314.
31. Foa EB, Dancu CV, Hembree EA, Jaycox LH, Meadows EA, Street GP. A comparison of exposure therapy, stress inoculation training, and their combination for reducing posttraumatic stress disorder in female assault victims. J Consult Clin Psychol 1999;67: 194–200.
32. Rauch SA, Defever E, Favorite T, et al. Prolonged exposure for PTSD in a Veterans Health Administration PTSD clinic. J Trauma Stress 2009;22:60–64.
33. Stein MB, Walker JR, Hazen AL, Forde DR. Full and partial posttraumatic stress disorder: findings from a community survey. Am J Psychiatry 1997;154:1114–1119.