One-Day Acceptance and Commitment Therapy Compared to Support for Depressed Migraine Patients: a Randomized Clinical Trial

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Abstract

In patients with migraine, depression is associated with poorer medical prognosis, decreased quality of life, and increased risk of suicidality and disability; yet, behavioral interventions have rarely been investigated. The current study compared the efficacy of two 1-day (5- to 6-h) interventions for co-occurring migraine and depression: (1) acceptance and commitment therapy plus migraine education (ACT-ED), and (2) support plus migraine education (S-ED). One hundred and thirty-six patients with comorbid depression and migraine were randomized to a treatment. One hundred and three (76%) completed the ACT-ED ($N = 56$) or S-ED ($N = 47$) workshop. Primary outcomes were depression diagnosis and symptoms. Secondary outcomes were anxiety symptoms, headache-related disability and general functioning, and quality of life. Assessments were completed at baseline and 3 and 6 months following the workshop. At the 6-month follow-up, on categorical outcomes, a significantly greater number of people in the ACT-ED condition no longer met criteria for a major depressive episode and exhibited a $\geq 50\%$ drop in symptoms on the Hamilton Rating Scale of Depression. Similarly, though, weaker results were found when examining depressive symptoms dimensionally. On secondary outcomes, people in the ACT-ED condition exhibited significantly greater improvements in anxiety, headache-related disability, and quality of social relationships, compared to S-ED. No differences between groups were observed in general functioning. A 1-day (5- to 6-h) ACT workshop can deliver substantial and lasting benefits to depressed migraineurs, over and above those provided by group support and education. This approach is an attractive alternative to weekly psychotherapy. [Clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02108678) # NCT02108678

Key Words Acceptance and commitment therapy (ACT) · Illness management · Migraine · Depression

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Introduction

Migraine is a chronic disorder that affects approximately 38 million US residents [1]. It is characterized by episodic, severe headache pain and functional impairment. The direct medical costs of migraine are estimated at 17 billion dollars annually [2], and productivity losses add another 13 billion dollars annually [1]. In addition to the pain and associated disability, migraine patients are at an elevated risk for psychiatric disorders [3]. Depression, in particular, is three times more common among migraineurs than in the general population; and this rate is even higher in migraine patients presenting to clinical settings [1–3]. This comorbidity is of major public health significance as it results in decreased quality of life, poorer response to migraine and depression treatment, and overall worse medical prognosis as well as increased risk for suicidality, medication overuse and disability [3]. Importantly, the economic burden of migraine doubles when there is depression [4]. Yet, despite its deleterious impact, depression in migraineurs is underdiagnosed and undertreated [6]. Anxiety disorders are also associated with migraine [7]. Migraine patients have a two-fold increased risk of an anxiety disorder diagnosis, highlighting the high comorbidity of depression and anxiety disorders with migraines [8]. Notably, effective therapeutic strategies directly targeting depression and anxiety in migraineurs are lacking.

Acceptance and commitment therapy (ACT) is a behavioral intervention with established efficacy in the treatment of chronic pain, depression, and anxiety and with growing evidence of efficacy in a range of other psychiatric and medical disorders [9]. Importantly, when presented as a *brief intervention*, ACT has resulted in positive outcomes [10, 11]. For example, in a small, uncontrolled pilot trial, patients with co-occurring depression and migraine were assigned to a 1-day ACT plus Education (ACT-ED) group *workshop* or to Treatment as Usual (TAU). Promising results were found with 77% of the participants in the ACT-ED arm remitting from depression compared to only 8% of those in TAU [12]. The intervention, based on ACT, targeted behavioral avoidance and promoted engagement in values-based living, processes implicated in depression and disability in chronic pain patients, including migraineurs [13]. The innovative “1-day workshop” format offered the potential for optimal treatment adherence and treatment completion, the lack of which is often the greatest obstacle to effective delivery of mental health services [14]. Presenting the treatment as a “workshop” was also better suited for individuals who may not be explicitly seeking specialized mental health care [15].

Building on this promising work, we conducted a randomized controlled trial contrasting the ACT-ED intervention to an active support plus migraine education (S-ED) workshop, in a larger group of patients with co-occurring major depressive disorder and migraine. The S-ED condition was intended to

control for treatment elements that pose rival explanations for the effectiveness of the ACT-ED condition, including nonspecific treatment elements such as therapist attention, expectation for improvement, and group support, as well as benefits of migraine education. This design allowed us to compare the efficacy of these two interventions and to assess whether there was an important additive effect of ACT training above the supportive and educational group environment. We hypothesized that, at the 6-month follow-up, patients in the ACT-ED workshop would exhibit a significantly greater decline in symptoms of depression and anxiety and improvements in functioning, compared to S-ED.

Methods

Participants

Participants were recruited from hospitals, including headache clinics and primary care clinics, and surrounding communities, via referrals, mass email, brochures, and posted flyers. Brochures and flyers stated: “If you have migraines and are having a hard time adjusting to your illness, consider participating in a research study....If you are eligible you would be invited to attend a 1-day workshop focused on ways to manage migraine and life stressors.” Those interested in the study completed an online web screening or a phone screening.

The screening inventory was completed by 4880 individuals, ages 18–70, with a history of migraine. Of those, 501 individuals met the following screening cutoffs: (1) obtained a score of 2 or more on the ID Migraine, a widely used 3-item screening tool with high positive predictive value for the presence of migraines [16]; (2) reported 4–12 migraine days over the previous month; (3) scored 10 or greater on the Patient Health Questionnaire-8 (PHQ-8) [17]; (4) no history of brain injury; (5) if currently using psychotropic or headache medications, use of these medications must have begun at last 4 weeks before the intake interview; (6) no history of schizophrenia, bipolar affective disorder or current substance abuse.

Of these, 177 people (35%) completed an in-person assessment, consisting of a diagnostic interview and self-report questionnaires. The remaining people who screened positive could not be reached ($n = 281$) or did not come in for an in-person assessment ($n = 43$). The eligibility criteria for the treatment phase included (1) a diagnosis of current major depressive episode on the Structured Clinical Interview for *Diagnostic and Statistical Manual for Mental Disorders – Fourth Edition* (SCID-IV; *DSM-IV* [18, 19]; (2) a score of 17 or greater on the Hamilton Rating Scale for Depression (HRSD) [20]; (3) a medical chart diagnosis of migraine; and (4) no imminent suicidality requiring urgent clinical attention. Following the in-person assessment, 41 patients were excluded (Fig. 1). Eligible participants ($N = 136$) were randomly

Fig. 1 CONSORT trial flow diagram

assigned to the ACT-ED ($n = 71$) or S-ED ($n = 65$) workshop. Of those, 56 attended the ACT-ED workshop; and 47 attended the S-ED workshop. Thus, 24% of those randomized to a workshop did not attend. All participants who came to the workshop completed it (100% completion of treatment protocol).

This study was fully approved by an Institutional Review Board, and all participants provided written informed consent. The study is also registered in clinicaltrials.gov (NCT02108678).

Design

Participants were assessed prior to the workshop and again 3 and 6 months postintervention. Assessors were blind to treatment condition. Eligible participants were randomly assigned to ACT-ED or S-ED, using the method of permuted blocks.

Treatments

The ACT-ED workshops lasted 5–6 h, included 4–8 patients, and involved training in ACT and education about migraine. The ACT component of the workshop emphasized approaches to managing troubling thoughts, feelings

and pain sensations (e.g., learning how to recognize and develop cognitive distance from unhelpful thoughts, such as “I can’t take this pain anymore,” and learning how to willingly face experiences that cannot be changed), while promoting effective and committed actions to achieve life goals. The education component (1 h), developed by a headache specialist (A.R.), involved educating participants about triggers and prodromes, risk factors for migraine chronification, effective use of medical treatments, and psychological and lifestyle factors known to contribute to migraine. Each ACT-ED workshop was implemented by two psychologists. The clinical content of the ACT workshop has been described in pragmatic detail by Dindo and colleagues [21]. A list of exercises completed during the workshop can also be found in Supplemental Document 1.

The S-ED workshop also lasted about 5–6 h, included 4–8 patients, and was led by two psychologists. The same educational topics listed above about migraine were presented, and participants discussed issues and experiences related to the topic. Additionally, diaphragmatic breathing was taught and practiced; and a passive progressive relaxation exercise (approximately 30 min) was completed.

The manuals for the ACT-ED and S-ED workshops are available upon request.

Fig. 2 Changes in depression symptoms, anxiety symptoms, and headache disability for 6 months following an ACT-ED or S-ED workshop

Outcome Measures

Primary Outcome: Depression

The main a priori outcome measures for this study were the 17-item HRSD [20] and the depression module of the SCID-IV [18, 19]. Response rates were assessed by examining the proportion of participants showing 50% or greater decline on the HRSD the proportion of participants who no longer met

depression criteria on SCID-IV. Symptom-level changes in depression were assessed by examining the HRSD total score.

Secondary Outcomes

Several secondary outcomes were assessed. The Structured Interview Guide for the Hamilton Anxiety Rating Scale (SIGH-A) was used to assess self-reported anxiety symptoms [22]. Headache-specific functioning was assessed with the Headache Disability Inventory (HDI) [23], which assesses the burden of headaches by inquiring about perceived impact of headaches on daily activities and functioning. Higher scores indicate greater impairment. General functioning was assessed with the 36-item World Health Organization Disability Assessment Schedule 2.0 (WHO-DAS 2.0) [24]. Lower scores indicate greater functioning. Quality of life was assessed with the World Health Organization Quality of Life (WHO-QOL). It assesses physical health, psychological well-being, social relationships and environment (e.g., satisfaction with living place and access to health care) [25].

Data Analyses

Demographic and clinical variables that describe study participant characteristics were compared between the two intervention groups. The two-sample *t* test was used to compare continuous variables, and Pearson's χ^2 test was used to compare categorical variables.

Generalized linear mixed model for binary data was used to assess the impact of treatment condition on SCID-IV diagnosis of depression, treatment response defined as > 50% reduction on HRSD or SIGH-A [26], and a reduction of ≥ 29 points on the HDI [23]. Treatment effect was estimated as odds ratio (OR) with 95% confidence interval and as number needed to treat (NNT).

Linear mixed-model analysis for repeated measures was used to compare the effect of treatment status on depressive symptom severity (HRSD), anxiety symptom severity (SIGH-A), headache-related disability (HDI), general functioning (WHO-DAS) and quality-of-life domains (WHO-QOL). The fixed effects in the linear mixed model were treatment status (ACT-ED versus S-ED), time (baseline, 3 months, and 6 months), and treatment-by-time interaction effect. Of interest in assessing the efficacy of ACT-ED over S-ED is to show a significant treatment-time interaction effect, which indicates differences in mean change from baseline over the two follow-up times in outcome measures between treatment groups. In addition, the linear mixed-model analysis also included performing tests of mean contrast to examine specific comparisons of interest, such as change over time within each treatment group and between-group comparison of means and mean changes at each time point. The estimate of treatment effect was presented as the difference in mean change

from baseline to 3 months and 6 months between treatment groups (with 95% confidence interval), and also as Cohen's *d* effect size.

All hypothesis tests were two-tailed, with Bonferroni adjustment applied to the *p* value (and confidence intervals) to account for treatment group comparisons assessed at two time points. Additionally, in testing for significance of within treatment group change from baseline, Bonferroni adjusted *p* value accounted for 4 tests, i.e., within-group change for 2 groups at 2 time points ($4 \times$ unadjusted *p* value). The *p* values reported in the tables for the marginal tests (within treatment group change and comparison of mean change between treatment groups at each time point) are the Bonferroni adjusted *p* values.

A *p* value < 0.05 was considered as statistically significant. All statistical analyses were performed using procedures from SAS version 9.4 (SAS/STAT 14.3, SAS Software, Inc., Carey, NC). Of note, linear mixed model for repeated measures using SAS Proc MIXED includes all data points available, not just those with both 3 and 6 months data. In the presence of missing data, under the assumption of missing at random (MAR), linear mixed model analysis which can handle incompletely observed subjects and uses a likelihood estimation method (i.e., SAS MIXED procedure) provides correct likelihoods and leads to valid estimates.

Results

Patient Characteristics

Table 1 presents demographic and clinical characteristics of study participants. Participants were mostly white, relatively well educated, and mostly female, consistent with the higher rates of both depression and migraine in women [7]. Almost all participants were taking acute medications (prescribed or over the counter) for their migraine-related pain. In contrast,

preventive migraine medications were being used by only a minority, also consistent with global data [27]. Approximately one-third of the participants in each group were also taking an antidepressant. There were no differences between participants in the ACT-ED and S-ED conditions on these variables (Table 1).

Primary Outcome (Depression)

Using the a priori definition of response for HRSD of $\geq 50\%$ reduction in symptoms, a significantly greater proportion of participants treated with ACT-ED responded to treatment compared to S-ED over the two follow-up times [overall treatment effect $F(1,97) = 8.39$; $p = 0.005$]. At 3 months, 62.8% in ACT-ED compared to 35.3% in S-ED responded to treatment ($OR = 3.10$; $NNT = 3.6$; $p = 0.021$). At 6 months 51.4% in ACT-ED versus 28.2% in S-ED exhibited an HRSD response ($OR = 2.70$, $NNT = 3.9$; $p = 0.059$) (Table 2).

On the SCID-IV, 100% of participants met diagnostic criteria for a current major depressive episode (MDE) At the 3- and 6-months follow-up, there were significantly fewer participants with current major depressive episode in the ACT-ED group than in the S-ED group [overall treatment effect $F(1,97) = 4.44$; $p = 0.038$]. At 3 months, 26.9 in ACT-ED and 40.7 in S-ED had current MDE ($OR = 0.54$, $p = 0.32$). At 6 months, 22.6% in ACT-ED and 45.8% in S-ED group had current MDE ($OR = 0.35$, $p = 0.044$) (Table 2).

Analyses of symptoms on the HRSD suggested a trend (nonsignificant) towards a treatment-by-time interaction effect, $F(2, 109) = 2.51$, $p = 0.086$. Assessment of this interaction, planned a priori, showed a significant mean decrease in severity of depressive symptoms in both ACT-ED and ED-S groups at 3 months and 6 months. The difference in mean change observed between treatment groups at 3 months was not significant ($p = 0.21$), though the effect size was moderate (0.34). At 6 months a greater mean decrease was seen in the ACT-ED

Table 1 Demographic Variables

Variable	ACT-ED (<i>n</i> = 56)	S-ED (<i>n</i> = 47)	<i>p</i> value
Age, years (mean/SD)	36.9 (14.9)	34.4 (12.6)	0.36
Female sex, <i>n</i> (%)	47 (84%)	38 (81%)	0.68
Caucasian race, <i>n</i> (%)	42 (75%)	36 (77%)	0.85
> 12 years of education, <i>n</i> (%)	32 (59%)	27 (57%)	0.67
Employed or in School, <i>n</i> (%)	44 (82%)	39 (83%)	0.42
Age of onset of migraines, years (mean/SD)	18.0 (10.2)	20.2 (11.1)	0.39
Taking antidepressant, <i>n</i> (%)	17 (32%)	15 (33%)	0.95
Number of migraine/headache days during month prior to baseline visit (mean/SD)	7 (3.2)	7.9 (3.5)	0.40
Taking abortive anti-migraine medication, <i>n</i> (%)	48 (86%)	42 (89%)	0.53
Taking preventive anti-migraine medication, <i>n</i> (%)	19 (34%)	17 (37%)	0.50

ACT-ED = Acceptance and Commitment Training plus Migraine Education; S-ED = Support plus Education

Table 2 Estimate of the mean proportion of the binary response outcome for HRSD, SCID-IV, SIGH-A, and HDI at 3 and 6 months follow-up from generalized linear mixed model analysis to compare the effect of ACT-ED versus S-ED

	ACT-ED (n = 56)	ED-S (n = 47)	ACT-ED vs. ED-S		
	Mean Proportion (95% CI)	Mean Proportion (95% CI)	Odds Ratio (95% CI)	NNT	p value
HRSD > 50% decline					
3 months	62.8% (48.3, 75.4)	35.3% (22.6, 50.5)	3.10 (1.15, 8.35)	3.6	0.021
6 month	51.4% (37.4, 65.2)	28.2% (16.5, 43.8)	2.70 (0.97, 7.49)	3.9	0.059
<i>Treatment effect: F(1,97) = 8.39</i>					0.005
SCID-IV depression					
3 months	26.9% (16.2, 41.1)	40.7% (27.3, 55.7)	0.54 (0.20, 1.47)	7.2	0.326
6 month	22.6% (13.0, 36.4)	45.8% (31.6, 60.7)	0.35 (0.12, 0.98)	4.3	0.044
<i>Treatment effect: F(1,97) = 4.44</i>					0.038
SIGH-A > 50% decline					
3 months	63.7% (48.0, 77.0)	41.8% (27.1, 58.2)	2.45 (0.85, 7.05)	4.6	0.113
6 month	51.8% (36.3, 67.0)	20.2% (10.0, 36.6)	4.25 (1.28, 14.03)	3.2	0.014
<i>Treatment effect: F(1,80) = 7.85</i>					0.006
HDI > 29 decline					
3 months	36.8% (24.4, 51.3)	11.5% (4.8, 25.4)	4.47 (1.23, 16.26)	4.0	0.019
6 month	37.7% (25.2, 52.0)	12.1% (4.9, 26.7)	4.40 (1.20, 16.18)	3.9	0.022
<i>Treatment effect: F(1,96) = 10.26</i>					0.002

NNT = Number needed to treat; ACT-ED = Acceptance and Commitment Training plus Migraine Education; S-ED = Support plus Education; HRSD = Hamilton Rating Scale for Depression; SCID-IV = Structured Clinical Interview for DSM-IV; SIGH-A = Structured Interview Guide for the Hamilton Anxiety Rating Scale; HDI = Headache Disability Inventory

group (-8.9 ; 95% CI $-1.7, -6.2$) compared to the S-ED group (-5.3 ; 95% CI $-8.3, -2.3$). The mean decrease in HRSD at the 6-month follow-up was 3.6 (95% CI $-0.1, 7.4$) more in ACT-ED than in ED-S (effect size = 0.46; $p = 0.055$; Table 3 and Fig. 2).

Secondary Outcomes

Anxiety

Evaluation of response to treatment on the SIGH-A, defined a priori as $\geq 50\%$ reduction in symptoms, showed a significant difference overall between the two treatment groups [$F(1,80) = 7.85$; $p = 0.006$]. At 3 months, 63.7% in ACT-ED compared to 41.4% in S-ED responded to treatment, (OR = 2.45; NNT = 4.6; $p = 0.11$). At 6 months, 51.8% in ACT-ED versus 20.2% in ED-S responded to treatment (OR = 4.25; NNT = 3.2; $p = 0.01$; Table 2). Participants in the ACT-ED condition showed significantly greater improvement over the two follow-up times in anxiety symptom severity compared to those in ED-S [treatment-by-time interaction: $F(2,113) = 7.10$, $p \leq 0.001$]. Assessment of this interaction effect showed a significant mean decrease in SIGH-A in both ACT-ED and S-ED groups at 3 months and 6 months, with a significantly greater decrease in the ACT-ED group than in the S-ED group at both follow-ups (Table 3 and Fig. 2).

Headache-Related Disability

Analysis of the HDI suggested a trend towards a treatment-by-time interaction effect [$F(2, 92) = 2.92$, $p = 0.059$]. There was a significant mean decrease in HDI score in both ACT-ED and ED-S groups at 3 months and 6 months. The mean decrease in HDI score at the 3-month follow-up was 9.1 (95% CI 0.5, 19.0) more in the ACT-ED than in the ED-S group (effect size = 0.44; $p = 0.067$; Table 4). The mean decrease in HDI score at the 6-month follow-up was 10.3 (95% CI: 0.2, 20.4) more in the ACT-ED than in the ED-S group (effect size = 0.48; $p = 0.043$; Table 4 and Fig. 2).

Using the a priori definition of a ≥ 29 decline in HDI total score, a significantly greater proportion of participants treated with ACT-ED exhibited a decline compared to ED-S over the two follow-up times [overall treatment effect $F(1,96) = 10.26$; $p = 0.002$]. The proportion that showed HDI ≥ 29 decline was 36.8% in ACT-ED group and 11.5% in ED-S at 3 months (OR = 4.47; $p = 0.02$). At 6 months, it was 37.7% in ACT-ED versus 12.1% in ED-S (OR = 4.40; $p = 0.02$) (Table 2).

WHO-QOL

Significant differences between ACT-ED and ED-S in mean score change over time were observed for WHO-QOL psychological well-being [treatment-by-time

Table 3 Estimate of mean and mean change from baseline at 3 and 6 months follow-up from linear mixed model analysis to compare the effect of ACT-ED versus S-ED on HRSD and SIGH-A

	ACT-ED (<i>n</i> = 56)		ED-S (<i>n</i> = 47)		ACT-ED vs. ED-S		
	Mean (SE)	Mean change (95% CI)	Mean (SE)	Mean change (95% CI)	Difference mean change (95% CI)	Effect size	<i>p</i> value
HRSD							
Baseline	19.3 (0.6)	–	18.9 (0.7)	–			
3 months	10.3 (1.0)	–9.0 [^] (–11.7, –6.4)	12.3 (1.0)	–6.5 [^] (–9.3, –3.7)	–2.5 (–6.1, 1.0)	0.34	0.205
6 month	10.4 (1.0)	–8.9 [^] (–11.7, –6.2)	13.6 (1.1)	–5.3 [^] (–8.3, –2.3)	–3.6 (–7.4, 0.1)	0.46	0.055
<i>Treatment*Time Interaction: F(2,109) = 2.51</i>							0.086
SIGH-A							
Baseline	22.5 (0.9)	–	20.3 (0.9)	–			
3 months	11.0 (1.2)	–11.4 [^] (–14.1, –8.7)	14.2 (1.2)	–6.1 [^] (–8.9, –3.2)	–5.4 (–8.9, –1.8)	0.73	0.002
6 month	11.5 (1.2)	–10.9 [^] (–14.0, –7.8)	15.6 (1.3)	–4.7 ^{**} (–8.0, –1.4)	–6.2 (–10.3, –2.1)	0.74	0.001
<i>Treatment*Time Interaction: F(2,113) = 7.10</i>							0.001

ACT-ED = Acceptance and Commitment Training plus Migraine Education; S-ED = Support plus Education; HRSD = Hamilton Rating Scale for Depression; SIGH-A = Structured Interview Guide for the Hamilton Anxiety Rating Scale

[^]Significant change from baseline Bonferroni adjusted *p* < 0.001

^{**}Significant change from baseline Bonferroni adjusted *p* < 0.01

Interaction: $F(2,143) = 3.07$; $p = 0.050$] and social relationships [treatment-by-time Interaction: $F(2,178) = 4.61$; $p = 0.011$]. A trend was observed for WHO-QOL environment [treatment-by-time Interaction: $F(2,180) = 2.73$; $p = 0.068$] (see Table 4). For psychological well-being, the ACT-ED group exhibited greater improvements than the ED-S group at both follow-up times (3.1 vs. 1.4; $p = 0.056$ at 3 months; 3.6 vs. 1.7; $p = 0.068$ at 6 months). Social relationships showed greater improvement in ACT-ED versus ED-S at 3 months (1.1 vs. –0.3; $p = 0.006$) but not at 6 months (1.5 vs. 0.4; $p = 0.128$). The same result was seen for environment with larger increase in ACT-ED versus ED-S at 3 months (1.9 vs. –0.1; $p = 0.045$) but with no significant difference at 6 months (2.2 vs. 1.0; $p = 0.535$). WHO-QOL physical health significantly increased over the two follow-up times in both groups, with no significant difference in mean score change between the two groups [treatment-by-time Interaction: $F(2,182) = 0.96$; $p = 0.385$].

WHO-DAS

Mean WHO-DAS score decreased over time in both the ACT-ED and ED-S groups, with no significant difference in the magnitude of change over time between the two groups [treatment-by-time interaction $F(2, 1.82) = 1.28$; $p = 0.282$]. At the 6-month follow-up, the improvement in the disability score was 9.6 (95% CI 4.3, 14.9) for ACT-ED and 6.1 (95% CI 0.3, 6.1) for ED-S (see Table 4).

Moderator Analyses

Gender, race, education, income, and medication use were examined as possible effect moderators of ACT-ED and S-ED. No significant effects were observed.

Of note, all the aforementioned analyses were also run on the full intent-to-treat sample; including all study participants who were randomized. Results of these intent-to-treat analyses are presented in supplemental Tables 1–3 (paralleling Tables 2, 3, and 4). Overall, the results of these analyses were very similar to the “completer” analyses (those who attended a workshop).

Discussion

This randomized controlled trial was designed to move us towards identifying an effective and efficient intervention for depression (as well as anxiety) and disability in patients with migraine. To that end, this study directly addressed the question of whether the previously demonstrated efficacy of group ACT workshops for depressed migraineurs is primarily due to nonspecific factors such as group support, therapist attention and education and to query whether ACT intervention provides added value over and above those nonspecific factors for this population. Therefore, 1-day ACT-ED and S-ED interventions were compared in a group of patients with comorbid depression and migraine with 3- and 6-month follow-up.

Table 4 Estimate of mean and mean change from baseline at 3 and 6 months follow-up from linear mixed model analysis to compare the effect of ACT-ED versus S-ED on Functional Outcomes

	ACT-ED (<i>n</i> = 56)		ED-S (<i>n</i> = 47)		ACT-ED vs. ED-S		
	Mean (SE)	Mean change (95% CI)	Mean (SE)	Mean change (95% CI)	Diff mean change (95% CI)	Effect size	<i>p</i> value
HDI Total Score							
Baseline	64.4 (2.5)	–	62.2 (2.8)	–			
3 months	46.0 (3.4)	–18.4 [^] (–25.7, –11.3)	52.9 (3.6)	–9.3* (–17.1, –1.4)	–9.1 (–19.0, 0.5)	0.44	0.067
6 month	41.9 (3.5)	–22.5 [^] (–29.9, –15.1)	50.0 (3.8)	–12.2** (–20.3, –4.0)	–10.3 (–20.4, –0.2)	0.48	0.043
<i>Treatment*Time Interaction: $F(2, 92) = 2.92$</i>							0.059
WHO-QOL Psychological well-being							
Baseline	17.4 (0.5)	–	17.6 (0.5)	–			
3 months	20.5 (0.6)	3.1 [^] (1.8, 4.3)	19.0 (0.7)	1.4* (0.1, 2.8)	1.7 (0.0, 3.3)	0.46	0.056
6 month	21.0 (0.6)	3.6 [^] (2.1, 5.0)	19.3 (0.6)	1.7* (0.1, 3.3)	1.9 (–0.1, 3.9)	0.44	0.068
<i>Treatment*Time Interaction: $F(2, 143) = 3.07$</i>							0.050
WHO-QOL Social relationships							
Baseline	9.4 (0.3)	–	9.6 (0.4)	–			
3 months	10.5 (0.3)	1.1** (0.4, 2.0)	9.3 (0.4)	–0.3 (–1.1, 0.6)	1.4 (0.4, 2.5)	0.62	0.006
6 month	10.9 (0.3)	1.5 [^] (0.6, 2.6)	10.0 (0.4)	0.4 (–0.6, 1.5)	1.1 (–0.2, 2.4)	0.38	0.128
<i>Treatment*Time Interaction: $F(2, 178) = 4.61$</i>							0.011
WHO-QOL Environment							
Baseline	28.4 (0.6)	–	29.2 (0.7)	–			
3 months	30.3 (0.7)	1.9** (0.4, 3.3)	29.1 (0.7)	–0.1 (–1.7, 1.4)	2.0 (0.0, 3.9)	0.47	0.045
6 month	30.6 (0.7)	2.2** (0.4, 4.1)	30.2 (0.7)	1.0 (–1.0, 3.0)	1.2 (–1.2, 3.7)	0.23	0.535
<i>Treatment*Time Interaction: $F(2, 180) = 2.73$</i>							0.068
WHO-QOL Physical health							
Baseline	21.5 (0.6)	–	21.0 (0.7)	–			
3 months	25.1 (0.7)	3.6 [^] (2.2, 5.1)	23.5 (0.7)	2.5 [^] (1.0, 4.1)	1.1 (–0.8, 3.0)	0.27	0.395
6 month	25.5 (0.7)	4.0 [^] (2.2, 5.8)	23.7 (0.7)	2.7** (0.8, 4.7)	1.3 (–1.2, 3.7)	0.24	0.477
<i>Treatment*Time Interaction: $F(2, 182) = 0.96$</i>							0.385
WHO-DAS Total							
Baseline	31.1 (2.0)	–	29.0 (2.2)	–			
3 months	23.2 (2.1)	–7.9 [^] (–12.1, –3.8)	24.9 (2.2)	–4.1 (–8.5, 0.4)	–3.9 (–9.4, 1.6)	0.33	0.227
6 month	21.5 (2.1)	–9.6 [^] (–14.9, –4.3)	22.9 (2.3)	–6.1* (–11.9, –0.3)	–3.5 (–10.6, 3.6)	0.23	0.537
<i>Treatment*Time Interaction: $F(2, 182) = 1.28$</i>							0.282

ACT-ED = Acceptance and Commitment Training plus Migraine Education; S-ED = Support plus Education; HDI = Headache Disability

[^]Significant change from baseline Bonferroni adjusted $p < 0.001$

**Significant change from baseline Bonferroni adjusted $p < 0.01$

*Significant change from baseline Bonferroni adjusted $p < 0.05$

This study showed that the ACT-ED intervention resulted in significant improvements in depression, based on the proportion of participants who responded to treatment (exhibited a drop of 50% or more on HRSD) and the proportion of participants who no longer met *DSM-IV* criteria for MDE. Although nonsignificant, a trend was observed with the ACT-ED group showing more improvements on depressive symptom severity (HSRD) than S-ED. It is not uncommon for categorical and dimensional

outcomes of depression to yield different results [28]. However, in the current study, the effect sizes on the dimensional outcomes were moderate to large. Thus, the overall message is similar across the categorical and dimensional measures of depression: ACT has a moderate advantage over S-ED.

The ACT-ED intervention also resulted in significantly greater improvements in anxiety symptoms. In terms of functioning and quality of life, significantly greater

improvements were observed in headache-related disability, psychological well-being, and quality of social relationships for the ACT-ED group compared to the S-ED group. No significant group differences were observed in general functioning.

In both the current investigation and the original pilot investigation, individuals with co-occurring depression and migraine who participated in the ACT workshop achieved a > 70% rate of remission for depression. In the previous trial, the ACT intervention was compared to treatment as usual; whereas here we have compared the total ACT workshop package (which includes ACT content, therapist attention, group dynamics and migraine education) against a strong comparator (which includes therapist attention, group dynamics, migraine education and opportunities for self-reflection but omits the ACT content). This replicates the previous finding regarding depression remission rates after one-time ACT intervention in this population, while extending previous research by suggesting that the addition of ACT coping strategies has important effects on distress and headache disability. This is particularly notable, given the known difficulty in finding advantages for psychological treatments over active control treatments [29]. At the same time, with a 54% remission rate of depression at 6 months for patients who participated in the support workshop, these findings highlight the power of a one-time group format in providing re-moralization to patients living with a difficult and isolating illness. Group therapy has been thought to provide a sense of universality [30] and may enhance a sense of common humanity, a foundation of self-compassion [31]. Further, educational interventions have been found to improve health outcomes for patients with migraine [32]. The strong finding of depression remission for the S-ED condition suggests that group support and education constitute a powerful intervention in themselves.

Weekly psychotherapy appointments have been a staple of behavioral intervention for generations. Since the advent of cognitive-behavioral therapy, depression has been thought to require 12–16 sessions of individual treatment. With new research highlighting an opportunity to provide briefer treatments, the question is naturally raised: are one-time interventions as helpful as ongoing sessions for people living with chronic and re-current conditions, such as migraine and depression? The effect sizes obtained in this study are comparable to those reported by a series of meta-analyses for weekly cognitive-behavioral therapy and other psychotherapeutic treatments for depression [33]. In addition, the effect sizes are generally higher than those obtained for pharmacological treatment of mild-to-moderate depression [34], without the risks of side-effects and the challenges of weaning. Furthermore, similar to our findings, a recent meta-analysis also showed that psychotherapeutic interventions for depression can have positive impacts on symptoms of anxiety [35]. This study adds to a growing body of literature showing that

brief psychotherapeutic interventions can be highly effective, transdiagnostically impactful and acceptable to medical patients [9]. For example, 1-day ACT interventions have shown promise in patients with diabetes, obesity, multiple sclerosis, and cardiovascular disease risk factors [11]. Notably, to the best of our knowledge, this is the first study to compare a 1-day ACT intervention to an active treatment condition in a population with comorbid psychiatric and medical problems, thus taking an important step forward for this burgeoning literature.

In addition to its efficacy, the ACT intervention featured in this line of research has several key pragmatic strengths. First, for patients with functional limitations and practical barriers such as transportation difficulties or family and work responsibilities [36], a 1-day workshop ensures treatment adherence and completion. A meta-analysis of 125 studies on outpatient psychotherapy found that 50% of patients drop out of treatment prematurely [37], and nearly 40% terminate treatment after the first or second visit [13]. Such high dropout levels are problematic because patients continue to experience symptoms and, thus, may increase healthcare utilization in other ways. Overall, the commonly encountered difficulties with treatment adherence and completion in psychotherapy were not an obstacle with the workshop format [38]. Once we got participants to the workshop, we were able to retain them for the whole treatment (100% treatment completion rate). At the same time, a sizable number of participants (24%) were eligible for a workshop but did not attend one. A greater understanding of the reasons for “no-shows” or what can be done for distressed patients who do not present for therapy is needed. It may be that interventions that can reach patients at home, such as web- or mobile-based applications, may be more effective at targeting patients who do not present to clinic. Similar to how we offer a “workshop” rather than “therapy,” which is less stigmatizing, e-health programs likely should also be presented in a manner that is acceptable to patients who are distressed but not explicitly seeking mental health care [39]. In the current context, it is also possible that patients did not want to attend a group intervention. Research has shown that potential clients sometimes express reservations about group psychotherapy, including fear of criticism, rejection, or the expectation to self-disclose [40].

The current study raises important questions about how best to assess improvements in functioning and quality of life, the sensitivity of generic measures of disability as compared to disease-specific measures of disability, and the value of identifying endpoints in trials that reflect the patient’s desired outcomes. This study found greater improvements for the ACT group in terms of the proportion of patients who showed improvements in headache-specific disability in comparison to the support group. In contrast, there were no differences between groups in general functioning. A generic measure of disability, such as the WHO-DAS may be too nonspecific to

capture changes that may result from an ACT workshop; although specific subscales such as well-being and quality of social relationships (aspects of quality of life) improved significantly more in ACT-ED than in S-ED. This finding aligns with a key therapeutic target of ACT interventions – helping patients clarify their values and engage in actions consistent with those values, and much of this work naturally centers around important relationships. A large amount of literature has shown that prioritizing meaningful relationships is linked with better mental and physical health outcomes [41]. Qualitative research may help to better identify what types of in behavior occur due to values-based interventions like ACT, whether these outcomes are meaningful to participants, and how they can be measured using standardized questionnaires.changes

Limitations and Future Directions

Consistent with previous ACT research, positive effects on distress and disability were maintained or strengthened at the final 6-month follow-up period [42]. During the workshop, participants are taught new ways to approach their thoughts and emotions and are given opportunities to practice behavioral skills in session. As participants continue to practice these new skills after the workshop, they may develop more flexible patterns of behavior, which positively impact well-being on an ongoing basis. Our clinical vision is to develop a one-time intervention with long-lasting impact; therefore, the longevity of the treatment effect must be empirically investigated. Future studies should examine whether the positive treatment effects obtained persist over longer periods of time than this study's 6-month follow-up, or whether they begin to wear off at certain times. This could provide important information about timing for booster sessions. Future studies should examine the effect of an ACT-ED intervention on migraine-related pain, medication use and healthcare utilization. Given the bidirectional influence of depression and migraine, an improvement in one disorder should result in improvement in the other.

Conclusion

Depression and/or anxiety in patients with migraine is of major public health significance because these mental health problems are common and result in greater disability and overall worse prognosis than migraine alone [43, 44]. Despite the high prevalence and deleterious impact, mental health problems are often underdiagnosed and undertreated in patients with migraine, due to poor recognition of distress, lack of evidence to guide interventions [5] and a dearth of behavioral treatments that are appealing to a population that does not see itself as needing mental health care. This

represents a missed opportunity, as both depression and anxiety are modifiable problems [45]; and psychological interventions have a long history of success in managing patients suffering from both mental health and medical conditions [46]. This study suggests that a 1-day workshop featuring ACT strategies, group support and migraine education offers a promising and efficient way forward for this patient population. It also highlights the noteworthy impact of group support and education in providing re-moralization, as well as the additional benefit can be attained from learning ACT.

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Compliance with Ethical Standards

The authors declare that that they have no conflicts of interest.

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