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The Effect of Telephone-Administered Cognitive-Behavioral Therapy on Quality of Life among Patients with Multiple Sclerosis

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Abstract

Background—Past research has found that a variety of physical, psychological, and social factors can affect quality of life (QOL). These previous findings suggest that interventions that address these factors could potentially improve QOL.

Purpose—The purpose of this study was to examine whether cognitive behavioral therapy (CBT) can improve QOL, and if so, explore which factors might mediate this effect.

Methods—This is a secondary analysis of a randomized controlled trial. One hundred twenty seven participants with multiple sclerosis (MS) and depression were randomly assigned to either a telephone-administered CBT (T-CBT) or telephone-administered supportive emotion focused therapy (T-SEFT) intervention.

Results—Patients assigned to T-CBT showed significantly greater improvements in QOL compared to those assigned to T-SEFT. The greater improvement in QOL among T-CBT recipients was mediated by improvements in depression and positive affect. There was also inconsistent support for the superior effect of CBT on QOL being mediated by improvement in fatigue.

Conclusions—T-CBT provided greater QOL benefits compared to T-SEFT, which controlled for non-specific treatment components. This study further suggests that T-CBT procedures specific to the management of depression and positive affect were uniquely useful in improving QOL.

Keywords

Multiple Sclerosis; Major Depression; Telemental Health; Cognitive Behavioral Therapy; Positive Affect; Mediation

Approximately 400,000 in the United States and 2.5 million people worldwide have been diagnosed with multiple sclerosis (MS), a debilitating disease of the central nervous system affecting muscle control and strength, vision, balance, sensation, and mental function (1). While MS does not usually reduce the length of life, it typically results in a substantial

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reduction in quality of life (QOL) (2). Thus, QOL has become an important target of interventions with MS patients.

The purpose of this study was to examine whether cognitive behavioral therapy (CBT) provides unique benefits for QOL, and if so, which factors might mediate this effect. Recent studies fairly consistently identify physical, psychological, and social symptoms that impact QOL among MS patients (2, 3). These factors are consistent with the World Health Organization's conceptualization of health as "not only the absence of infirmity and disease but also a state of physical, mental, and social well-being" (4) which was the initial inspiration for the construct of health-related QOL. Accordingly, in the current study we identified factors that might mediate an effect of CBT on QOL, including physical (i.e., fatigue), psychological (i.e., depression), and social functioning (i.e., social support). Given the importance of well-being in contrast to the absence of symptoms, we also examined positive affect and participants' adaptive coping skills which are presumably improved in CBT and might be mediators of any improved QOL.

Among the physical symptoms experienced by people with MS, fatigue is the most common. Indeed, up to 92% of patients report fatigue as their most significant complaint (5). With respect to mental health, depression is very common among persons with chronic illnesses, with MS patients having a lifetime prevalence of 50% and an annual prevalence of 15–25% (6). Positivity (i.e., increasing awareness of positive events, gratitude, etc.), however, has been found to promote benefit-finding in depressed MS patients (7). There is also support for the stress buffering effects of coping (8) and social support (8, 9).

Each of the factors described above has been shown to have an effect on QOL in patients with MS. Both fatigue and depression are independently associated with reduced QOL in MS (10). Social support has been shown to make a significant and unique contribution to QOL beyond other variables, including disease severity and cognitive impairment (3). Positivity and positive affect have also been found to be predictors of greater QOL in MS patients (11).

These findings suggest that interventions that treat depressive symptoms and fatigue, teach adaptive coping strategies, and improve positive affect and social support can potentially improve QOL. Each of these factors has been shown to be responsive to psychological intervention. There is a growing body of literature showing that depression among patients with MS is responsive to CBT, both when administered face-to-face (12, 13) or over the telephone (14, 15). Many of the trials of CBT for MS have also included modules that teach skills to manage other symptoms of the disease, including fatigue (16–18). Likewise, CBT has been found to improve satisfaction with social support (19), develop coping strategies (20, 21), and to produce significant increases in positive affect (15). Finally, psychological interventions have been shown to improve QOL (22).

This report is an examination of a secondary aim that was part of the original grant proposal, in which telephone-administered CBT (T-CBT) was compared to telephone-administered Supportive Emotion-Focused Therapy (T-SEFT). The primary outcomes have been previously reported (15). The a priori hypothesis of this study was that patients who received T-CBT would show greater improvements in QOL compared to patients who received T-SEFT. Because the focus of the trial was the treatment of depression, we hypothesized that any treatment differences in QOL would be partially mediated by changes in depression during the treatment period.

We conducted exploratory mediation analyses to examine additional factors that might account for any increased improvement in QOL among patients who received T-CBT compared to those who received T-SEFT. The exploratory mediators correspond to

treatment modules contained in the T-CBT manual, including fatigue, positive affect, adaptive coping, and social support.

Methods

Procedure

The current study was approved by the University of California San Francisco and the Kaiser Permanente Human Subjects Review Committees. A detailed description of the methods is provided in the report of the primary outcomes (15). MS patients recruited through Kaiser Permanente Medical Care Group of Northern California were identified through the organization's database, sent an invitation letter, and were screened via telephone communication for inclusion and exclusion criteria. Patients were also recruited through announcements in the newsletters of regional chapters of the National Multiple Sclerosis Society and completed the screening process when they called the study's toll-free number.

Study inclusion criteria were: 1) a diagnosis of MS confirmed by a neurologist; 2) functional impairment as measured by the Guy's Neurological Disability Scale (score of 3 or more on at least one area of functioning) (23); 3) depressive symptoms as measured by the Beck Depression Inventory-II (score of 16 or more) (24) and the Hamilton Rating Scale for Depression (Hamilton; score of 14 or more) (25, 26); 4) proficiency in the English language; and 5) being 18 years of age or older.

Patients were excluded if they 1) met the criteria for dementia using a neuropsychological assessment described in the primary analysis (15); 2) were currently receiving psychotherapy; 3) showed evidence of serious psychopathology, including psychosis, current substance abuse, or suicidal ideation; 4) had a recent experience of MS exacerbation; 5) had physical or intellectual deficits; and 6) used medications that affect mood with the exception of antidepressants.

All patients provided verbal and written informed consent. Patients recruited from the National MS Society's announcements also completed a release of information, which was utilized to confirm the MS diagnosis with the patient's neurologist. After patients' informed consent forms and baseline assessments were completed, they were randomized to one of two 16-week telephone-administered psychotherapies (50-minute sessions): T-CBT or T-SEFT. Randomization was stratified based on whether the participant was currently diagnosed as having a major depressive disorder and using antidepressant medications.

Treatment Conditions

T-CBT, which includes a patient workbook, is based on standard CBT principals applied to the needs of people with MS (27, 28). The goal of T-CBT is to teach skills, such as behavioral activation, cognitive restructuring, and problem solving that help manage thoughts and behaviors that contribute to depression, improve skills in managing stressful life events, and resolve interpersonal difficulties. In addition, T-CBT included a variety of treatment modules targeting specific needs of MS patients, including adaptive coping, social support, positivity (i.e., increasing awareness of positive events, gratitude, etc.), and fatigue management (29).

T-SEFT is an adaptation of client centered, process-experiential psychotherapy, which is a manualized, validated treatment (30). Adaptations included telephone administration and the elimination of specific Gestalt therapy tasks (i.e., empty chair technique). The goal of T-SEFT was to increase the participants' level of experience of their internal world. Therapeutic tasks included maintaining attention on empathic attunement, developing the

therapeutic bond, and facilitating direct expression of present emotional experience and current needs. Cognitive interventions or skills training were prohibited in this intervention.

Furthermore, because antidepressant medication was not an exclusion criterion, therapists in both treatment arms were prohibited from discussing anything having to do with attitudes, feelings, or adherence behaviors related to antidepressant medications.

Psychologist's Training & Supervision

All treatments were administered by nine doctoral-level psychologists with at least one year of postdoctoral clinical experience. Psychologists were nested in treatment arm to avoid the influence of treatment preference, therapeutic orientation, or therapist bias. The five T-CBT therapists had been trained in CBT; the four T-SEFT therapists endorsed adherence to experiential principals including that the therapeutic relationship is the principal vehicle for change in psychotherapy. All psychologists received two hours of weekly group supervision by a more senior psychologist whose theoretical orientation and training was consistent with therespective treatment model. To monitor therapist adherence to the treatment models, two sessions from each patient were rated by blinded research assistants on a modified version of the Cognitive Therapy Scale (31).

Assessment

Self-report materials were mailed to participants, while interview assessments were conducted over the telephone by clinical evaluators. Both were completed on the same day. Participants were paid $10 to $50 per assessment, pending on the time point and the length of the assessment. Assessments occurred at baseline, mid-treatment (week 8), and post-treatment (week 16).

Quality of Life—QOL is conceptualized as a global construct. It is measured using a single item from the Multiple Sclerosis Quality of Life instrument (32). The question asks “Overall, how would you rate your own quality-of-life? (on a scale from “0” worst possible QOL “as bad or worse than being dead” to “10” best possible QOL). Single item QOL measures are often used in medical populations and have been shown to have good validity, reliability, sensitivity, and ease of application (33, 34). Furthermore, global single-item QOL indicators are sensitive to change over time and have been shown to be comparable to multi-item scales (35, 36).

Depression—Severity of depressive symptoms was assessed using a telephone-administered version of the Hamilton (26) and the self-reported Beck Depression Inventory-II (BDI-II) (24), which was administered by mail.

Exploratory Mediating Factors—The Modified Fatigue Impact Scale (Fatigue) is a 21 item measure of fatigue commonly used in MS research (35). The participants’ adaptive coping skills were measured using the Brief COPE (36). Participants’ positivity was measured using the Positive Affect subscale of the Positive and Negative Affect Scale (Positive Affect) (37) and consists of 10 items. Social support was measured using the Satisfaction scale from the UCLA Social Support Inventory (Satisfaction) (38).

Data Analyses

All analyses were conducted on an intent-to-treat basis. Data from the 16 week treatment period was used because it was expected that the largest treatment differences would occur during this period. The current study used a mixed-effects model which allowed us to include all participants in the analysis and which makes use of all observed data during the treatment period. A mixed-effects model provides valid inferences in the presence of

missing data assuming the missing data are missing at random which we believe to be a reasonable assumption in this study. Initial analyses compared baseline demographics between treatment groups using t-tests and chi-square tests of independence, and baseline diagnoses were compared across treatment groups.

Data across the three time points were analyzed using a mixed-effects repeated measures model with random subject-specific intercepts (39). These models evaluated the effects of treatment (T-CBT or T-SEFT), over time by focusing on the treatment by time interaction. Mediators entered our models as time-varying covariates. We used the framework of Muller and colleagues (40) to identify those variables which mediate the moderating effects of treatment on QOL.

Muller and colleagues specify four criteria for mediated moderation. In the context of our analysis, these criteria are: 1) an overall treatment effect on QOL as measured by a significant treatment by time interaction; 2) a significant treatment by time effect on the mediator; 3) the mediator has a significant effect on QOL when included in a model with treatment; and 4) after adjusting for the mediator, the treatment effect is reduced. Only when these four criteria were satisfied for each of the mediators investigated, did we calculate the effect of mediation using MacKinnon and colleagues' product of coefficients method (41). Bias-corrected 95% percent confidence intervals for the mediated effect were calculated using bootstrapping (42).

Results

Participants

A flow chart showing the progress of participants through the trial is available in the primary outcome report (15). Of the 748 patients who completed the initial telephone screening, 223 met the preliminary criteria for a full eligibility assessment, of which 150 were found eligible for randomization. Of the eligible 150 patients, 23 (15.3%) refused randomization, 62 were randomized to T-CBT, and 65 were randomized to T-SEFT.

The baseline characteristics of participants randomized to the two treatment groups are available in the primary outcome results (15). There were no significant differences in patient characteristics across treatment groups. Analyses revealed that employment status was significantly associated with BDI-II score at baseline (p=.045) but not at post-treatment (p=.210). No other demographic, diagnostic, medication, or disability variable was associated with any outcome variable at baseline (p>.06 for all), and none of these variables were associated with treatment assignment (p>.36 for all). Therefore, no demographic, diagnostic, medication, or disability variables were included in subsequent analyses in the current study.

Attrition

Seven participants (5.5%) did not complete the 16 weeks of therapy (three in the T-CBT group and four in the T-SEFT group). Of these seven participants, six dropped out by their own choice and one participant (T-CBT group) was discontinued and referred to a community provider after a traumatic event. Of these seven participants, five agreed to continue with follow-up assessments (two in the T-CBT group and three in the T-SEFT group), while two dropped out of therapy and assessments (one in each group).

QOL Outcomes

There was no significant difference between the two treatment groups on QOL scores at baseline (Est. = −.03, SE = .32, p=.93). Participants' QOL score improved significantly over

the course of treatment (Est. = .37, SE = .12,*p*=.003). There was a significant time X treatment interaction effect on QOL, such that patients receiving T-CBT experienced greater increases in QOL scores compared with patients receiving T-SEFT (Est. = .51, SE = .17, *p*=. 004). The time X treatment interaction remained significant in two analyses controlling for depression using either the BDI-II (*p*=.009) or the Hamilton (*p*= .007; see Table 1).

Depression as a Mediator

The model, examining whether change in depression mediated the effect of treatment assignment on change in QOL, was tested twice using the framework of Muller and colleagues (40), once using the BDI-II and once using the Hamilton (see Table 2). All criteria for mediation were met for the HRDS (p<.01), however, one of the criteria for mediation using the BDI-II was not met.

Exploratory Analyses of Mediational Effects

Because the trial targeted depressive symptoms, all subsequent meditational analyses controlled for the effects of depression measured at all time points. Each meditational analysis was run twice, once controlling for BDI-II and once for Hamilton. The results of the exploratory meditational analyses are displayed in Table 3. Positive Affect met all mediation criteria and was a significant mediator of the relationship between treatment assignment and QOL outcomes, controlling either for the effects of the BDI-II (*p*<.01) and the Hamilton (*p*<. 05).

The Fatigue scale met the criteria for mediation and was significant when controlling for depression using the Hamilton (*p*<.05), but did not meet the mediation criteria when using the BDI-II. The Brief COPE and Satisfaction also did not meet criteria as mediators when controlling for the BDI-II or the Hamilton.

Discussion

The current study found greater improvements in QOL in MS patients who completed T-CBT, compared to T-SEFT, even after controlling for the effects of depression. Previous research has shown that psychological interventions are effective at improving QOL among patients with MS (22). In addition, treatments that explicitly cultivate positive feelings may be more successful in improving well-being than other treatments (43). However, this is, to the best of our knowledge, the first study to show that a CBT intervention provides greater improvements in QOL compared to another psychological intervention (T-SEFT). This suggests that specific procedures in T-CBT may have unique benefits for QOL.

Given the unique contribution T-CBT had on QOL, we explored additional potential effects of CBT that might mediate this effect. The hypothesis that the effect of T-CBT on QOL would be mediated by depression received inconsistent support. Analyses using the Hamilton to assess depression supported the mediation hypothesis while analyses using the BDI-II did not. The lack of a mediation effect using the BDI was due to a failure to find a time X treatment interaction effect on the BDI-II, which was consistent with the findings reported in the original trial (15). Furthermore, the mediation by the Hamilton was only partial. This suggests that T-CBT likely affects factors independent of depression that in turn can potentially impact QOL. The T-CBT treatment (27, 28) used in this study taught techniques to improve behavioral and cognitive coping, strengthen social support, develop fatigue management skills, and increase meaning and positive affect. Accordingly, we examined these factors as potential mediators of the effects of T-CBT on QOL

Positive affect was consistently found to be a unique significant mediator of treatment on QOL even after controlling for depression. Fatigue was found to be a significant mediator of

treatment on QOL when controlling for depression using the Hamilton, however, there was no meditational effect when controlling for depression using the BDI-II. Thus, the findings on fatigue as a mediator independent of depression are inconclusive. The remaining exploratory analyses of mediators, including adaptive coping and social support, showed no evidence of mediation.

Many studies have found that behavioral treatments improve positive affect (44, 45). While positive affect is associated with depression, it is also an independent construct (46) that can have independent effects on QOL (11). Indeed, treatments that focus primarily on improving positivity tend to improve well-being and QOL (43). There are a variety of potential explanations why positive affect might exert an influence on QOL independent of depression. Positive affect has been associated with benefit finding, which can occur independent of depression and could improve QOL (7). Fredrickson's Broaden-and-Build theory would suggest that positive affect might encourage approach, exploration and a broadening of one's mindset and perspectives (47). A clearer understanding of how CBT can produce improvements in positive affect could open new avenues to improving QOL.

The current study has several limitations. This secondary analysis used a sample of patients with MS with depression, which represent a disabled group for whom telemental health interventions have been shown to be effective in past research (14, 15). Therefore, it is unclear whether these findings would generalize to a broader group of patients without chronic illness or disability. Nevertheless, this study supports the a priori hypothesis that T-CBT would result in greater improvements in QOL compared to T-SEFT. This study used a single item measure of QOL, which, while supported as a meaningful methodology (33, 34), may not generalize to measures of QOL that are based on measurement of multiple components of QOL. Another limitation is that the mediation analyses, with the exception of depression, were exploratory, and had not been decided a priori. Nevertheless, this paper supports a growing literature suggesting that treatments that focus on improving positive affect can produce unique contributions to QOL.

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Table 1

Effects of Time X Treatment Interaction on QOL Covarying the Effects of Depression

Effects	Estimate	*SE*	*p*
Model Controlling for BDI			
Intercept	7.033	0.317	<.0001
BDI-II	−0.107	0.009	<.0001
Treatment	−0.150	0.263	0.570
Time	−0.161	0.117	0.172
Time X Treatment	0.405	0.154	0.009
Model Controlling for the Hamilton			
Intercept	6.195	0.397	<.0001
Hamilton	−0.099	0.016	<.0001
Treatment	−0.145	0.297	0.627
Time	−0.027	0.128	0.834
Time X Treatment	0.454	0.166	0.007

Table 2

Mediation of depression on effects of treatment assignment on quality of life (QOL)

Mediator	DV	Mediation Criteria				Effect of mediation (95% CI)
		Estimate of time* treatment in model 1 (95% CI)	Estimate of time* treatement in model 2 (95% CI)	Estimate of mediator in model 3 (95% CI)	Effect of time* treatment after adjusting mediator (95% CI)	
Hamilton	QOL	0.510** (0.168, 0.852)	−1.271* (−2.375, −0.166)	−0.099*** (−0.131, −0.068)	0.454** (0.126, 0.781)	0.126** (0.031, 0.253)
BDI-II		0.510** (0.168, 0.852)	−0.951 (−2.519, 0.618)	−0.107*** (−0.126, −0.089)	0.405** (0.101, 0.708)	NA

Model 1: QOL = time + treatment + **time*treatment**

Model 2: Mediator = time + treatment + **time*treatment**

Model 3: QOL = time + treatment + time*treatment +**Mediator**

NA = Not Applicable: One mediation criterion not met

* p<.05

** p<.01

*** p<.001

Table 3

Exploratory Mediation Analyses

Mediator	DV	Covariate	Mediation Criteria				Effect of mediation (95% CI)
			Estimate of time* treatment in model 1 (95% CI)	Estimate of time* treatment in model 2 (95% CI)	Estimate of mediator in model 3 (95% CI)	Effect of time* treatment after adjusting mediator (95% CI)	
Positive Affect	QOL	BDI-II	0.405** (0.101, 0.708)	1.412* (0.316, 2.508)	0.067*** (0.041, 0.094)	0.308* (0.010, 0.606)	0.095** (0.019, 0.197)
Fatigue			0.405** (0.101, 0.708)	−1.883 (−3.778, 0.012)	−0.013 (−0.029, 0.003)	0.374* (0.068, 0.680)	NA
Satisfaction			0.405** (0.101, 0.708)	0.443 (−0.449, 1.334)	0.059*** (0.027, 0.091)	0.382* (0.079, 0.685)	NA
Brief COPE			0.405** (0.101, 0.708)	−0.443 (−2.262, 1.375)	0.034*** (0.015, 0.052)	0.544** (0.182, 0.907)	NA
Positive Affect	QOL	Hamilton	0.454** (0.126, 0.781)	1.229* (0.112, 2.346)	0.102*** (0.075, 0.129)	0.322* (0.007, 0.636)	0.125* (0.016, 0.266)
Fatigue			0.454** (0.126, 0.781)	−1.809* (−3.586, −0.033)	−0.032*** (−0.049, −0.015)	0.390* (0.064, 0.716)	0.058* (0.0001, 0.148)
Satisfaction			0.454** (0.126, 0.781)	0.456 (−0.479, 1.390)	0.091*** (0.058, 0.124)	0.408* (0.083, 0.733)	NA
Brief COPE			0.454** (0.126, 0.781)	−0.387 (−2.230, 1.456)	0.031** (0.010, 0.052)	0.564** (0.170, 0.958)	NA

Model 1: QOL = BDI (Hamilton) + time + treatment + **time*treatment**

Model 2: Mediator = BDI (Hamilton) + time + treatment + **time*treatment**

Model 3: QOL = BDI (Hamilton) + time + treatment + time*treatment +**Mediator**

NA = Not Applicable: One mediation criterion not met

* p<.05

** p<.01

*** p<.001