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Effectiveness of Behavioral Activation Treatment for Depression and HbA1C in Diabetics type II

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Abstract

Behavioral activation is the principal non-pharmacologic method for the management of depression, but its usefulness for depressed patients with diabetes remains unknown. The aim of this study is to assess the efficacy of behavioral activation therapy (BA) for depression in patients with diabetes. Patients with type 2 diabetes and major depression (n = 29) were randomized to 16 sessions of behavioral activation (n = 15) and control group (n = 14). All patients participated in a diabetes education program to control for the effects of supportive attention and the possible influence of enhanced diabetes control on mood. The main outcome was depression, measured with the Beck Depression Inventory (BDI-II) assessed at 0, 2, 4, 6, 8, 10, 12, 14, 16 and 4 months, and the glycemic control was measured by using hemoglobin A1C levels, Outcomes were assessed immediately after treatment and 4 months after treatment . The percentage of patients achieving remission of depression (Beck Depression Inventory score < 9) was greater in the BA group than in the control group: post-treatment 75% of patients in the BA group (9 of 12) compared with 14.2% of controls (2 of 14) achieved remission (difference, 60.8 percentage points (P < 0.01); at follow-up 66.6% of patients in the BA group (8 of 12) compared with 15.3% of controls(2 of 13) achieved remission (P = 0.03). Post-treatment HbA1C levels were not different in the two groups, but follow-up mean HbA1C levels were significantly better in the BA group than in the control group (9.5% compared with 10.9%; P = 0.03). The combination of Behavioral activation and supportive diabetes education is an effective non-pharmacologic treatment for major depression in patients with type 2 diabetes. It can successfully be disseminated into routine practice settings in Iran and it may also be associated with improved glycemic control .

Key words: Behavioral activation, depression and type II diabetics

Introduction

Data from controlled studies, suggest that depression is more prevalent in diabetic patients than in the general population and that it is associated with poor glycemic control and decreased compliance with therapy (Kovacs, Mukerji, Drash & Iyengar, 1995; Carney, Rich, Freedland, Saini, Velde, & Simeone et al., 1988; Jacobson, Rand & Hauser, 1985; Lloyd, Wilson & Forrest, 1997; Lustman, Griffith, Clouse, Freedland, Eisen & Rubin et al 1997; Lustman, Clouse & Freedland, 1998). Depression has also been associated with an increased risk for complications of diabetes, particularly cardiovascular disease and retinopathy (Kovacs et al., 1995; Carney et al., 1988; Jacobson et al., 1985; Lloyd, Wilson et al., 1997). The mechanisms of these associations are not fully understood, but it is plausible that alleviation of depression improves glycemic control and

thereby decreases the risk for complications. Pharmacotherapy for depression may be poorly tolerated or may be insufficient to produce full remission in as many as 50% of diabetic patients with major depression (Lustman, et al., 1997; Lustman et al., 1998; Popkin, Callies & Mackenzie, 1987). The usefulness of non-pharmacologic approaches to the management of depression, such as psychotherapy, has not been systematically studied.

Approximately two thirds of patients who have both diabetes and major depression do not receive specific antidepressant treatment, in part because their physicians tend to attribute their depression to poorly controlled or advancing diabetes (Lustman & Harper, 1987; Kovacs, Obrosky, Goldston & Drash, 1997). Therapy for these patients still largely centers on medical management, which may include emotional support and diabetes education; this approach is probably suboptimal.

Major depressive disorder is a common mental health problem (American Psychiatric Association, 1994) and there are many studies that have demonstrated the effectiveness of antidepressant medication in treating it (Blacker, 1997; Fein, Paz, Rao & Lagrassa, 1988; Hirschfeld & Schatzberg, 1994; Schwartzberg, 1996). Thus, antidepressants have become the standard treatment for depression (American Psychiatric Association, 2000; Olfson, Marcus, Druss & Pincus, 2002), despite their limitations such as problems with side-effects, refusal by patients to take them and considerable relapse after discontinuation. Psychological treatments might offer a viable alternative (Dobson, Hollon, Dimidjian, Schmaling, Kohlenberg & Gallop et al., 2008; Hollon & Shelton, 2001; Gloaguen, Cottraux & Cucherat, 1998). In non-Western countries, the use of antidepressant medication is even more common, due to the limited availability of psychotherapy. This means there is a need for better dissemination of relatively simple but effective psychological treatments. Behavioral activation is such a candidate, given its effectiveness and relatively simple protocol.

Behavioral activation is based on the Behavioral component of cognitive–Behavioral therapy (CBT) for treating depression (Beck, Rush, Shaw & Emery, 1979).A study by Jacobson et al found that Behavioral activation was as effective as a full CBT package for treating depression (Jacobson, Dobson, Truax, Addis, Koerner & Gollan et al., 1996). In a subsequent trial by the same research group, Dimidjian et al compared Behavioral activation with antidepressant medication and CBT. They found that Behavioral activation was as effective as antidepressant medication, and even outperformed CBT, especially in individuals who were more severely depressed (Dimidjian, Hollon, Dobson, Schmaling, Kohlenberg & Addis et al., 2006). Moreover, participants originally treated with antidepressant medication and later a pill placebo experienced more relapse at the 2-year follow-up than individuals treated with Behavioral activation or CBT (Dobson et al., 2008). Thus, for prevention of recurrence, Behavioral activation and CBT were superior to medication discontinuation. Finally, more recently, two meta-analyses unanimously found that Behavioral activation interventions are as effective as CBT.

The present study was set up to document the effectiveness of Behavioral activation when implemented in clinical practice in Iran after a short period of training. We reasoned that there is a need for psychological treatment for depression in Iran as an alternative to antidepressant medication, which although readably available is not very popular due to its association with mental illness (creating stigma) and because of side effects. From the effective psychological treatments available, Behavioral activation seemed the most easy to implement. Training and treatment were based on the published Behavioral activation protocol, (Martell, Dimidjian & Herman-Dunn, 2010; Martell, Addis & Jacobson, 2001) and none of the developers of Behavioral activation or specialists were involved. Thus, our study was designed to determine efficacy of Behavioral activation (BA) added to supportive diabetes education. A secondary aim was to determine whether remission of depression is associated with improved glycemic control.

Methodology

Participants

Participants included 29 people with type 2 diabetes mellitus who were 18 to 60 years of age were eligible for participation if they were able to answer questions, fill out study forms, and give informed consent, selected from 100 referrals. The diagnosis of type 2 diabetes was made according to the criteria developed by the American Diabetes Association (American Diabetes Association, 1998) and was confirmed by a statement from the patient's primary physician. Patients also had to a primary diagnosis of major depressive disorder according to the DSM-IV-TR, (American Psychiatric Association, 2000) confirmed by the Structured Clinical Interview for the DSM-IV-TR (SCID-CT); (First, Williams, Spitzer & Gibbon, 2007) and had to have a score of at least 17 on the Beck Depression Inventory (BDI-II), and written consent to participate in the study. Exclusion criteria were: a lifetime diagnosis of bipolar disorder or psychosis; organic brain syndrome; intellectual disability; substantial and imminent suicide risk; a current (within the past 6 months) diagnosis of alcohol or drug misuse or dependence; were currently taking psychoactive medications; unstable medical condition; pregnancy or a plan to become pregnant; and inability to read and understand the study's instruments.

Participants diagnosed with major depressive disorder through telephone screening were referred to the mental health clinic for further assessment. Psychiatrists confirmed diagnoses and checked the eligibility of participants who completed the assessment. When eligibility was confirmed, participants were randomised by an independent coordinator. Twenty-nine participants were randomly assigned to each condition. Participants were treated at the Mental Health Clinic in saqqez, Kurdistan Province. The study was conducted from March 2013 to December 2013.

Therapist

Behavioral activation was conducted by a clinical psychologist (MS), the first author (B.M[1]); Training in Behavioral activation was provided by L.M[2], ph.d clinical psychologist, in 60 h over 4weeks.

Treatments

Behavioral activation

The Behavioral activation model we used was based on the two Behavioral activation manuals by Martell et al (Martell et al., 2010; Martell et al., 2001). Behavioral activation interventions are behavior-based and specific cognitive interventions are prohibited. The focus is on the participant's behaviors and the environmental context in which the behaviors take place; acting according to goals, not to feelings; and using an activity chart to schedule people's activities and follow the relationship between activity and mood. Identifying secondary problems such as avoidance patterns and depressive ruminations are important because they play a role in maintaining depression. Most individuals with depression withdraw from social activities, thereby minimising distress in the short term but creating long-term difficulties. Behavioral activation tries to break down the pattern of avoidance and utilizes Behavioral techniques to target depressive ruminations. Behavioral activation therapists deal with ruminating as a behavior rather than engaging with or challenging the contents of ruminative thoughts. Participants received 16 sessions over 12 week (Jacobson et al., 1996; Dimidjian et al., 2006). For the first 4 week, there were two sessions per week, and for the following 8 week there was one session per week.

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Measurements

Assessment of Depression

The presence of the major Axis I clinical syndromes was assessed by using the National Institute of Mental Health Diagnostic Interview Schedule (DIS) (Robins, Helzer, Cottier & Goldring, 1989), and these syndromes were diagnosed according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (Diagnostic and Statistical Manual of Mental Disorders, 1987). The reliability and validity of the DIS in psychiatric and epidemiologic studies have been extensively reported (Robins, Helzer, Croughan, Williams & Spitzer, 1981). Evidence also indicates that the DIS is sensitive and useful for patients with diabetes, in whom the somatic manifestations of the medical disease (such as fatigue, weakness, sleep disturbances, and sexual dysfunction) mimic the symptoms of a psychiatric disorder (Lustman, Harper, Griffith & Clouse,1986; Lustman, Freedland, Carney, Hong & Clouse, 1992).

The severity of current symptoms of depression was measured by using the BDI (Beck & Beamesderfer, 1987). This measure asks patients to provide a self-rating from 0 to 3 on each of 21 items; these ratings are added together to produce a total score. The BDI has been studied extensively and has been shown to be a reliable and valid measure of the severity of depression (Beck, Steer & Garbin, 1988). Depression manifests similarly on this instrument in diabetic and psychiatric patients, particularly with regard to the cognitive symptoms of depression (Lustman et al., 1992). The BDI-II was taken by evaluators who were masked to group. Assessments were conducted at baseline, and at 2, 4, 6, 8, 10, 12, 14, 16 and 4 months. In accordance with the Dimidjian et al study (2006), each session was preceded by the BDI-II (Behavioral activation group), administered by assistants who were masked to group; for participants who dropped out of treatment we used these data as the last observation in the analysis.

Assessment of Diabetes

Glycosylated hemoglobin (HbA1C) levels were measured to assess average glycemic control in the 120-day period before testing (Goldstein, Little, Wiedmeyer, England & McKenzie, 1986; Santiago, Davis & Fisher, 1987; Ladenson, Chan & Kilzer, 1985). Total HbA1C levels were measured with the Pierce Glyco-Test (Pierce Chemical, Rockford, Illinois), an affinity assay that removes confounding by hemoglobin variants, such as hemoglobin F. The range of HbA1C levels for normal, nondiabetic persons in the Barnes-Jewish Hospital outpatient laboratory is 4.4% to 6.3%. In this laboratory, the between-run coefficients of variation for values greater than 6.6% are all 5% or less, the recommended standard (Baynes, Bunn, Goldstein, Harris & Martin, 1993). The presence of complications of diabetes (neuropathy, retinopathy, and nephropathy) was determined by a physician-investigator on the basis of review of each patient's medical history, current symptoms, physical examination results, and objective test results (which were obtained through review of clinical records).

Assessment of Compliance

Compliance with self-monitoring of blood glucose levels was determined by using electronic memory glucometers, which recorded the date, time, and result of blood glucose testing. Patients were instructed to test their blood glucose levels per day on two nonconsecutive days each week.

Study Design

Patients were informed that depression in diabetes can be a cause or a consequence of poor glycemic control and that the study would determine whether focusing on the behavioral or the physical side of the problem was the most effective way to relieve depression. These concepts were familiar to most patients and were generally well accepted. No patients declined further evaluation because they were unwilling to accept random assignment. Patients who met the inclusion criteria and gave informed consent underwent a 2-week period of glucometer training and baseline

assessment, after which they were randomly assigned to study groups. The randomization pattern was determined by a computer algorithm, and assignments were concealed in sealed envelopes.

During the 12-week treatment period, all patients participated in a diabetes education program by meeting in 1-hour, biweekly, individual sessions with a certified diabetes educator. A variety of diabetes self-care topics were covered in these sessions, and diet and exercise regimens were systematically reviewed and modified as needed. Physicians were given HbA1C and glucometer data from our study to facilitate management. The diabetes education program was designed to control for the nonspecific effects of supportive attention as well as the potential influence of enhanced self-care and glycemic control on mood and ideation.

Patients were randomly assigned to receive BA or to receive no specific antidepressant treatment other than the diabetes education program. Patients in the BA group received an hour of treatment weekly for 12 week from a clinical psychologist (MS) for the first 4 week there were two sessions per week, and for the following 8 week there was one session per week. Study outcomes were measured immediately after the end of the 12-week treatment period and at a follow-up evaluation 4months later. At each evaluation, assessments of diabetic control and depression were made and scored independently of one another. The study personal who monitored patient progress were not involved in treatment, and assessors were blinded to treatment assignments. No additional study protocol treatment was provided after the end of the 12-week treatment period. Patients who remained depressed at that point (BDI score > 9) were referred to their primary physician for antidepressant medication or to a psychotherapist. Glycemic control and severity of depression were measured again at the 4months follow-up visit, and patients were restudied at that time with an abbreviated psychiatric interview.

Statistical Analysis

Differences in the demographic and clinical characteristics of patients receiving BA and controls were determined in the intention-to-treat and completer samples by using the Fisher exact test for categorical data and the Student Mest for continuous data. The results of an intention-to-treat analysis of the depression outcomes are provided for the purpose of comparison (Frank, Karp & Rush, 1993; Rush & Prien, 1995). The analyses of study outcomes focused on the completer sample. Analyses of covariance (ANCOVAs) were used to determine the effects of treatment on symptoms of depression and glycemic control after treatment and at 4 months follow-up with beginning levels of the dependent measures (BDI score and HbA1C level) as the covariates. The post-treatment and follow-up BDI data were not normally distributed. Consequently, the scores were categorized and Fisher exact tests were used to analyze the data. We used ANCOVA for a secondary analysis after the continuous BDI data were transformed into van der Waerden normalized ranks (SAS Procedures Guide, 1993). We also studied HbA1C levels by using f-tests of mean change scores over various intervals (for example, from before to after treatment or after treatment to follow-up). A repeated-measures analysis of variance (ANOVA) was used to determine the effects of treatment on compliance with the protocol for self-monitored blood glucose levels.

The clinical significance of individual depression outcomes (per BDI) was judged by using two standard conventions: A post-treatment score of 9 or less was used to denote remission of depression (Beck et al., 1988). The clinical significance of the treatment findings was judged by using the approach described by Braitman (Depression Guideline Panel, 1997). In this approach, a 95% CI is calculated around the point estimate (the difference between the percentages of patients responding to the two treatments). A number is specified that indicates the minimum difference between treatment responses needed to conclude that the experimental treatment has a clinically important advantage. This number is then compared with the CI around the point estimate. A claim that a treatment has clinically significant effects is supported if the CI falls entirely above the value

representing the smallest important difference. On the basis of meta-analyses of acute-phase trials of treatment for depression, the smallest clinically important point estimate was set at 15% (Frank et al., 1993; Depression Guideline Panel, 1997; Preskorn, 1996). Less is known about the sustained efficacy of different treatments for depression once treatment has been discontinued. Thus, discussion of the clinical significance of BA was limited to the post-treatment findings.

Results

Participation Data and Demographic and Clinical Characteristics

One hundred patients gave informed consent and were evaluated to determine their eligibility (Figure 1). Fifty-six of these patients were excluded from participation, and 29 satisfied all inclusion criteria and were randomly assigned to study groups after completion of baseline assessment. Of the 71 excluded patients, 39 (55%) had scores lower than 14 on the BDI, 11 (15.4%) had exclusionary comorbid psychiatric conditions, 21 (29.5%) were receiving psychoactive medication and were unwilling or unable to discontinue it.

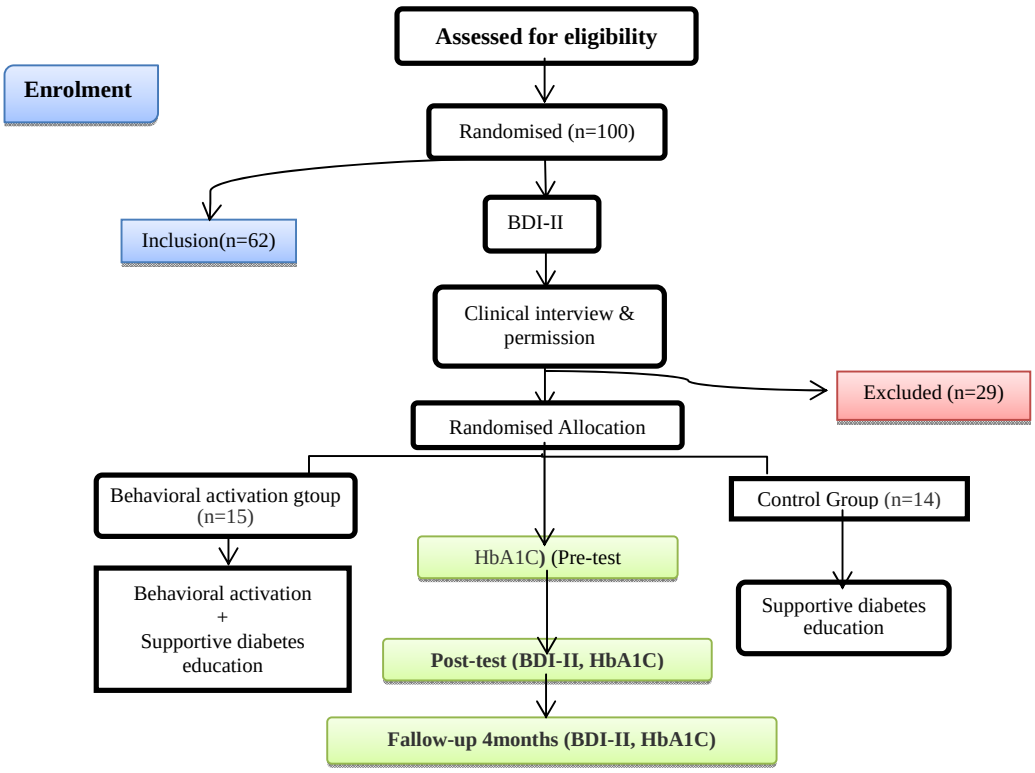

Figure. 1 CONSORT 2013 flow diagram

Of the 29 patients who were randomly assigned to treatment, 24 (82.7%) completed the 12 weeks of treatment and 5 (17.2%) discontinued participation prematurely. Of the 5 dropouts, 3 were in the CBT group and 2 were in the control group. No differences of more than 20% were seen between dropouts and completers on any of the measured demographic, depression, and clinical characteristics (age, sex, marital status, education, previous episodes and treatment of depression, duration of diabetes, type of diabetes treatment, and HbA1C levels and BDI scores before

treatment). No evidence of differential attrition was seen. Follow-up data were obtained on all. Only 3 of 11patients (27.2%) who were depressed after the 12-week treatment period received treatment for their depression during the 4monthss follow-up interval.

Selected demographic, depression, and diabetes characteristics of the 24 patients who completed treatment are shown in the Table1. Of the three variables, only duration of diabetes was associated with a measure of depression outcome. Patients with longer duration of diabetes were not less likely to achieve remission of depression but were less likely to realize a reduction in the severity of depression symptoms (P = 0.03).

Table1. Selected characteristics of the Study Sample

Characteristic	Behavioral activation group(n=15)	Control group (n=14)
Age mean (years)	52.3	49.8
Sex(female)	53.3%(8 of 15)	57.1%(8 of 14)
Married(not married)	53.3 % (46.7%)	57.1% (42.9%)
Mean duration of type 2 ± SD, y	8.9 ± 10.1	7.7 ± 9.2
Mean glycosylated hemoglobin ± SD, %	7.5 ± 9.9	7.7 ± 9.5
Mean previous episodes of depression ± SD, n	4.8 ± 3.5	4.1 ± 5.2
Mean level of education y	11.5	10.6
Mean weight. kg	71.8	69.5
Mean duration of diabetes, y	7.7	6.9
Mean Beck Depression Inventory Score	24.4	25.1

None of the differences between groups were statistically significant.

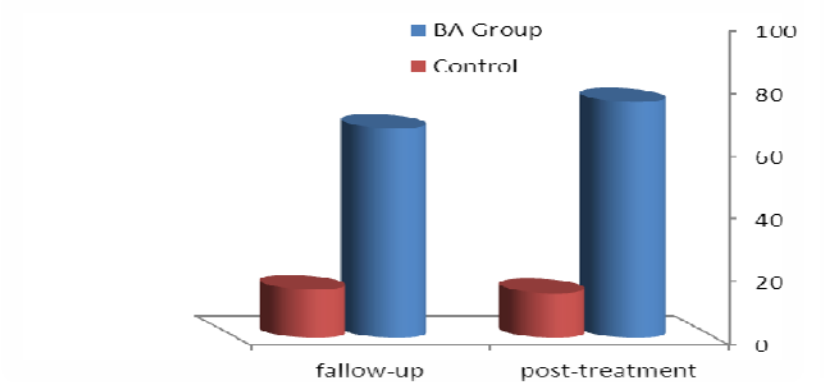

Figure 2. Percentages of patients with depression in remission depression at post-treatment and follow-up evaluations: A Beck Depression Inventory score of 9 or less was used to define remission. A greater percentage of patients receiving behavioral activation therapy (BA) had remission at post-treatment and follow-up evaluations.

Effect of Treatment on Depression

In this analysis, dropouts were treated as if they did not achieve remission. At the post-treatment evaluation, the percentage of patients achieving remission of depression (BDI score < 9)

was greater in the BA group than in the control group (75% [9 of 12] compared with 14.2% [2 of 14] difference, 60.8 percentage points ; P<0.01). At the 4months follow-up evaluation, the percentage of patients in remission was greater in the BA group than in the control group (66.6% [8 of 12] compared with 15.3% [2 of 13] difference, 51.3 percentage points; P = 0.03). Depression outcomes were further studied by using an ANCOVA. Reduction in depression symptoms was greater, at both post-treatment and follow-up evaluations, in the BA group than in the control group (P < 0.01 for post-treatment comparison and P = 0.01 for 4 months comparison).

Association of Treatment with Glycemic

Control No statistically significant difference was seen in post-treatment HbA1C levels, adjusted for pretreatment HbA1C levels, between the BA group (n = 11) and the control group (n = 14) (10.2% compared with 9.9%; P = 0.17). At follow-up, similarly adjusted mean HbA1C levels were lower in the BA group (9.5%) compared with 10.9%; P = 0.03). Change score analysis confirmed this finding; in the 4 months after treatment, HbA1C levels decreased by 0.7% in the BA group and increased by 0.9% in the control group (P = 0.04).

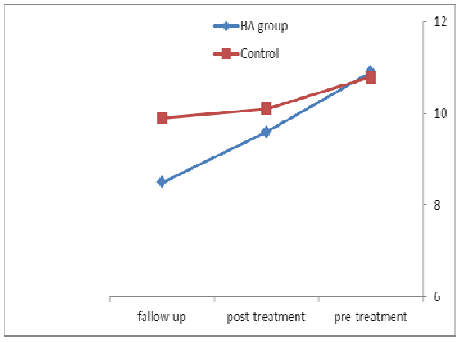

Figure 3. Absolute change in glycosylated hemoglobin (HbA1C) levels from pretreatment to post-treatment evaluations and from post-treatment to follow-up evaluations

Association of Depression Remission with Glycemic

Control an analysis comparing responders with nonresponders was used to estimate the association of change in depression with change in glycemic control. Responders (n=18) were patients whose depression remitted (BDI scores<9) at both post- treatment and follow-up evaluations. Nonresponders (n=11) were patients with manifest depression (BDI scores > 14) at both evaluation points. Covariate-adjusted mean HbA1C levels were lower in the nondepressed group at both the post-treatment (8.5% compared with 10.9%; P=0.003) and follow-up (9.2% compared with 12.1%; P=0.006) evaluations.

Association of Treatment with Compliance with Blood Glucose Monitoring

All patients practiced by using a memory glucometer for a week before randomization. Analysis of the pretreatment data showed no statistically significant differences in compliance with self-monitoring of blood glucose levels in the BA group and the control group (65.4% compared with 66.7%; *P* > 0.2). A repeated-measures ANOVA was used to determine the association of treatment with weekly compliance over the 12 weeks treatment period**.** The ANOVA showed no statistically significant main effects (that is, effects of treatment or time). A time-by-treatment-group interaction indicated that over the 12 weeks treatment period, compliance with self-monitoring of blood glucose levels declined in the BA group compared with the control group *(P* = 0.03).

Discussion

Until now, behavioral activation has been tested by the developers and by only one independent study (Jacobson et al., 1996; Dimidjian et al., 2006; Ekers, Richards, McMillan, Bland & Gilbody, 2011). In our study, behavioral activation therapists were not trained and supervised by behavioral activation experts but by a non-expert using the published protocol, which is encouraging regarding the feasibility of its dissemination around the globe. Behavioral activation interventions are relatively simple and easy to understand for individuals with depression, and do not require difficult or complex skills on the part of participants or therapists (Lejuez, Hopko, LePage, Hopko & McNeil, 2001). It could therefore be considered as a first-choice treatment, with potentially good cost-effectiveness.

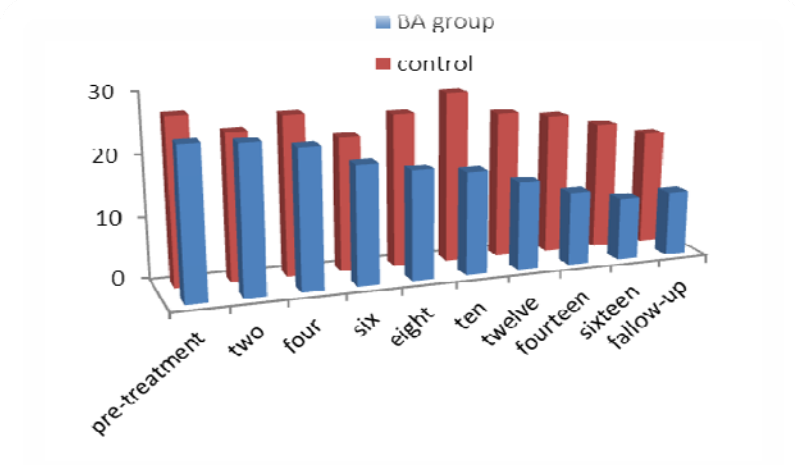

Figure 4. Compliance with the protocol for self-monitoring of blood glucose levels {SMBG). Over the 10-week treatment period, compliance declined in the group receiving cognitive behavioral therapy (CBT) compared with controls (P = 0.01). White bars represent the CBT group; striped bar represent controls

Our study shows that BA combined with diabetes education is an effective non-pharmacologic treatment for major depression in patients with diabetes. The finding of depression remission in 75% of the sample compares favorably with the outcomes reported in depressed, medically well out-patients receiving BA (Murphy, Simons, Wetzel & Lustman, 1984; Hollon, Shelton & Davis, 1993; McKnight, Nelson-Gray & Barnhill, 1992) and with the response to conventional antidepressant medication seen in the only controlled trial of depression in diabetes available to date (Lustman et al., 1997). Although the brevity of the follow-up interval limits our ability to make long-term projections, the data suggest that BA combined with diabetes education may produce a more favorable prognosis for patients with depression and diabetes than that seen in earlier follow-up studies of diabetic patients with untreated (Lustman, Griffith & Clouse, 1981) difference in efficacy in the BA and control groups was also clinically significant. Our 15-percentage point (15%) criterion for the smallest clinically important difference between treatments is based on meta-analyses of the literature on depression treatment (Frank et al., 1993; Depression Guideline Panel, 1997; Preskorn, 1996). The 95% CIs for the difference between the percentage of patients in each study group that were in remission (14.2 to 75 percentage points). This suggests that the addition of BA offers a genuine clinical advantage in the management of depression in diabetes compared with the nonspecific intervention used in the controls. Controls received an educational

intervention aimed at improving diabetes self-care. This intervention is frequently used in clinical practice to improve glycemic control, instill feelings of self-control, and thereby create a sense of well-being. During the 12-week treatment period, patients in the control (education-only) group were substantially more compliant with self-monitoring of blood glucose levels and evidenced a mean improvement in HbA1C levels of 0.5%. Despite increased attention and measurable short-term improvements in diabetes control and compliance, however, no one of controls achieved remission of depression. This response rate is no better than the rate reported with placebo and control treatment in meta-analyses of the literature on treatment of depression (Frank et al., 1993; Depression Guideline Panel, 1997; Preskorn, 1996). Depression is uniquely important in diabetes because its association with poor glycemic control increases the risk for retinopathy and cardiovascular disease. These associations, reported in both cross- sectional and prospective studies (Lustman et al., 1997, 1998, 1986, 1992), have led to clinical trials designed to determine whether alleviating depression improves medical outcome. In a recent placebo-controlled trial of nortriptyline, remission of depression was associated with clinically important improvements in HbA1C levels (Lustman et al., 1997). Our study also suggests that remission of depression may favorably affect HbA1C levels, but it does not reveal the mechanism involved in this association. Improvement in depression may have salutary effects on a variety of behavioral practices (such as sleep practices, dietary practices, and physical activity) or physiologic paths (such as alterations in autonomic tone, hypothalamic-pituitary-ad- renal axis activity, or neurotransmitter function) involved in glucose regulation. An improvement in glycemic control in the BA group was evident at follow-up but not at the post-treatment evaluation. Improvement in glycemic control may have lagged behind improvement in depression because of the biology of HbA1C formation and because the interval between HbA1C measurements taken before and after treatment spanned only 70 days. The HbA1C level is a "weighted" measure of mean blood glucose levels over the preceding 120-day period (Santiago et al., 1987; Goldstein, Little, Lorenz, Malone, Nathan & Peterson, 1995). Although more recent events contribute relatively more than earlier events to the final result, approximately 25% of the variance in HbA1C levels is determined by the mean blood glucose level in the third and fourth months (days 60 to 120) before measurement (Goldstein et al., 1995). Thus, post-treatment HbA1C levels reflected points in time before study entry when all patients were depressed, as well as points in time early in treatment when many patients were still depressed. In contrast, follow-up HbA1C values better captured the beneficial influence of BA on glycemic control because they reflected a 120-day period during which substantially more of the BA group remained free of depression. Congruence in the time intervals assessed by measures of HbA1C and depression (or any psychosocial factor) is methodologically important. Incongruence in these intervals may help explain the inconsistent relation of depression to glycemic control observed in some previous studies (Marcus, Wing, Guare, Blair & Jawad, 1992; Peyrot & Rubin, 1997). The addition of BA to diabetes education had a statistically significant adverse effect on compliance with self-monitoring of blood glucose levels during the 12 weeks of treatment, an effect that we had not anticipated and cannot readily explain. We suspect that even though all patients received diabetes education, those who also received BA viewed the depression intervention as the focus of treatment. As a consequence, their attention to self-monitoring of blood glucose levels decreased. Behavioral activation therapy routinely included homework assignments directing patients to record their all activities and increase various physical and social activities. Thus, it is possible that the participation of the BA group in diabetes education complicated an already complex regimen and was more than the patients could handle. It is a well-established principle of compliance that any action that complicates a treatment regimen (such as adding a medication or using divided rather than single-dose schedules) usually decreases compliance with other components of treatment (Eisen & Miller,

1990; Shope, 1981; Matsui, 1997). The generalizability of our findings is uncertain. First, our study was limited to a relatively small number of patients, and the 95% CIs around the point estimates spanned a wide range of plausible true values. When depression was measured in terms of the percentage of patients judged to be clinically improved, the lower limit of the 95% CI was 17%, a value close to that established for the smallest clinically important difference in the percentage of patients responding to the two treatments. Second, our follow-up interval was limited to the 4months immediately after treatment. Third, we cannot exclude the possibility that BA and diabetes education interacted in a way that potentiated antidepressant effectiveness; analogous inter- actions may have occurred in many clinical trials. Further studies comparing BA and diabetes education, individually and in combination, are needed to answer such questions and to see whether successful BA alone is sufficient to produce glycemic improvement. Fourth, it is worth noting that patients in the BA group had education almost a full year longer than controls. The difference in education was not statistically significant, but the extra educational experience may have contributed to improved outcome in the BA group. Finally, treatment was administered by a single clinical psychologist experienced in the use of BA. Whether treatment would be as effective when administered by other therapists is uncertain. In conclusion, our study shows that BA combined with diabetes education is an effective non- pharmacologic treatment for major depression in patients with type 2 diabetes. This therapy was associated with improvement in glycemic control despite its association with a decline in self-monitoring of blood glucose levels. Additional investigations of larger patient samples are needed to fully characterize the covariation of depression and glycemic control. Nevertheless, our study offers further evidence linking health and emotional function by suggesting that improved mental health is related to improved medical outcome. Our findings support the importance of treating depression in patients with comorbid medical illness.

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Implications of this study

The findings of our study suggest that behavioral activation is a simple and effective intervention for depression that can be easily disseminated to routine practice settings, similar to what has been demonstrated in Western countries. The fact that the behavioral activation was delivered effectively by therapists with a minimum of training and supervision is very encouraging, taken together with the superior effects in the subgroup of participants with more severe depression, it speaks for its timely dissemination to other routine practice settings as well. It has even been suggested that behavioral activation can be provided by healthcare professionals who had no previous experience with providing psychotherapy which further increases possibilities for its implementation.

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