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Preventing Late-life Depression in Age-Related Macular Degeneration

Barry W. Rovner, M.D. and **Robin J. Casten, Ph.D.**
Departments of Psychiatry and Neurology (BWR), and Psychiatry and Human Behavior (RJC), Jefferson Medical College, Jefferson Medical College, Philadelphia, PA

Abstract

Objective—To determine whether problem-solving treatment (PST) can prevent depressive disorders in patients with age-related macular degeneration (AMD).

Design—Two hundred six patients with AMD were randomly assigned to PST (n = 105) or usual care (n = 101). PST therapists delivered six PST sessions over 8 weeks in subjects' homes.

Measurements—Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition Diagnoses of Depressive Disorders, Hamilton Depression Rating Scale scores, and rates of relinquishing valued activities were assessed at 2 months for short-term effects and 6 months for maintenance effects.

Results—The 2-month incidence rate of depressive disorders in PST-treated subjects was significantly lower than controls (11.6% versus 23.2%, respectively; OR = 0.43; 95% CI [0.20, 0.95]). PST also reduced the odds of relinquishing a valued activity (OR = 0.48; 95% CI [0.25, 0.96]); this effect mediated the relationship between treatment group and depression. By 6 months most earlier observed benefits had diminished. Secondary analyses showed that a minimal level of depressive symptoms were disabling and predicted incident depressive disorders.

Conclusion—PST prevented depressive disorders and loss of valued activities as a short-term treatment but these benefits were not maintained over time. To sustain PST's effect, an intervention that uses a problem-solving framework to enhance rehabilitative skills may be necessary.

Keywords

Problem-solving treatment; vision loss; age-related macular degeneration; depression

Preventing depression in older people might seem improbable given the medical problems, disability, and social losses that many experience and the view that depression is an inevitable consequence of aging. Although most older persons will never, in fact, become depressed, many have medical problems and physical disabilities or stressful life events, chronic life difficulties, or poor coping skills that increase their risk. Developing targeted early interventions for these persons may prevent them from becoming depressed.

We have focused on preventing depression in persons with vision loss due to age-related macular degeneration (AMD). AMD is the leading cause of severe vision loss in older adults, with almost two million having advanced disease (neovascular or "wet AMD," or

Send correspondence and reprint requests to Barry W. Rovner, M.D., Jefferson Hospital for Neuroscience, 900 Walnut Street, 4th Floor, Philadelphia 19107, PA. barry.rovner@jefferson.edu.

geographic atrophy or "dry AMD") and over seven million having early signs.[1] The number affected will double by 2020, dramatically increasing the population of visually impaired people. Vision loss deprives them of the primary means by which they engage the world and prevents many from pursuing valued activities. This threatens their sense of self and self-efficacy and may lead to depression. Our strategy to prevent depression focuses on preserving or redefining valued activities using problem-solving approaches. In this article, we describe the results of our National Institute of Mental Health-funded clinical trial "Preventing Depression in AMD" and discuss future directions for depression prevention in AMD.

The clinical trial compared the efficacy of problem-solving treatment (PST) with usual care to prevent depressive disorders in patients with recent diagnoses of neovascular AMD.[2] It was a selective preventive intervention in that it targeted patients at higher than average risk for depression but who had no current symptoms.[3] We tested the hypothesis that PST would reduce the incidence of depressive disorders at 2 months (short-term effects) and at 6 months (maintenance effects) compared with usual care and, secondarily, would prevent loss of valued activities.

PST is a manual-driven psychological treatment that teaches problem-solving skills.[4] It addresses negative perceptions that may interfere with finding practical solutions to problems and teaches the following problem-solving skills: 1) defining problems; 2) establishing realistic goals; 3) generating, choosing, and implementing solutions; and 4) evaluating outcomes. Subjects are encouraged to use these skills routinely to develop practical compensatory strategies to achieve valued functional goals and thereby prevent depression.[5,6] PST-trained therapists (two nurses, one master's level counselor) delivered six 45–60-minute in-home PST sessions over 8 weeks.

METHODS

We recruited subjects from the retinovitreous clinics of Wills Eye Hospital in Philadelphia. The inclusion criteria were age over 64 years, neovascular AMD in one eye diagnosed within the preceding 6 months, and preexisting AMD in the fellow eye. We chose these parameters to identify nondepressed patients with recent bilateral visual impairment who were at high risk for depression. From December 2001 to July 2005, we identified 602 potentially eligible patients; of these, 206 (34.2%) were randomized to the PST (N = 105) or usual care (N = 101) group. The major reasons for nonparticipation (N = 396) were refusal (N = 263; 66%); inability to contact (N = 53; 13%); cognitive impairment (N = 19; 5%); depression (N = 14; 4%); and other (N = 47; 12%). Nonparticipating patients were similar to enrolled subjects on their demographics characteristics, visual acuity, and responses to a screening measure of depression. During the trial, 17 (8.3%) subjects dropped out of the study (11 PST and 6 controls). The primary outcome was a *Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition* diagnosis of major or minor depression. Research nurses administered the Modified Schedule for Affective Disorders and Schizophrenia and the Structured Interview Guide for the Hamilton Depression Rating Scale (HDRS) to rule out depression at baseline and to diagnose depressive disorders at 2 and 6 months.[7,8] We used the 24-item HDRS to quantify depressive symptoms.[8] We measured vision disability (i.e., self-reported difficulty level on vision-dependent daily activities) using the National Eye Institute Vision Function Questionnaire (NEI VFQ-17).[9] Its items rate difficulty on tasks such as reading newsprint and pursuing hobbies; subjects also rated the personal value of all tasks.

RESULTS

We found that at 2 months, PST subjects had half the incidence rate of depressive disorders as controls (11.6% versus 23.2%; OR = 0.43; 95% CI [0.20, 0.95]). We also found that fewer PST subjects had relinquished a valued activity than controls (23.2% versus 37.4%; OR = 0.48; 95% CI [0.25, 0.96]). We then tested a mediation model to determine whether relinquishing a valued activity mediated the relationship between PST and depression using a logistic regression with depression diagnosis at 2 months as the outcome. The treatment group was entered on the first step and significantly predicted depression (OR = 2.31, 95% CI 1.06, 5.06). This relationship diminished when activity loss was added (OR for treatment group = 2.04, 95% CI 0.92, 4.54); activity loss, however, was significant (OR = 2.55, 95% CI 1.18, 5.50). These results suggest that PST prevented depression to the extent that it prevented loss of a valued activity.

The number of patients needed to be treated with PST to prevent one case of depression was nine (95% CI 5, 72). The large confidence interval reflected the size of the sample and the low incidence rate of depression. There were no significant differences in HDRS score change over time between treatment groups.

At 6 months, there was no difference in depression rates in PST versus control subjects (21.1% versus 27.4%; OR = 0.65; 95% CI [0.33, 1.39]). As at 2 months, however, PST subjects were almost half as likely to relinquish valued activities as controls (30.5% versus 44.2%; OR = 0.53, 95% CI 0.28, 1.01).

DISCUSSION

We found that PST prevented depressive disorders as a short-term preventive treatment but that its effect did not persist over time. There was, nevertheless, substantial evidence that PST was not the same as usual care. For one, we observed the hypothesized 50% risk reduction at 2 months and found that preventing the loss of valued activities mediated the relationship between PST and depression. We underestimated, however, the incidence of depression following cessation of treatment. This suggests that booster treatments for all PST subjects, or rescue treatments for those with low-level depressive symptoms, may have been necessary to sustain PST's ability to prevent depressive disorders. The former is a continuation of the selective intervention strategy that targets an asymptomatic high risk group, whereas the latter is an indicated preventive strategy in that it targets patients with what may be early signs of depression.[3]

When we examined depression as a continuous measure of symptoms, we found no significant changes or differences between treatment groups. This was expected given that we enrolled nondepressed subjects; although a notable minority developed a depressive disorder over time, the preponderance of HDRS scores in the sample remained low throughout the study.

From a research design perspective, the clinical trial demonstrated that systematic sampling, successful randomization and masking, protocol-driven treatment, assessment of multiple relevant outcomes, and maintenance of treatment fidelity are feasible in psychosocial intervention studies. It adds to other studies demonstrating the value of depression management strategies to treat and, as our data suggest, prevent depression in older patients.[10–13] The study also suggested that a practical, problem-solving intervention like PST may prevent depression in other disabling conditions such as heart disease, cancer, and stroke, where disability and loss of valued activities increase the risk for depression.

Minimal Depression Is Disabling and Increases the Risk for Depressive Disorders

In a secondary analysis of our data, we examined the effect of minimal depressive symptoms on levels of disability and the incidence of more severe depressive disorders.[14] Many studies have identified the high prevalence and disabling consequences of depressive symptoms that do not meet criteria for major depression (variably termed minor, subthreshold, or subsyndromal depression).[15] Lyness et al. recently found that subsyndromal depression produces clinically significant impairments and increases health service utilization and medical costs.[16] Relying on *Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition* definitions of major or minor depression only, however, would omit a substantial proportion of affected older persons. Others have similarly reported that depressive symptoms predict future declines in functional status and onset of major depression.[17–21]

Although the "Preventing Depression in AMD" trial did not enroll patients with clinically significant depressive symptoms, subjects did have varying low levels of symptoms that we quantified using the HDRS.[8] Total possible scale scores range from 0 to 50; scores greater than 14 indicate moderate-severe depression and scores less than 7 are normal. The mean for our sample was 2.2 (SD: 2.2) and 95.5% of subjects had scores within the normal range.

We identified 49 subjects (23.8%) whose baseline HDRS scores were one SD above the mean for this sample (i.e., ≥4). Their average HDRS score was 5.4 (SD 1.7); median: 5.0; range: (4, 12). We called these subjects "minimally depressed" and found that they had significantly greater difficulty performing vision-dependent daily living activities than subjects with fewer symptoms even though they had similar visual acuity and medical problems.[14]

We also found that minimal depressive symptoms strongly predicted incident depressive disorders. Thirty-four of the 49 (69%) subjects with HDRS greater than 4 (versus 24.4% with scores less than 4) developed a depressive disorder over the next 6 months. Their mean HDRS score, in fact, although in the top 25th percentile of the sample, was less than the HDRS score of seven that is taken as normal. The incidence rate for depressive disorders at 2 or 6 months for these subjects, compared with those with lower HDRS scores were: 75.6% versus 17.8%, respectively (OR = 14.27; 95% CI [6.40, 31.80]). Table 1 shows the baseline HDRS symptoms that a regression analysis demonstrated independently and significantly predicted incident depression at 2 or 6 months. Subjects who reported a "depressed mood" alone were significantly more likely to develop a depressive disorder than those who denied depressed mood and correctly predicted 74.9% of the cases. Endorsing hypochondria, insomnia, and guilt identified an additional 6.8% of cases. Adding other HDRS symptoms did not improve the model. These data suggest that these four symptoms, taken together, correctly classified 81.7% of patients who developed a depressive disorder and may identify patients at risk.

Thus, minimally depressed patients with AMD, who would not be considered depressed according to current diagnostic criteria, are at high risk to develop more severe depressive disorders and to suffer decrements in vision function that cannot be accounted for by the severity of their eye disease or general medical problems. Although we and others have previously reported the adverse effects of severe depression in AMD and other disorders, we now find that even minimal depressive symptoms adversely affect function.[17–22]

Future Directions for Prevention Depression in AMD

Although PST prevented depression, we believe its effect was short-lived because its emphasis on independent problem-solving (i.e., having subjects develop their own solutions, often without knowledge of low vision resources) did not optimize their remaining vision and thereby limited its effectiveness. We found, for example, that PST did not increase

optical device use, low vision rehabilitation consultation, or home modifications. We believe that PST as a "talking treatment," rather than one of education and demonstration, restricted its ability to access these compensatory strategies. To prevent depression more effectively over time, we believe that an intervention that builds on the strengths of a problem-solving framework (i.e., reframing problems into goal-oriented tasks) and enhances rehabilitative skills may be necessary.

We are now developing a low vision rehabilitation intervention that is designed to improve patients' ability to continue valued activities and prevent depressive disorders. In it, an occupational therapist (OT) will collaborate with a low vision optometrist to develop and implement a care plan based on a patient's rehabilitation potential and personal rehabilitation goals. The optometrist will evaluate remaining vision and magnification needs, prescribe optical devices, and provide the OT with an initial care plan. The OT will subsequently meet with subjects in their homes and use a problem-solving approach that reframes patients' depressive perceptions (over which they feel they have no control) into goal-directed tasks that they can control. The hypothesis is that this treatment will enable patients with AMD to continue valued goals via enhanced compensatory strategies and problem-solving skills, and thereby to prevent depression. Because depression in AMD is a frequent, painful consequence of vision loss, integrating disease management strategies for both conditions is necessary. Our plan to incorporate depression management directly into low vision care provides, we believe, an optimal approach to meet this need and may well serve as a model for other rehabilitative interventions.

We plan to recruit patients with subthreshold depressive symptoms because of their increased risk for more severe depressive disorders. This then is an indicated prevention intervention because it targets people who already have detectable signs of depression but do not meet diagnostic criteria.[3] The primary research question of the intervention's efficacy drives our plan to use categorical diagnoses rather than depressive symptoms as the primary outcome. Although we recognize that depressive phenomena are not easily fitted to categories, the categorical approach seems best suited to assess a clinical treatment's efficacy because it generates syndromes with discernable treatment and prognostic implications. Where we to rely on change in depressive symptoms as the primary outcome, we would obtain only a relative, not an explicit, sense of the intervention's efficacy that may lack clinical meaning.

Our approach to disability assessment is innovative in that we will measure targeted vision outcomes, which identifies and quantifies specific vision-related goals as outcomes.[23,24] This approach is likely to be more sensitive to treatment effects than summary scores on multisymptom measures that mix unvalued and valued activities and may obscure improvements in specific valued activities. It recognizes that different subjects select different goals and pinpoints and evaluates change in the goals that subjects value, and has the face validity, clinical relevance, and flexibility to convey meaningful change in response to rehabilitative interventions. The secondary study hypothesis is that intervention subjects will report less difficulty with targeted vision goals compared with controls over time.

CONCLUSION

Preventing depression in older persons depends on distinguishing states of demoralization that arise from adverse life circumstances from pathologic mood disorders that may reflect underlying brain disease. Although recent genetic and neuroimaging studies increasingly question the validity of this distinction, our current state of knowledge and experience working with patients with AMD suggest that depression in these patients represents an understandable reaction to the loss of valued activities and resulting disability. Although we

have focused on AMD, our goal is to contribute to the development of interventions for patients with chronic diseases in which depression and disability are common. Interventions that target only depression or disability, however, may be less than fully effective because, in AMD at least, patients experience vision loss, depression, and disability as a single syndrome. They do not distinguish their mood from their function in the way that researchers isolate and measure these constructs separately. For them, tangibles such as reading and socializing are difficult to separate from intangibles such as moods or intentions. In fact, these activities inseparably join how they feel with what they do. Our focus on preserving valued activities as a strategy to prevent depression is based on these observations.

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TABLE 1

Hamilton Depression Rating Scale Symptoms at Baseline that Predict Depressive Disorders at 2 or 6 Months

HDRS Symptom	OR	CI
Depressed mood	16.7	4.26–65.41
Hypochondria	3.3	1.56–6.85
Insomnia	2.5	1.18–5.10
Guilt	6.7	1.63–27.77