The Effects of Venlafaxine on Social Activity Level in Depressed Outpatients

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Background: Although most depression treatment outcome scales focus on symptoms, depression also affects daily functioning, social activity, and quality of life. We examined the effects of venlafaxine on social activity, general life functioning, and depressive symptoms in 2 placebocontrolled clinical trials of venlafaxine.

Method: Subjects were 600 outpatients with major depression (DSM-III-R criteria). Treatment outcomes were examined separately in each study, primarily because of differing lengths of follow-up.

Results: Treatment with venlafaxine significantly improved activity level, general life functioning, and depressive symptoms. Treatment accounted for statistically significant changes in both activity level and general life functioning even after controlling for changes in depression.

Conclusion: We provide evidence that social activity is a behavioral domain distinct from depressive symptoms and that venlafaxine improves social activity level and general life functioning in addition to its positive effects on depressive symptoms in outpatients with major depression. *(J Clin Psychiatry 1999;60:157–163)*

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Reprint requests to: Ralph R. Turner, Ph.D., Phase V Technologies, Inc., 20 Walnut St., Wellesley Hills, MA 02181. A lthough depression affects daily functioning, social activities, and quality of life in addition to mood and neurovegetative symptoms,¹ most outcome measures of depression treatment focus exclusively on symptoms.²⁻⁷ Treatment may improve symptoms without improving social functioning.⁸ Because social activities and daily functioning may influence relapse through their effects on social support, improvements in activity level and general life functioning are important indicators of treatment response,⁹ particularly in long-term studies, since therapies may improve symptoms over a few weeks while functioning may improve more slowly.¹⁰

Several studies suggest that symptoms and functional limitations are at least somewhat distinct and are best assessed independently. For example, Mintz and associates¹¹ have demonstrated that symptomatic improvement may not translate directly into improved work functioning following treatment of depression. These investigators compiled data from 10 published treatment studies of over 800 patients. They found that although symptom reduction was not related to the length of treatment (with brief and longer term treatments being equally effective), work outcomes were related to treatment duration, reaching maximum improvement after 4 to 6 months of treatment. Giller and associates¹² reported similar results. Other studies have demonstrated that symptom severity in depression is strongly associated with functional impairment.^{13–15} In the realm of social functioning, Weissman and colleagues¹⁶ found that meaningful changes in the social adjustment of depressed individuals in treatment may not emerge for as long as 8 months.

When considered together, these findings support the assertion that symptoms and functional limitations or disability are at least somewhat distinct. Evidence from these converging sources indicates that just as symptoms typically appear first during the development of a depressive disorder and are followed by functional impairments, during recovery, symptoms appear to improve first, followed by improved functioning. The unique temporal trajectories of symptoms and functional status (including activities and social and work functioning) in onset and remission point to the importance of assessing both in treatment outcomes studies.

Daily social activities have been linked to depression in children,¹⁷ adults,^{18–20} and individuals with chronic illness.²¹ These findings consistently point to a reduction in the frequency and intensity of social contacts in depressed individuals. This association between depression and activity level has led several investigators and professional organizations to suggest that involvement in activities is an important aspect of treatment for depression.^{22,23}

However, treatment studies often fail to include an activity indicator when assessing treatment efficacy, perhaps because available measures are demanding. For example, the Social Rhythm Metric²⁴ and the Rochester Interaction Record²⁵ require prospective recording of activities in a daily diary by study participants. Although diary measures provide unique opportunities to examine activity levels in detail,²⁶ and have been used to study activities in dysphoric individuals²⁷ and effects of antidepressants,²⁸ daily reports place considerable demands on research participants and investigators.²⁹ Some questionnaires, such as the Activity Pattern Indicators³⁰ and the Katz Adjustment Scale,³¹ are less demanding but still lengthy, and may be burdensome for individuals experiencing a psychiatric disorder.

The current study was designed to measure changes in activity level and general life functioning associated with effective treatment of depressive symptoms. Indicators of general life functioning and activity level were incorporated into 2 clinical trials of venlafaxine. Venlafaxine is a selective serotonin norepinephrine reuptake inhibitor indicated for the treatment of depressive mood disorders. It has a neuropharmacologic profile distinct from other currently available antidepressants,³² but has demonstrated antidepressant efficacy.33-36 Within the context of these clinical trials, we examined evidence for whether social activity is an aspect of depression distinct from mood and neurovegetative symptoms. First, we sought to determine whether activity level improved with effective treatment for depression. Second, we examined the relationship between activity level and depressive symptoms to determine if changes in activity following treatment are independent of changes in depressive symptoms. If activity changes were mediated by symptom changes, controlling for symptom changes would eliminate the effect of treatment on activity level.³⁷ If, on the other hand, the effect of venlafaxine on activity level remained statistically significant after controlling for changes in depressive symptoms, that would be evidence that depressive symptoms and activity level are distinct domains. We predicted that self-reported activity level would change in response to pharmacologic treatment, and that these changes would be correlated with but not redundant to changes in both depressive symptoms and general life functioning.

METHOD

Participants and Study Designs

Participants were outpatients meeting DSM-III-R criteria for major depression. They were enrolled in 1 of 2 Wyeth-Ayerst clinical trials, referred to as Studies I and II, and gave written informed consent to participate.

Study I inclusion criteria were as follows: Participants were outpatients, aged 18 to 65 years, meeting DSM-III-R criteria for major depression, with a minimum score of 20 on the Hamilton Rating Scale for Depression (HAM-D)⁴ and depressive symptoms for at least 1 month. Nonpregnant women of childbearing potential were required to use effective contraception.

Potential Study I participants were excluded if they had hypersensitivity to venlafaxine; a myocardial infarction within 6 months; history or presence of clinically significant hepatic or renal disease; history of seizure disorder; a history of any psychotic disorder not associated with depression; were acutely suicidal; had used any investigational or antipsychotic drug within 30 days; had used any monoamine oxidase inhibitor (MAOI) or electroconvulsive therapy (ECT) within 14 days or were currently using any other antidepressant, anxiolytic, or sedative-hypnotic drug; had a history of drug or alcohol dependence within 2 years; were participating in formal psychotherapy during the study period; or had clinically significant abnormalities.

Study II inclusion criteria were as follows: Participants were outpatients, 18 years and older, meeting DSM-III-R criteria for major depression, with a minimum score of 20 on the HAM-D and depressive symptoms for at least 1 month. The exclusion criteria for Study II were identical to those for Study I (see above).

Study I was a double-blind, placebo-controlled, dosage-determination study of 3 b.i.d. doses of venlafaxine in 312 outpatients. Following a 7-day single-blind placebo washout period, 78 patients were randomly assigned to placebo, 79 to 25 mg/day of venlafaxine (12.5 mg b.i.d.), 76 to 50–75 mg/day of venlafaxine (25–37.5 mg b.i.d.), and 79 to 150–200 mg/day of venlafaxine (75–100 mg b.i.d.). The 210 women (67.3%) in the trial ranged in age from 18 through 64 years (mean \pm SD = 37.3 \pm 9.96), and the 102 men (32.7%) ranged in age from 19 to 64 years (mean \pm SD = 40.8 \pm 10.8).³⁸ Of the 312 patients, 232 (74.4%) completed the full 42 days of treatment, and there were no treatment differences in the rate of discontinuation from therapy. Two hundred fifty-six patients had data available for longitudinal analysis.

Study II was a double-blind, placebo-controlled, dosage-comparison of b.i.d. and t.i.d. dosing of venlafaxine in 288 outpatients. Following a 7-day single-blind placebo washout period, 96 patients were randomly assigned to placebo, 94 to venlafaxine b.i.d., and 98 to venlafaxine t.i.d. Doses were titrated upward to a maximum dose of 200 mg/day if patients had not responded to 150 mg/day by day 15. The 174 women (60.4%) in the trial ranged in age from 18 to 67 years (mean \pm SD = 38.79 \pm 9.87), and the 114 men (39.6%) ranged in age from 22 to 68 years (mean \pm SD = 44.72 \pm 11.37). One hundred eighty-seven patients (64.5%) completed the full 56 days of treatment, and there were no treatment differences in the dropout rate. Data from 251 patients were available for longitudinal analysis.

Measures

The 21-item HAM-D^{4,39} was a primary efficacy parameter in Studies I and II. Higher scores indicate greater depression. In Study I, the HAM-D was administered at baseline and study days 7, 14, 21, 28, and 42 and analyzed for efficacy after 42 days of therapy. In Study II, the HAM-D was administered at study days 1, 7, 14, 21, 28, 42, and 56 and analyzed for efficacy after 56 days of therapy. Patients in Study II were significantly less depressed at baseline (Study I mean \pm SD HAM-D score = 25.65 \pm 3.74; Study II mean \pm SD HAM-D score = 24.92 \pm 3.46; t = 2.47, df = 599, p < .01). The difference was less than 1 point, corresponding to a small effect size of 0.20.⁴⁰

The 10-item Montgomery-Asberg Depression Rating Scale (MADRS)^{6,7} was the other primary efficacy parameter in Studies I and II. Higher scores indicate greater depression. Baseline results confirmed that patients in Study II were less depressed (Study I mean \pm SD MADRS score = 29.12 \pm 5.49; Study II mean \pm SD MADRS score = 26.82 \pm 4.78; t = 5.44, df = 596, p < .001). The nearly 3-point difference corresponded to an effect size of 0.45.

The General Life Functioning (GLF) scale is a 13-item, 6-point Likert scale, summed and scored so that higher scores represent higher quality of life, requiring reverse scoring of several items. Developed for use in the National Institute of Mental Health (NIMH) Treatment of Depression Collaborative Research Program,⁴¹ the GLF consists of 7 items from Dupuy⁴² and 6 items developed for the NIMH study. A recent study in elderly patients with recurrent major depression reported high internal consistency for the total scale ($\alpha = .92$).⁴³ After factor analysis, the authors recommended using the scale total score.

We repeated the psychometric analysis of the GLF since there were no published data on its properties when we initiated our study. The Cronbach α^{44} was .86 in the combined sample. Patients on Study II had higher general life functioning than those in Study I (Study I mean ± SD GLF score = 41.88 ± 8.93; Study II mean ± SD GLF score = 44.05 ± 7.54;) (t = 3.21, df = 596, p < .001). This difference constituted an effect size of 0.26.

The Activities Questionnaire (AQ) was designed for this study (Appendix 1). Its 10 items measure housekeeping, leisure, personal finance, community activities, work and school activities, and social interactions. Items were drawn from the psychopathology and social behavior literature and from a review of existing scales including the Katz Adjustment Scale,³¹ the Activity Pattern Indicators,³⁰ and the Social Adjustment Scale.⁴⁵ A complete description of the AQ and data regarding its factor structure, reliability, and convergent validity are available from the authors. The AQ was administered in both studies at baseline and at the primary efficacy endpoint (Study I, day 42; Study II, day 56).

The AQ demonstrated adequate internal consistency ($\alpha = .78$) and formed 2 factors labeled "social interaction" ($\alpha = .76$) and "task-related activity" ($\alpha = .58$). These 2 factors were subjected to a confirmatory factor analysis using a multiple groups solution, which indicated that the model was a good fit (goodness-of-fit index = 0.986). The 2-factor model was compared to a 1-factor model of the scale total score and fit the data better ($\chi^2 = 81.9$, df = 34, for the 2-factor model versus $\chi^2 = 168$ for the 1-factor model; Akaike information criterion was 124 for the 2-factor model and 208 for the 1-factor model—both statistics indicate better fit with lower values); it also fit equally well in men and women. Because of the reasonable reliability of the scale total, however, we retained the total in the analyses presented below.

Scores on the AQ are obtained by taking the mean across the items constituting the total AQ scale, and the items in each factor separately. The AQ is scored from 1-6, with a higher score corresponding to higher activity levels. One item is reverse-scored. The item anchors differed slightly for each item due to differences in wording across questions.

Consistent with the depression and general life functioning scale results, patients in Study II showed higher activity levels at baseline than those in Study I (Study I mean \pm SD AQ score = 2.39 \pm 0.68; Study II mean \pm SD AQ score = 2.51 \pm 0.66; t = 2.10, df = 593, p < .04). The largest mean difference was only 0.12, corresponding to an effect size of 0.17.

Data Analysis

Treatment effects in Studies I and II were examined separately. Change scores were calculated for all measures, including AQ scale factors, by subtracting the endpoint score from the baseline. For the depression measures, interim scores were substituted for the endpoint in a last-observation-carried-forward analysis (LOCF) if the endpoint was missing. If there were less than 21 days of follow-up data, the patient was considered lost to followup. Some patients who terminated early had exit scores for the AQ and GLF scales, which were used in the calculation of change scores. Treatment effects for the AQ, its subscales, and the GLF were computed in analysis of variance models, using planned comparisons of the differ-



ences between placebo and the active treatment groups combined. To test the hypothesis that AQ and GLF provided additional information about the effects of treatment above and beyond changes in depression, hierarchical multiple regression analyses were conducted in which changes in AQ (total score and each factor assessed separately) or GLF scores were regressed on changes in HAM-D or MADRS scores (the 2 measures were assessed separately) with treatment (dummy coded) entered in a second step. In this way, the incremental variance contributed by treatment to changes in activity or general life functioning beyond the effects of changes in depression could be tested.

RESULTS

Associations Between Depression, Activities, and General Life Functioning

There was a modest relationship at baseline between the depression measures and AQ and a slightly higher relationship with GLF. The correlations between AQ and GLF scores were moderate (Table 1). The AQ showed a stronger correlation with the GLF than with either the MADRS (t = 9.65, df = 588, p < .001) or the HAM-D (t = 12.41, df = 588, p < .001).

Treatment-Related Changes in Activity, General Life Functioning, and Depression

In Study I, the mean \pm SD reduction in depression was -11.26 ± 7.87 on the HAM-D and -13.5 ± 10.0 on the MADRS, while the mean \pm SD improvement on the AQ was 0.65 ± 0.82 over 42 days of treatment and 8.06 ± 10.42 on the GLF, corresponding to effect sizes of 1.43, 1.35, 0.79, and 0.77 for the HAM-D, MADRS, AQ, and GLF, respectively. For the AQ subscales, the mean ± SD improvement in social interaction was 0.59 ± 0.88 and in task-related activity was 0.74 ± 1.00 , corresponding to effect sizes of 0.67 and 0.74. Effect sizes above 0.8 are considered large by convention.⁴⁰ Effect sizes above 0.2 are considered clinically meaningful. Venlafaxine treatment significantly improved the AQ score when compared with placebo (t = -2.44, df = 265,p < .02, effect size = 0.42), as was the case for social interaction (t = -1.96, df = 265, p = .05, effect size = 0.35) and task-related activity (t = -2.70, df = 266, p < .01, effect size = 0.40) as well.

In Study II, the mean \pm SD reduction in depression was -9.26 ± 8.38 on the HAM-D and -10.24 ± 10.39 on the MADRS, while the mean \pm SD improvement on the AQ was 0.54 ± 0.86 , and 5.70 ± 11.60 on the GLF over 56 days, corresponding to effect sizes of 1.10, 0.98, 0.63, and 0.49. Social interaction (mean \pm SD = 0.53 ± 1.14) and task-related activity scores (mean \pm SD = 0.55 ± 0.88) also improved, corresponding to effect sizes of 0.46 and 0.62, respectively. Venlafaxine treatment resulted in sig-

| Table 1. Rela Depression, | ationships and Quality | at Baseline y of Life Sc | Between oresª | n Activity, | |
|------------------------------|------------------------|-----------------------------|------------------|-------------|-------|
| M | 10 | C : - 1 | T1- | TIAM D | 3.4.4 |

| Measure | AQ | Social | Task | HAM-D | MADRS | | | |
|---|--------|--------|--------|--------|--------|--|--|--|
| AQ | | | | | | | | |
| Social | 0.93* | | | | | | | |
| Task | 0.73* | 0.44* | | | | | | |
| HAM-D | -0.15* | -0.12 | -0.14 | | | | | |
| MADRS | -0.30* | -0.25* | -0.27* | 0.59* | | | | |
| GLF | 0.63* | 0.53* | 0.58* | -0.27* | -0.42* | | | |
| $^{a}N = 591$ (Studies I and II combined). Abbreviations: AO = Activity | | | | | | | | |
| Questionnaire, GLF = General Life Functioning Scale, | | | | | | | | |
| HAM-D = Hamilton Rating Scale for Depression, | | | | | | | | |
| MADRS = Montgomery-Asberg Depression Rating Scale, | | | | | | | | |
| Social = Social interaction factor of the AQ, Task = task-related | | | | | | | | |
| activity factor of the AQ. All coefficients signifigant at $p < .01$, except | | | | | | | | |
| *p < .001. | | | | | | | | |

nificant improvements on the AQ compared with placebo (t = -2.7, df = 250, p < .01), and on the social interaction (t = -2.5, df = 249, p < .05) and task-related activity factors (t = -2.37, df = 251, p < .05) as well.

The effects of treatment on the GLF scores were similar across the 2 studies. The treatment effect (planned comparison) between the placebo and the 3 treatment arms combined was significant for Study I (t = -2.45, df = 274, p < .02, effect size = 0.35) and Study II (t = -2.65, df = 253, p < .01, effect size = 0.35).

Tables 2 and 3 present the associations between the change scores for depression, activity, and general life functioning following treatment. Both tables show that a positive change in activity levels was moderately associated with an improvement in depression.

To determine whether the effects of treatment on AQ and GLF scores could be explained completely by changes in depression, a series of multiple regression analyses was conducted. In Study I, when controlling for changes in MADRS scores, treatment accounted for significant incremental variance only for changes in taskrelated activity, and showed a trend for changes in the total AQ score (Table 4). In Study II, when controlling for MADRS change scores, treatment accounted for significant incremental variance on changes in AQ, social interaction, and task-related activity. Similar patterns of significance were observed for the regression models controlling for HAM-D change scores and GLF scores. In Study I, when controlling for changes in the HAM-D, treatment accounted for significant incremental variance on the changes in AQ (t = 2.27, df = 266, p < .02, $\Delta R^2 = 0.01$) and task-related activity (t = 2.58, df = 268, p < .01, $\Delta R^2 = 0.02$), with a trend on social interaction $(t = 1.73, df = 266, p < .08, \Delta R^2 = 0.01)$. When controlling for changes on the MADRS, the treatment effect on changes in the GLF was not significant, but it was significant when the HAM-D was the control variable (t = 2.22, df = 276, p < .03, $\Delta R^2 = 0.01$).

In Study II, when controlling for changes in the HAM-D, treatment accounted for significant incremental

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| Treatment in Study I ^a | | | | | | |
|-----------------------------------|--------|--------|--------|--------|--------|--|
| Measure | AQ | Social | Task | HAM-D | MADRS | |
| AQ | | | | | | |
| Social | 0.95* | | | | | |
| Task | 0.78* | 0.56* | | | | |
| HAM-D | -0.49* | -0.40* | -0.52* | | | |
| MADRS | -0.54* | -0.45* | -0.55* | 0.88* | | |
| GLF | 0.75* | 0.66* | 0.72* | -0.60* | -0.65* | |
| $^{a}N = 256.$ | | | | | | |
| *p < .001. | | | | | | |

Table 2. Relationships Between Activity, Depression, and Quality of Life Change Scores After 42 Days of Treatment in Study I^a

| Table 3. Relationships Between Activity, Depression, | |
|--|--|
| and Quality of Life Change Scores After 56 Days of | |
| Treatment in Study II ^a | |

| Measure | AQ | Social | Task | HAM-D | MADRS |
|----------------|--------|--------|--------|--------|--------|
| AQ | | | | | |
| Social | 0.94* | | | | |
| Task | 0.81* | 0.58* | | | |
| HAM-D | -0.61* | -0.50* | -0.63* | | |
| MADRS | -0.64* | -0.55* | -0.63* | 0.92* | |
| GLF | 0.78* | 0.70* | 0.69* | -0.70* | -0.73* |
| $^{a}N = 251.$ | | | | | |
| *p < .001. | | | | | |

variance on the changes in AQ (t = 2.92, df = 249, p < .01, $\Delta R^2 = 0.01$), social interaction (t = 2.50, df = 248, p < .01, $\Delta R^2 = 0.02$), and task-related activity (t = 2.50, df = 250, p < .01, $\Delta R^2 = 02$). When controlling for changes in depression, the effect of incremental variance of treatment on changes in GLF scores was significant, whether controlling for MADRS scores (t = 2.61, df = 252, p < .01, $\Delta R^2 = 0.01$) or HAM-D scores (t = 3.01, df = 252, p < .01, $\Delta R^2 = 0.02$).

DISCUSSION

We found evidence for the reliability, validity, and responsiveness of the AQ and the GLF as outcome measures in 2 depression treatment studies. Treatment with venlafaxine resulted in improvements in total AQ, social interaction, task-related activity, and GLF measures. After controlling for the effects of improvements in depressive symptoms, venlafaxine still contributed to improvements in total AQ, social interaction, task-related activity, and GLF scores over 56 days of follow-up in Study II. Similar trends were observed over 42 days of follow-up in Study I, but the effect was not always statistically significant. Although the incremental variance was small $(R^2 = 0.01 - 0.02)$, we believe the effects of treatment on activity level are clinically meaningful. The fact that the statistical results were stronger in the study with an additional 2 weeks of follow-up is consistent with the observation that functioning takes longer to improve than symptoms.¹⁰ This conclusion would be strengthened if we had observed the same results over a longer period of fol-

Table 4. Multiple Regression Analysis of the Effects ofTreatment on Activity Change Scores When Controlling forChanges in Depression^a

| Measure | В | b | R ^{2b} | ΔR^2 | t | р |
|------------------------|-------|-------|-----------------|--------------|--------|-------|
| AQ Total | | | | | | |
| MADRS-42 | 0435 | 5333 | | | -10.36 | .0001 |
| Treatment ^c | .1752 | .1270 | 0.30 | 0.01 | 1.76 | .08 |
| MADRS-56 | 0525 | 6369 | | | -13.30 | .0001 |
| Treatment ^c | .2263 | .1238 | 0.43 | 0.02 | 2.59 | .01 |
| Social Interaction | | | | | | |
| MADRS-42 | 0393 | 4506 | | | -8.25 | .0001 |
| Treatment ^c | .1468 | .0710 | 0.22 | 0.01 | 1.3 | .19 |
| MADRS-56 | 0456 | 5428 | | | -10.32 | .0001 |
| Treatment ^c | .2190 | .1175 | 0.32 | 0.01 | 2.24 | .03 |
| Task-Related | | | | | | |
| Activity | | | | | | |
| MADRS-42 | 0536 | 5416 | | | -10.64 | .0001 |
| Treatment ^c | .2444 | .1044 | 0.32 | 0.01 | 2.05 | .04 |
| MADRS-56 | 0682 | 6222 | | | -12.74 | .0001 |
| Treatment ^c | .2498 | .1029 | 0.41 | 0.01 | 2.11 | .04 |

^aAbbreviations: MADRS-42 = change in MADRS score over 42 days of treatment in Study I, MADRS-56 = change in MADRS score over 56 days of treatment in Study II. Each analysis was run separately in a stepwise approach with depression change scores entered first, then treatment.

 ${}^{b}R^{2}$ is for the model with both variables entered.

^cTreatment is dummy-coded.

low-up. Our findings suggest that (1) venlafaxine improves activity level and general life functioning over short periods of follow-up, (2) that improvement in activity level and general life functioning occur in the context of improvement in depressive symptoms, and (3) that improvements in depressive symptoms do not entirely account for improvements in activity level and general life functioning.

That changes in depressive symptoms do not fully account for improvements in activity level and general life functioning suggests that the latter are behavioral domains distinct from depressive symptoms. Further evidence for the distinction of these domains from depressive symptoms comes from the relatively modest correlations between baseline activity levels and depression, coupled with higher relationships between the change scores. One explanation for this pattern might be that social activity is facilitated by positive affect, not suppressed by negative affect. In laboratory⁴⁶ and field studies,47,48 low positive affect has been distinguished from high negative affect, and positive affect has been uniquely linked to daily social activity. Future treatment outcome studies might benefit from distinguishing how changes in positive and negative affect differentially mediate treatment-related changes in social activities.

There are several limitations to our research that point to areas worthy of further investigation. By including only outpatients with depression without significant comorbidities, we cannot be certain that our findings will generalize to the wider population of depressed individuals, who frequently may have substance abuse or other psychiatric difficulties. Second, we did not assess the effects of psychotherapy on activity level, and are therefore unable to say whether similar benefits on activity level would also occur if the treatment were psychotherapy instead of medication.

Depression treatment research that relies solely on symptom outcomes may overlook important treatmentrelated behavioral changes that occur somewhat independently of subjective distress or neurovegetative symptoms. For example, a depressed individual may show improvements in social functioning while experiencing a sad mood, appetite loss, or other signs or symptoms of depression. Depressed mood can be a proxy for diffuse vulnerability^{49,50} and may remain relatively stable despite changes in daily activities, or may improve while activity levels remain stable. However, even nonmood indicators are not completely free of negative affectivity.⁵¹ Although depression is characterized by decreased activity and social withdrawal,⁵² the activity-related features of depression may fluctuate with only moderate correspondence to changes in other features of depression. As Clark and Watson note, "... many individuals continue to function despite their internal misery."51(p226)

In summary, social interaction, task-related activity, and general life functioning were relatively distinct from the symptoms of depression and yet were responsive to effective treatment. In seeking to understand the full impact of depression and its treatments on patients, investigators should consider expanding the scope of measured outcomes beyond symptoms. Activity level and general life functioning are both examples of such outcomes.

Drug name: venlafaxine (Effexor).

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Appendix 1. 10-Item Activity Questionnaire

Social Interaction

- 1) How much time have you spent in leisure activities such as sports, gardening, or hobbies?
- 2) How active have you been in community activities (lodges, church, neighborhood, town meeting, and such)?
- 3) How frequently have you socialized with people you know (coworkers, friends, neighbors?)
- 4) How frequently have you kept in touch with people by phone or letter?
- 5) How much interaction (talking together, family projects, family outings, and the like) have you had with members of your family?
- 6) How frequently have you visited people or entertained at your home?
- 7) When you have been with friends, relatives, or coworkers, how involved have you been in conversation or activities?
- Task-Related Activities
 - 8) How active have you been at work, at school, or in household tasks? 9) How much effort has it taken to carry out your work, school, or
- household tasks? 10) How well have you kept up with household business activities such as paying bills, shopping, or getting things repaired?
- 1 =Next to no time at all 6 = A great deal of time 1 = Extremely inactive 6 = Extremely active1 = Extremely infrequently 6 = Extremely frequently1 = Extremely infrequently 6 = Extremely frequently6 = A great deal of interaction 1 =Next to no interaction at all 6 = Extremely frequently1 = Extremely infrequently1 =Not involved at all 6 = Extremely involved1 = Extremely inactive 6 = Extremely active1 = Hardly any effort at all 6 = An enormous effort; I haven't been able to cope 1 = Not well at all
 - 6 =Very well