Changes in Depressive Symptoms and Social Functioning in the Sequenced Treatment Alternatives to Relieve Depression Study

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Abstract: Major depressive disorder (MDD) profoundly affects social functioning, including the ability to enjoy social activities with peers, friends, and family members. We sought to compare changes in social functioning and depressive symptoms in the first level of the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study. Adult outpatients (N = 2876) with diagnoses of MDD were treated using flexible doses of citalopram for up to 14 weeks. We compared the change over the course of treatment in the social activities item of the Work and Social Adjustment Scale to the change in individual items of the Quick Inventory of Depressive Symptoms–Self-Rated (QIDS-SR). Improvement in social functioning was modestly positively correlated with improvement in sad mood, concentration/decision making, involvement, and energy/fatigability. Only 16% to 22% of the variance in the change in social functioning was accounted for by these symptoms, and only 32% was accounted for by the total QIDS-SR score. In this large real-world sample of outpatients treated using citalopram, changes in depressive symptoms do not entirely explain improvements in social functioning.

Key Words: Major depressive disorder, citalopram, social adjustment.

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Psychosocial and functional impairments are common in major depressive disorder (MDD) and are likely to result in negative psychosocial outcomes, including unemployment and decreased social contacts (Hirschfeld et al., 2002; Weissman, 2000). However, the exact nature of the relationship between MDD symptoms and deficits in psychosocial functioning remains to be established. Although there is a modest association between decreases in clinical symptoms and improvements in social functioning during acute treatment using antidepressants, social functioning often does not return to baseline (Weissman, 2000). A small number of studies have investigated long-term social functioning impairments during or after treatment using antidepressants; these suggest that long-term impairments in social functioning may persist even in patients whose depression is determined to be in clinical remission (Kennedy et al., 2007). In level 1 of the STAR*D trial, greater baseline symptom severity was associated with lower health-related quality of life as assessed across multiple domains (Trivedi et al., 2006b). Interestingly, Rapaport et al. (2005) found that symptom measures in mood and anxiety disorders were associated with baseline quality of life; however, the symptom measures accounted for only a small proportion of the variance in quality of life.

We sought to make a similar comparison for social functioning in a large sample of patients with MDD before and after selective serotonin reuptake inhibitor treatment. To this end, we compared changes in social functioning as measured by the social leisure activities item of the Work and Social Adjustment Scale (WSAS), with changes in depression symptoms in level 1 of STAR*D trial (Mundt et al., 2002). We hypothesized that changes in symptom measures during citalopram treatment would be associated with changes in social functioning measures but would account for only a small proportion of the variance in the improvements in social functioning.

METHODS

The rationale, design, and detailed methods for the first level of STAR*D have been previously described (Rush et al., 2004; Trivedi et al., 2006a). The study protocol was approved by individual institutional review boards, and all patients provided written informed consent. The generalizability of our results was increased by limiting eligibility to patients who sought care as part of routine medical or psychiatric treatment (*i.e.*, patients were not recruited through advertising) and by having broad inclusion and minimal exclusion criteria. Outpatients aged 18 to 75 years diagnosed with nonpsychotic MDD with a baseline 17-item Hamilton Depression Rating Scale (Hamilton, 1960; Hamilton, 1967) score of 14 or greater were eligible. Eligible patients (n = 2876) were treated with the selective serotonin reuptake inhibitor citalopram for up to 14 weeks. Citalopram was started at 20 mg/day and titrated to a target dose of 60 mg/day by week 6, with flexibility to titrate more slowly if necessary.

The WSAS is a five-item scale used to assess work, home management, social leisure activities, private leisure activities, and close relationships; Cronbach α measure of internal consistency for the scale ranges from 0.70 to 0.94, and test-retest correlation is 0.73 (Mundt et al., 2002). In STAR*D, the WSAS was administered using an interactive voice response (IVR) system, which has been shown to correlate highly (0.81–0.86) with the clinician-administered version (Mundt et al., 2002). The current analysis focused on the social activities item: "3. Because of my [disorder], my social leisure activities (with other people, such as parties, bars, clubs, outings, visits, dating, home entertainment) are impaired," which was rated using a scale ranging from 0 ("not at all") to 8 ("very severely impaired").

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This report represents secondary analyses of the STAR*D trial. The STAR*D study is registered at Clinical Trials as Sequenced Treatment Alternatives to Relieve Depression (STAR*D; http://clinicaltrials.gov/ct2/home; NCT00021528).

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The QIDS-SR is a well-validated 16-item self-rated scale of depressive symptoms (Rush et al., 2003), which captures the nine criteria used to diagnose major depressive episode in the *DSM-IV*. It was also administered using the IVR system. Scores for individual items range from 0 to 3; the score for the entire instrument ranges from 0 to 27.

Patients who had QIDS-SR and WSAS scores for entry and exit (n = 1846) were included in this post hoc analysis. We compared the change (exit–entry) in the social activities item of the WSAS (item 3) to the change in individual items of the QIDS-SR. The Pearson product-moment correlation was computed between the change in WSAS item 3 and the change in each QIDS-SR item (for a total of 16 separate correlations); for these correlations, α was adjusted using the Bonferroni correction, yielding an α of 0.003 (= 0.05/16). In addition, the Pearson product-moment correlation was computed between the change in WSAS Item 3 and the change in total QIDS-SR score. Proportion of variance was calculated as the square of Pearson r.

RESULTS

The STAR*D level 1 analyzable sample of 2876 has been reported elsewhere (Trivedi et al., 2006a). Of these 2876 patients, 1846 had both baseline and exit assessments of the WSAS. Table 1 shows the baseline characteristics of the 1846 patients included in this analysis; these were not significantly different from the characteristics of the full sample (n = 2876).

For WSAS Item 3, mean change (exit–entry) was −1.9 ± 2.8 (n = 1846, $p < 0.0001$), with change values ranging from −8 (improvement) to 8 (worsening). For the 16-item QIDS-SR, total mean change (exit–entry) was −6.3 ± 6.7 (n = 1846, $p < 0.0001$), with change values ranging from −25 (improvement) to 13 (worsening).

Table 2 shows Pearson product moment correlation (r) and the proportion of the variance (r^2) in WSAS item 3 accounted for by the change in individual QIDS-SR items. Change in social functioning was modestly correlated with 4 of the 14 individual QIDS-SR items: sad mood (r = 0.48, $p < 0.001$), concentration/decision making (r = 0.44, $p < 0.001$), involvement (r = 0.42, $p < 0.001$) and energy/fatigability (r = 0.40, $p < 0.001$). As Table 2 shows, however, only 16% to 23% of the variance in the change in social functioning was accounted for by each of these items individually. The remainder of the items each explained 10% or less of the variance in the change in social functioning. Although the change in the WSAS social activities item was more highly correlated with the change in total QIDS-SR score (r = 0.58, $p < 0.001$), the change in depressive symptoms overall only accounted for 34% of the variance in the change in social functioning.

TABLE 1. Patient Sample Descriptive Characteristics

Measure	N = 1846
Age (mean ± SD), yrs	42.3 ± 12.9
Female sex (n, %)	1183 (64.1)
Race (n, %)	
White	1435 (77.7)
Black	298 (16.1)
Other	113 (6.1)
Hispanic	205 (11.1)
Years of education (mean ± SD)	13.7 ± 3.2
Employment status (n, %)	
Employed	1014 (54.9)
Unemployed	707 (38.3)
Retired	125 (6.8)
Monthly household income (mean ± SD)	2461 ± 3073
Medical insurance (n, %)	
Any private	946 (52.8)
Public only	224 (12.5)
None	620 (34.6)
Marital status (n, %)	
Never married	484 (26.2)
Married/cohabiting	826 (44.7)
Divorced/separated	471 (25.5)
Widowed	65 (3.5)
Psychiatric care (n, %)	1184 (64.1)

TABLE 2. Pearson Product Moment Correlation (r) and Proportion of Variance Accounted for (R^2) Between Change in WSAS Item 3 and Individual QIDS-SR Items or Total QIDS-SR Score for the Entire Sample (n = 1846)

	Item	r	R^2	p
1	Sleep-onset insomnia	0.3168	0.1003	<0.0001
2	Midnocturnal insomnia	0.2667	0.0711	<0.0001
3	Early-morning insomnia	0.2082	0.0433	<0.0001
4	Hypersomnia	0.0837	0.0070	0.0003
5	Mood (sad)	0.4804	0.2308	<0.0001
6/7	Appetite	0.2016	0.0407	<0.0001
8/9	Weight	0.1175	0.0138	<0.0001
10	Concentration/decision making	0.4428	0.1961	<0.0001
11	Outlook (self)	0.3088	0.0953	<0.0001
12	Suicidal ideation	0.2882	0.0831	<0.0001
13	Involvement	0.4159	0.1730	<0.0001
14	Energy/fatigability	0.3993	0.1594	<0.0001
15	Psychomotor slowing	0.2578	0.0665	<0.0001
16	Psychomotor agitation	0.2377	0.0565	<0.0001
–	$QIDS\text{-}SR_{16}$ total	0.5800	0.3364	<0.0001

Bonferroni-corrected α = 0.003.
QIDS-SR indicates Quick Inventory of Depressive Symptomatology–Self-report; WSAS, Work and Social Adjustment Scale.

DISCUSSION

Rapaport et al. (2005) compared baseline symptom measures with baseline quality of life measures in an array of mood and anxiety disorders and found that "illness-specific symptoms" accounted for only a small to modest proportion of the variance in quality of life, leading them to conclude that quality of life is a "related but semi-independent component of *DSM-IV* syndromes" (p. 1176). In this study, we sought to determine the extent to which improvements in social functioning, as opposed to the broader concept of quality of life, were related to improvements in MDD symptoms.

In this large (n = 1846), real-world sample of outpatients, all QIDS-SR items (except for the infrequently reported increased appetite and weight gain) were significantly correlated (Bonferroni-corrected α = 0.003) with change in the social activities item of the WSAS (Table 2). However, even the most highly correlated items (sad mood, concentration/decision making, involvement, and energy/fatigability) individually account for only 16% to 23% of the variance in social functioning. The less highly correlated items (sleep onset insomnia, self-outlook, suicidal ideation, psychomotor slowing, midnocturnal insomnia, decreased appetite, psychomotor agitation, early morning insomnia, hypersomnia, decreased weight, and increased appetite) individually account for only 1% to 10% of the variance. Even the change in total QIDS-SR score accounted for only 34%

of the variance in the change in WSAS item 3. It should be noted, as well, that the wording of the WSAS instructions (which explicitly ask subjects to evaluate the effect of their disorder on their social functioning) would be expected to bias subjects into linking social functioning and depression symptoms. As such, the proportion of variance in social functioning accounted for by depression symptoms, which we report here, is likely to be an overestimate.

Similar to the results here, our analysis of changes in social functioning and depression symptoms in a double-blind, randomized, placebo-controlled trial comparing *Hypericum perforatum* to sertraline showed that only 25% of the variance in the change in social functioning, measured using the Sheehan Disability Scale (Sheehan et al., 1996), was accounted for by the variance in the change in depression symptoms during the 8-week acute phase (Denninger et al., 2008). These and our current results seem to support the conclusion by Rapaport et al. (2005) that quality of life measures capture a component of mood and anxiety disorders partially distinct from symptom measures.

Our study has several limitations. First, our use of WSAS item 3 as a proxy measure of social functioning may define social functioning too narrowly, given that item 3 refers only to social leisure activities. Second, there are no studies, to our knowledge, correlating WSAS item 3 scores to total scores on other validated social functioning scales. Finally, we have not controlled for comorbid anxiety disorders, symptoms of which can also contribute to deficits in social functioning and quality of life (Rapaport et al., 2005).

CONCLUSIONS

In sum, the current results support the idea that social functioning measures capture a component of MDD that is distinct from symptom-based measures. Social functioning measures may provide a window into patients' recovery that incompletely overlaps with measures of depression symptoms. Further research is needed to determine the optimal way to track and directly remediate quality of life and social functioning deficits.

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Inc, Methylation Sciences, Neuronetics Inc, Novartis AG, Nutrition 21, Organon Pharmaceuticals, PamLab LLC, Pfizer Inc, PharmaStar, Pharmavite LLC, Precision Human Biolaboratory, Prexa Pharmaceuticals Inc, PsychoGenics, Psylin Neurosciences Inc, Ridge Diagnostics Inc, Roche, RCT Logic LLC, Sanofi-Aventis US LLC., Sepracor Inc, Schering-Plough Corporation, Solvay Pharmaceuticals Inc, Somaxon Pharmaceuticals Inc, Somerset Pharmaceuticals Inc, Synthelabo, Takeda Pharmaceutical Company Limited, Tetragenex Pharmaceuticals Inc, TransForm Pharmaceuticals Inc, Transcept Pharmaceuticals Inc, Vanda Pharmaceuticals Inc, and Wyeth-Ayerst Laboratories. 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Wyeth-Ayerst Laboratories. Dr. Fava has equity holdings in Compellis, and receives royalty/patent or other income from the following: patent for the Sequential Parallel Comparison Design and patent application for a combination of azapirones and bupropion in MDD, copyright royalties for the Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire, Sexual Functioning Inventory, Antidepressant Treatment Response Questionnaire, Discontinuation Emergent Signs and Symptoms, and the State vs Trait, Assessability, Face Validity, Ecological Validity, and Rule of Three P's Criteria.

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