

Concise Associated Symptoms Tracking Scale: A Brief Self-Report and Clinician Rating of Symptoms Associated With Suicidality

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Objective: US Food and Drug Administration (FDA) warnings recommend monitoring negative symptoms associated with the initiation of antidepressant medications as these symptoms may interfere with full recovery and pose safety concerns. There is currently no brief, reliable rating instrument for assessing treatment-emergent, negative symptoms. We evaluated the psychometric properties of 2 versions of the newly developed 17-item Concise Associated Symptom Tracking (CAST) scale, the CAST Clinician Rating (CAST-C) and CAST Self-Rated (CAST-SR), which are brief instruments designed to measure the 5 relevant associated symptom domains (irritability, anxiety, mania, insomnia, and panic).

Method: The study enrolled 265 outpatients with major depressive disorder (MDD), from July 2007 through February 2008, into an 8-week, open-label trial with a selective serotonin reuptake inhibitor. Diagnosis of MDD was determined by the Psychiatric Diagnostic Screening questionnaire and an MDD checklist based on *DSM-IV-TR* criteria. Suicidality (suicidal ideation with associated behaviors) is 1 of 9 symptoms of MDD (depressed mood, loss of interest, appetite or weight change, sleep disturbance, reduced concentration or indecisiveness, fatigue or decreased energy, psychomotor agitation or retardation, feelings of worthlessness or excessive guilt). Psychometric evaluations were conducted on both versions of the CAST.

Results: Cronbach α was .80 (CAST-C) and .81 (CAST-SR). Factor analysis identified 5 factors for each scale: (1) irritability, (2) anxiety, (3) mania, (4) insomnia, and (5) panic. When the item that cross-loaded on 2 factors was eliminated, the 16-item solution had a better goodness of fit (CAST-C: 0.90 vs 0.87; CAST-SR: 0.88 vs 0.84). Cronbach α for the 16-item versions was .77 (CAST-C) and .78 (CAST-SR). The 5 associated CAST symptom domains correlated well with other standard measures of these domains.

Conclusions: The 16-item CAST-C and CAST-SR demonstrated excellent psychometric properties. These are potentially useful measures for monitoring treatment-emergent negative symptoms associated with antidepressants, as recommended by the FDA.

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There is growing concern that antidepressant treatment may have a paradoxical effect on a minority of patients, that it may induce not only suicidal states but also a range of negative symptoms that could be precursors of serious adverse events including suicide.^{1–4} Early case reports described an antidepressant-induced state characterized by akathisia-like restlessness, suicidal ideation, and strong, self-destructive impulses.^{5–7} Teicher et al⁸ detailed 9 clinical mechanisms by which antidepressants could induce or exacerbate suicidal tendencies and these negative symptoms: (1) energizing patients to act on preexisting suicidal ideation, (2) worsening depression, (3) inducing akathisia with associated self-destructive or aggressive impulses, (4) inducing panic attacks, (5) switching patients into manic or mixed states, (6) producing severe insomnia or significantly interfering with sleep pattern, (7) inducing an obsessional state, (8) producing an organic personality disorder with borderline features, and (9) exacerbating or inducing electroencephalogram irregularities or other neurologic disturbances.

In October 2004, the available evidence led the US Food and Drug Administration (FDA) to introduce a preliminary product labeling change concerning the use of antidepressants in children and adolescents.⁹ This FDA advisory suggests that, during the “initial few months” of a course of antidepressant therapy or at times of dose changes, “patients should be observed for worsening suicidality and unusual changes in behavior, including anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania and mania.”⁹ In June 2005, the FDA extended its version of the warning used in selective serotonin reuptake inhibitor (SSRI) product labeling to include adults.¹⁰ The warning states:

The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality.¹⁰

Collectively, these negative symptoms associated with antidepressant use are commonly referred to as an “activation syndrome.” In a large prospective study of outpatients

Clinical Points

- Clinicians should monitor patients treated with antidepressants for symptoms associated with treatment-emergent suicidal ideation.
- The Concise Associated Symptoms Tracking (CAST) scale allows for efficient screening of the activation syndrome (ie, irritability, anxiety, mania, panic, insomnia).
- The CAST is a brief self-report instrument that allows for the assessment of domains thought to be associated with changes in suicidal risk.

with nonpsychotic major depressive disorder (MDD), Harada et al¹¹ found that 4.3% of patients developed symptoms consistent with the activation syndrome.

The literature offers several interpretations or explanations of the activation syndrome outlined in the FDA warning. Akiskal et al¹² suggested that the activation syndrome is a function of misdiagnosis, pointing out that the symptoms of agitated, activated, or otherwise excited depression overlap considerably with a bipolar mixed state. Additionally, Chun and Dunner¹³ pointed out that the rate of antidepressant-induced hypomania in MDD is within the rate of misdiagnosis of bipolar depression as unipolar. Thus, some portion of the activation syndrome may also be explained by the presence of an undiagnosed *DSM-IV* Axis I disorder characterized by significant mood lability, as found in borderline personality and bipolar disorders. However, the majority of these events appear to be secondary to antidepressant initiation.

The symptoms identified in the 2005 FDA warning can be grouped into 5 broad domains of treatment-emergent symptoms that constitute the activation syndrome: (1) irritability (irritability, hostility, aggressiveness), (2) anxiety (anxiety, akathisia), (3) mania (hypomania, mania, impulsivity), (4) panic (panic attacks), and (5) insomnia (insomnia). As with suicidality,^{14,15} valid and reliable scales are available to assess each of the symptom domains^{14,16–32} constituting the activation syndrome. However, an evaluation of all these symptom domains would take a significant amount of time to administer, score, and interpret, which would be impractical for daily use in a clinical setting. In addition, currently available instruments depend on assessment through extensive interviews and have not been sensitive to change with treatment. To be useful in practice, any procedure used to monitor treatment-emergent adverse events that could be associated with suicide-related phenomena must be able to detect these symptoms and monitor them over time as they occur in individual patients. There is currently no easy-to-use, validated, brief measure with acceptable psychometric properties to assess all 5 domains identified in the FDA warnings.

To address this gap, we developed a 17-item instrument, the Concise Associated Symptoms Tracking (CAST) scale, including a clinician-rated (the CAST Clinician Rating [CAST-C] scale) and a self-report (the CAST Self-Rated [CAST-SR] scale) version. The CAST includes questions about irritability, anxiety, mania, insomnia, and panic—domains thought to be associated with increased risk for suicide-related events and behaviors. The items in the CAST were designed to be rated using a Likert scale.

The current report utilized data from the Suicide Assessment Methodology Study to address the following questions:

(1) What is the distribution of the CAST scores? (2) Do the items cluster in a manner that is consistent with the 5 broad domains of the activation syndrome? (3) Is the CAST a reliable measure? and (4) Is the CAST a valid measure?

This report summarizes the available psychometric data on the newly developed clinician-rated and self-rated versions of the CAST. A scale

to measure suicidal ideation as recommended by the FDA warnings will be presented in a separate report.

METHOD

Study Population

The study enrolled eligible, consecutive, care-seeking adult outpatients with nonpsychotic MDD, 18–75 years of age, at 6 primary and 9 psychiatric care sites across the United States. Major depressive disorder was diagnosed clinically and confirmed using the Psychiatric Diagnostic Screening Questionnaire (PDSQ)^{33,34} and an MDD checklist from the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision (*DSM-IV-TR*). Eligible participants scored ≥ 14 on the baseline 17-item Hamilton Depression Rating Scale (HDRS₁₇).^{21,22} Participants with general medical conditions were eligible as long as their general medical conditions did not contraindicate the SSRI treatment. Patients were not eligible if they had bipolar disorder; schizophrenia; schizoaffective disorder; MDD with psychotic features (lifetime); a current primary diagnosis of anorexia nervosa, bulimia nervosa, or obsessive-compulsive disorder; current substance abuse or dependence; or a well-documented history of nonresponse (in the current major depressive episode) to 2 adequately delivered SSRI treatments (in terms of both dose and duration). Patients were also ineligible if they had taken antidepressants in the 2 weeks prior to screening (4 weeks for fluoxetine and 6 weeks for monoamine oxidase inhibitors). After receiving a complete description of the study and prior to participation, all participants provided written informed consent.

Study Description

One of the primary objectives of the multicenter National Institute of Mental Health–sponsored Suicide Assessment Methodology Study (clinicaltrials.gov identifier: NCT00532103) was to evaluate easy-to-use and parsimonious clinician- and patient-oriented measures of suicidality and associated symptoms. The secondary objectives of the study were (1) to describe and measure the occurrence and course of treatment-emergent suicidality and associated symptoms in depressed outpatients after initiation and dose escalation of SSRI pharmacotherapy and (2) to evaluate and

compare suicidality assessment methods in representative clinical psychiatric and primary practice settings. The Suicide Assessment Methodology Study was conducted across 15 sites following approval from each of the institutional review boards and monitored by a data monitoring and safety board. Participants were treated with an open-label SSRI antidepressant and monitored for 8 weeks. The SSRIs used in the study included citalopram, escitalopram, fluoxetine, paroxetine, paroxetine controlled release, or sertraline, with the choice of SSRI used in treatment made at the discretion of the individual participant's physician.

Measurement-based care^{35–37} was based on information from each clinic visit regarding (1) depressive symptom severity and (2) side effects and medication tolerability. Depressive symptom severity was assessed using the 16-item Quick Inventory of Depressive Symptomatology—Clinician Rating (QIDS-C₁₆),^{29,38} which uses a structured interview based upon the 9 *DSM-IV-TR* criteria for a major depressive episode (scores ranging from 0 to 27, with higher numbers indicating greater severity). Side effects and medication tolerability were measured using the Systematic Assessment for Treatment Emergent Events—Systematic Inquiry,²⁴ a 55-item self-report that rates the most commonly reported side effects expected with the study medications; the 3-item Frequency, Intensity and Burden of Side Effects Rating,³¹ a self-report measure that provides global ratings of frequency, intensity, and overall burden due to side effects attributable to the antidepressant treatment; and a self-rated medication treatment adherence questionnaire to assess adherence to the prescribed antidepressant.

Assessments

At the screening/baseline visit, clinical research coordinators collected sociodemographic and clinical information and completed the HDRS₁₇. At baseline, participants also completed the PDSQ, a 125-item forced-choice (symptom present or absent) self-report *DSM-IV* Axis I screening questionnaire and the Self-Administered Comorbidity Questionnaire.³⁰

Throughout the course of the study, depression severity was assessed using the QIDS-C₁₆. Suicidal ideation was measured using the Modified Scale for Suicidal Ideation,¹⁴ an 18-item, clinician-administered scale that monitors intensity of ideation, courage, and competence to attempt and to talk and write about death over the past year. We also used the Positive and Negative Suicide Ideation inventory,²⁵ a 20-item, self-report measure of positive and negative thoughts related to suicide attempts that contains positive and negative ideation subscales. Additionally, we used the Concise Health Risk Tracking (CHRT) scale, including the CHRT Clinician Rating (CHRT-C) and the CHRT Self-Report (CHRT-SR) scales, a 12-item scale that rates current suicidal thoughts and plans.

Symptoms representing the 5 broad domains measured by the CAST (irritability, anxiety, mania/hypomania, insomnia, and panic) were collected with other assessments. Irritability was assessed using item and item total

scores from the Clinician-Administered Rating Scale for Mania (10-item mania scale)¹⁶ and the Impulsivity Rating Scale,²³ a 7-item, fully anchored scale with items rated from 0 to 3 (higher scores indicating more impulsivity). Anxiety was evaluated using the Beck Anxiety Inventory (BAI),¹⁹ a 21-item patient self-report of physiologic hyperarousal (and cognitive anxiety) over the last week with items ranging from 0 (not at all) to 3 (severely—I could barely stand it) and the Barnes Akathisia Rating Scale.¹⁷ Anxious depression was defined as major depressive disorder with high levels of anxiety symptoms, as reflected in an HDRS₁₇ 6-item, anxiety/somatization factor score ≥ 7 (psychic anxiety, somatic anxiety, gastrointestinal somatic symptoms, general somatic symptoms, hypochondriasis, and insight).^{39–41} Symptoms of mania and hypomania were evaluated using the Clinician-Administered Rating Scale for Mania, the Impulsivity Rating Scale, and a Psychosis Screen, a 6-item, clinician-rated scale that assesses the presence of hallucinations (auditory, visual) and delusions (persecution, grandiose, somatic, guilt) during the last 2 weeks. Insomnia was assessed using the 3 insomnia items from the QIDS-C₁₆. Panic symptoms were measured using the BAI.

The CAST-C and CAST-SR were administered as well. Both include items reflecting several domains: (1) irritability, (2) anxiety, (3) mania, (4) insomnia, and (5) panic. Each of the 17 items was provided as a statement to reflect patient status in the preceding 24 hours and was rated on a 5-point, fully-anchored Likert scale, with responses ranging from “strongly agree” to “strongly disagree” (Figure 1).

Protocol clinic visits were to occur at weeks 0, 2, 4, 6, and 8. The QIDS-C₁₆ and Frequency, Intensity, and Burden of Side Effects Rating were also collected by telephone at weeks 1, 3, 5, and 7. Participants were evaluated using the CHRT-C and CAST-C via telephone on Mondays, Wednesdays, and Fridays during the first 2 weeks following medication initiation and following a dose increase (week 4 or later). During all clinic visits, including baseline, the clinical research coordinators also collected information on depression severity using the QIDS-C₁₆; suicidal ideation using the CHRT-C, CHRT-SR, Positive and Negative Suicide Ideation, and Modified Scale for Suicidal Ideation (the latter only at baseline and weeks 4 and 8); associated symptom domains using the CAST-C, CAST-SR, BAI, Barnes Akathisia Rating Scale, Clinician-Administered Rating Scale for Mania, Impulsivity Rating Scale, and Psychosis Screen; and medication side effects using the Frequency, Intensity, and Burden of Side Effects Rating and Systematic Assessment for Treatment Emergent Events—Systematic Inquiry.

Analytic Methods

Descriptive statistics are used to describe the sample, percentages for discrete characteristics, and measures of central tendency for continuous characteristics. All analyses were conducted separately for the CAST-C and the CAST-SR. Spearman rank-correlation coefficients were used to assess inter-item correlations. Factor analyses were conducted using principal component factor rotation. The

Figure 1. Concise Associated Symptoms Tracking (CAST) Scale

Please read this series of statements and rate the extent to which each of the statements describes how you have been feeling or acting in the past 24 hours.

For example, if you feel the statement very accurately describes how you have been feeling in the past 24 hours, you would give a rating of "Strongly Agree." If you feel the statement is not at all how you have been feeling in the past 24 hours, you would give a rating of "Strongly Disagree."

	Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
1. I feel anxious all the time.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. I have been feeling really good lately.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. I feel as if I am going to have a heart attack.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. I wish people would just leave me alone.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. I have been having more trouble sleeping than usual.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. I am feeling restless, as if I have to move constantly.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. I suddenly feel very confident.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. I am more talkative than normal.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. I feel very uptight.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. I find myself saying or doing things without thinking.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. I feel very tense and I cannot relax.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12. I can feel my heart racing.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13. Lately everything seems to be annoying me.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14. I slept very little last night.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15. I cannot sit still.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
16. I find people get on my nerves easily.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
17. I have been having lots of great ideas.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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Goodness-of-Fit Index was used to assess the fit of the factor structure. The Goodness-of-Fit Index ranges between 0 and 1, with higher scores indicating a better fit. Pearson correlation coefficients were used to assess the association of the total score of the CAST with each of the factors and to estimate the discriminant and concurrent validity by estimating the correlations of the CAST total score with other measures of mood disorders, suicidal ideation, and general medical comorbidity burden.

RESULTS

The study enrolled 265 men (29%) and women (71%) outpatients diagnosed and initially treated for MDD with an SSRI, of which 239 completed the CAST-C and CAST-SR. The sample's sociodemographic and clinical characteristics were typical for a sample of real world outpatients with MDD (eTable 1).

Exploratory Factor Analyses

An examination of the results indicated that 5 orthogonal factors should be retained for the CAST-C and CAST-SR. The 5 factors included the following domains: irritability, anxiety, mania, insomnia, and panic (Table 1). In both versions, the factor loadings indicated that each item is indeed related to the symptom domain it is intended to assess: items 4, 9, 10, 13, and 16 are related to the irritability domain; items 1, 6, and 15 are related to the anxiety domain; items 2, 7, 8, and 17 are related to the mania/hypomania domain; items 5 and 14 are related to the insomnia domain; and items 3 and 12 are related to the panic domain.

Within the 5-factor solution, item 11 (feel tense, cannot relax) was associated with 2 factors in both CAST versions. Subsequent analyses were performed with and without this item. Exploratory analysis of the 16-item version of the CAST-C and CAST-SR (without item 11) provided an excellent goodness of fit (Goodness-of-Fit Index: 0.90 and 0.88,

Table 1. Factor Analysis Results for 17- and 16-Item CAST-C and CAST-SR^a

Item No.	Item	All Items (GFI=0.8727)					Less Item 11 (GFI=0.8977)				
		Irritability	Anxiety	Mania	Insomnia	Panic	Irritability	Anxiety	Mania	Insomnia	Panic
CAST-C											
1	I feel anxious all the time	.29	.67	-.06	.12	.16	.28	.63	-.06	.14	.19
2	I have been feeling really good lately	-.22	-.08	.72	.16	-.08	-.23	-.08	.71	.16	-.08
3	I feel as if I'm going to have a heart attack	.11	.10	.01	.16	.84	.11	.09	.01	.16	.84
4	I wish people would just leave me alone	.53	-.08	-.26	.30	.24	.53	-.08	-.26	.30	.23
5	I have been having more trouble sleeping than usual	.12	.22	-.01	.86	.08	.12	.21	-.01	.86	.09
6	I am feeling restless; as if I have to move constantly	.13	.75	.15	.22	.18	.15	.77	.14	.22	.19
7	I suddenly feel very confident	-.08	-.04	.78	.07	.10	-.08	-.02	.77	.06	.09
8	I am more talkative than normal	.08	.15	.64	-.10	.23	.08	.14	.64	-.09	.24
9	I feel very uptight	.58	.35	-.20	.09	.27	.57	.31	-.20	.10	.29
10	I find myself saying or doing things without thinking	.62	.00	.17	.06	.26	.61	-.04	.17	.08	.28
11	I feel very tense and I cannot relax	.50	.55	-.05	.14	.20					
12	I can feel my heart racing	.09	.37	.06	-.05	.68	.09	.36	.05	-.05	.69
13	Lately everything seems to be annoying me	.83	.19	-.00	.08	-.06	.85	.20	-.00	.08	-.05
14	I slept very little last night	.12	.21	.02	.85	.03	.12	.20	.02	.85	.04
15	I cannot sit still	.03	.82	.06	.12	.04	.05	.84	.05	.12	.06
16	I find people get on my nerves easily	.77	.22	-.04	-.01	-.12	.79	.24	-.05	-.02	-.11
17	I have been having lots of great ideas	.09	.08	.69	-.13	-.17	.09	.08	.69	-.13	-.16
Eigenvalue		4.63	2.29	1.50	1.26	1.09	4.10	1.49	2.29	1.25	1.08
CAST-SR											
		All Items (GFI=0.8432)					Less Item 11 (GFI=0.8790)				
		Irritability	Anxiety	Mania	Insomnia	Panic	Irritability	Anxiety	Mania	Insomnia	Panic
1	I feel anxious all the time	.37	.60	-.05	.01	.21	.36	.60	-.05	.02	.22
2	I have been feeling really good lately	-.25	.01	.64	.04	-.11	-.25	.01	.64	.03	-.11
3	I feel as if I'm going to have a heart attack	.18	.08	.03	.11	.81	.17	.09	.03	.12	.81
4	I wish people would just leave me alone	.55	.19	-.17	.02	.11	.56	.21	-.17	.03	.11
5	I have been having more trouble sleeping than usual	.18	.14	-.04	.85	.13	.17	.14	-.05	.85	.14
6	I am feeling restless; as if I have to move constantly	.15	.84	.10	.19	.14	.15	.84	.09	.20	.14
7	I suddenly feel very confident	-.18	-.06	.80	.04	.14	-.18	-.06	.81	.03	.14
8	I am more talkative than normal	.10	.11	.66	.02	.31	.12	.13	.66	.02	.31
9	I feel very uptight	.65	.29	-.06	.11	.26	.64	.29	-.07	.12	.28
10	I find myself saying or doing things without thinking	.59	.08	.18	.03	.26	.58	.08	.17	.03	.27
11	I feel very tense and I cannot relax	.58	.42	-.06	.23	.21					
12	I can feel my heart racing	.07	.27	.03	.09	.77	.05	.26	.03	.09	.77
13	Lately everything seems to be annoying me	.87	.06	-.05	.15	-.07	.87	.08	-.06	.16	-.06
14	I slept very little last night	.13	.15	.05	.88	.07	.12	.14	.05	.88	.07
15	I cannot sit still	.10	.88	.05	.11	.09	.10	.88	.05	.12	.10
16	I find people get on my nerves easily	.81	.03	-.09	.10	-.07	.83	.05	-.10	.11	-.06
17	I have been having lots of great ideas	.09	.04	.71	-.07	-.14	.09	.03	.71	-.07	-.13
Eigenvalue		4.87	2.34	1.43	1.07	1.24	4.32	2.34	1.42	1.07	1.24

^aFactor loadings > .4 are shown in bold.

Abbreviations: CAST-C=Concise Associated Symptoms Tracking Clinician Rating, CAST-SR=Concise Associated Symptoms Tracking Self-Rated, GFI=Goodness-of-Fit-Index.

respectively) for the 5-factor solution, with no cross-loading items and a consistent factor structure across both versions of the CAST. The results of the analyses of the 17-item version (with item 11) also found high goodness of fit for the CAST-C and CAST-SR (Goodness-of-Fit Index: 0.87 and 0.84, respectively).

Distribution of Responses to Items

Table 2 provides the distribution of items endorsed in the 2 versions of the CAST measure. Using CAST scoring (1 [strongly disagree] to 5 [strongly agree]), the CAST-C and CAST-SR items ranged from mean ± SD scores of 1.0 ± 0.8 and 1.0 ± 0.9, respectively, for item 2 (feeling really good lately) to 2.7 ± 1.2 and 2.7 ± 1.2, respectively, for item 5 (more trouble sleeping than usual).

Reliability

Table 3 provides inter-item correlations for both the CAST-C and the CAST-SR. The Cronbach α for the 17- and 16-item versions of the CAST-C were high: .80 and .77, respectively. Cronbach α for the 17- and 16-item versions of the CAST-SR were also high: .81 and .78, respectively. There was also a high agreement between the clinician-rated and self-rated items (Table 4), with κ ranging from 0.59 to 0.78.

Correlation of CAST-C and CAST-SR With Other Measures

The 5 CAST-C and CAST-SR domains correlated well with other standard measures of depressive severity and assessments of potential precursor symptoms (BAI, Clinician-Administered Rating Scale for Mania, HDRS₁₇, Impulsivity Rating Scale, PDSQ, QIDS-C₁₆) (Table 5).

Table 2. Distribution of Items Endorsed for CAST-C and CAST-SR (n = 239)

Item No.	Item	Strongly Disagree		Disagree		Neutral		Agree		Strongly Agree		Mean ± SD
		n	%	n	%	n	%	n	%	n	%	
CAST-C												
1	I feel anxious all the time	11	4.6	63	26.4	36	15.1	101	42.3	28	11.7	2.30 ± 1.12
2	I have been feeling really good lately	61	25.5	132	55.2	32	13.4	13	5.4	1	0.4	1.00 ± 0.80
3	I feel as if I'm going to have a heart attack	55	23.0	130	54.4	23	9.6	25	10.5	6	2.5	1.15 ± 0.98
4	I wish people would just leave me alone	22	9.2	64	26.8	51	21.3	76	31.8	26	10.9	2.08 ± 1.18
5	I have been having more trouble sleeping than usual	13	5.4	40	16.7	25	10.5	92	38.5	69	28.9	2.69 ± 1.21
6	I am feeling restless; as if I have to move constantly	18	7.5	79	33.1	43	18.0	74	31.0	25	10.5	2.04 ± 1.17
7	I suddenly feel very confident	59	24.7	138	57.7	25	10.5	14	5.9	3	1.3	1.01 ± 0.84
8	I am more talkative than normal	45	18.8	137	57.3	27	11.3	24	10.0	6	2.5	1.20 ± 0.94
9	I feel very uptight	10	4.2	63	26.4	31	13.0	106	44.4	29	12.1	2.34 ± 1.12
10	I find myself saying or doing things without thinking	21	8.8	88	36.8	32	13.4	83	34.7	15	6.3	1.93 ± 1.15
11	I feel very tense and I cannot relax	9	3.8	55	23.0	26	10.9	108	45.2	41	17.2	2.49 ± 1.13
12	I can feel my heart racing	28	11.7	117	49.0	21	8.8	58	24.3	15	6.3	1.64 ± 1.15
13	Lately everything seems to be annoying me	11	4.6	46	19.2	43	18.0	98	41.0	41	17.2	2.47 ± 1.12
14	I slept very little last night	14	5.9	55	23.0	16	6.7	94	39.3	60	25.1	2.55 ± 1.25
15	I cannot sit still	18	7.5	113	47.3	37	15.5	59	24.7	12	5.0	1.72 ± 1.07
16	I find people get on my nerves easily	6	2.5	45	18.8	31	13.0	103	43.1	54	22.6	2.64 ± 1.10
17	I have been having lots of great ideas	43	18.0	119	49.8	37	15.5	36	15.1	4	1.7	1.33 ± 0.99
CAST-SR												
1	I feel anxious all the time	16	6.7	63	26.4	42	17.6	90	37.7	28	11.7	2.21 ± 1.16
2	I have been feeling really good lately	68	28.5	118	49.4	36	15.1	15	6.3	2	0.8	1.02 ± 0.87
3	I feel as if I'm going to have a heart attack	76	31.8	106	44.4	29	12.1	24	10.0	4	1.7	1.05 ± 1.00
4	I wish people would just leave me alone	19	7.9	60	25.1	60	25.1	75	31.4	25	10.5	2.11 ± 1.14
5	I have been having more trouble sleeping than usual	14	5.9	33	13.8	28	11.7	90	37.7	74	31.0	2.74 ± 1.20
6	I am feeling restless; as if I have to move constantly	29	12.1	73	30.5	39	16.3	67	28.0	31	13.0	1.99 ± 1.26
7	I suddenly feel very confident	73	30.5	109	45.6	40	16.7	12	5.0	5	2.1	1.03 ± 0.93
8	I am more talkative than normal	65	27.2	111	46.4	29	12.1	25	10.5	9	3.8	1.17 ± 1.06
9	I feel very uptight	21	8.8	60	25.1	44	18.4	87	36.4	27	11.3	2.16 ± 1.18
10	I find myself saying or doing things without thinking	32	13.4	71	29.7	46	19.2	69	28.9	21	8.8	1.90 ± 1.21
11	I feel very tense and I cannot relax	18	7.5	52	21.8	26	10.9	99	41.4	44	18.4	2.41 ± 1.23
12	I can feel my heart racing	49	20.5	97	40.6	24	10.0	55	23.0	14	5.9	1.53 ± 1.22
13	Lately everything seems to be annoying me	15	6.3	43	18.0	40	16.7	99	41.4	42	17.6	2.46 ± 1.16
14	I slept very little last night	20	8.4	50	20.9	12	5.0	87	36.4	70	29.3	2.57 ± 1.33
15	I cannot sit still	34	14.2	91	38.1	40	16.7	62	25.9	12	5.0	1.69 ± 1.15
16	I find people get on my nerves easily	15	6.3	39	16.3	30	12.6	104	43.5	51	21.3	2.57 ± 1.17
17	I have been having lots of great ideas	57	23.8	97	40.6	49	20.5	27	11.3	9	3.8	1.31 ± 1.07

Abbreviations: CAST-C = Concise Associated Symptoms Tracking Clinician Rating, CAST-SR = Concise Associated Symptoms Tracking Self-Rated.

The BAI contains items that reflect physiologic hyperarousal as well as cognitive symptoms of anxiety. As such, BAI scores were correlated with the panic factor of the CAST-C (0.53) and CAST-SR (0.59), as well as the anxiety factor (CAST-C: 0.48) (CAST-SR: 0.51). The HDRS₁₇ anxiety subscale score, which, like the BAI, assesses panic symptoms as well as cognitive anxiety, was also correlated with the CAST panic factor (CAST-C: 0.31) (CAST-SR: 0.30) and anxiety factor (CAST-C: 0.33) (CAST-SR: 0.31). The CAST irritability factor was correlated with the Impulsivity Rating Scale total scores (CAST-C: 0.40) (CAST-SR: 0.39), as well as the Clinician-Administered Rating Scale for Mania irritability item (CAST-C: 0.30) (CAST-SR: 0.30). The 3-item insomnia questionnaire on the QIDS-C₁₆ was used to define insomnia, and it was correlated with the CAST insomnia factor (CAST-C: 0.53) (CAST-SR: 0.51). The PDSQ provided consistent results, with generalized anxiety most highly correlated with the CAST anxiety factor (CAST-C: 0.41) (CAST-SR: 0.41), and panic disorder most highly correlated with the CAST panic factor (CAST-C: 0.63) (CAST-SR: 0.65). The Clinician-Administered Rating Scale for Mania and the PDSQ mania scales were not as well correlated with the mania factor or

the other 4 factors, perhaps due to the complex mixture of items contained within the Clinician-Administered Rating Scale for Mania.

The CHRT evaluates suicidal ideation and plans, social support, and hopelessness. Clinically significant correlations ($r \geq 0.30$) between the CAST-SR irritability factor and the CHRT-SR total score (0.45) and CHRT-SR hopelessness factor (0.49) were found. The same findings were paralleled in the comparison of the CAST-C irritability factor and the CHRT-C total score (0.37) and CHRT-C hopelessness factor (0.49).

DISCUSSION

The treatment-emergent symptoms included in the 2005 FDA antidepressant use warning—which may represent precursors to emerging suicidality—can be placed into 5 broad domains: (1) anxiety, akathisia; (2) panic attacks; (3) insomnia; (4) irritability, agitation, hostility, aggressiveness, impulsivity; and (5) hypomania and mania. These symptom domains are directly queried in both versions of the CAST. An examination of the psychometric properties of

Table 3. Pearson Inter-Item Correlations for the CAST-C (above diagonal) and CAST-SR (below diagonal)

Item No.	Item	Item No.																
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1	I feel anxious all the time	1.00	-.08	.26	.19	.32	.48	-.07	.11	.39	.22	.61	.31	.34	.23	.39	.31	-.02
2	I have been feeling really good lately	-.05	1.00	.00	-.21	.00	.00	.45	.28	-.26	-.06	-.15	-.10	-.17	.04	.01	-.18	.35
3	I feel as if I'm going to have a heart attack	.28	.01	1.00	.27	.21	.32	.02	.14	.28	.19	.26	.46	.15	.19	.15	.09	-.06
4	I wish people would just leave me alone	.26	-.20	.28	1.00	.23	.19	-.17	-.08	.34	.27	.28	.06	.38	.20	.12	.30	-.18
5	I have been having more trouble sleeping than usual	.27	-.09	.21	.16	1.00	.34	.05	.03	.28	.14	.32	.14	.21	.68	.23	.14	-.11
6	I am feeling restless; as if I have to move constantly	.45	-.03	.27	.27	.29	1.00	.14	.20	.33	.18	.43	.31	.27	.31	.63	.25	.10
7	I suddenly feel very confident	-.13	.46	.06	-.15	-.03	.08	1.00	.41	-.17	.01	-.09	.11	-.06	-.00	.01	-.06	.34
8	I am more talkative than normal	.15	.21	.22	-.01	.13	.21	.46	1.00	.04	.16	.13	.13	.07	-.02	.17	.00	.25
9	I feel very uptight	.48	-.14	.34	.38	.32	.38	-.11	.09	1.00	.38	.55	.28	.44	.21	.29	.42	-.10
10	I find myself saying or doing things without thinking	.28	-.13	.19	.26	.18	.19	-.01	.32	.38	1.00	.40	.19	.37	.17	.13	.25	.12
11	I feel very tense and I cannot relax	.53	-.19	.27	.34	.36	.43	-.09	.05	.60	.44	1.00	.33	.43	.30	.37	.38	.03
12	I can feel my heart racing	.29	-.09	.50	.07	.19	.35	.11	.18	.28	.22	.34	1.00	.16	.17	.30	.18	.04
13	Lately everything seems to be annoying me	.35	-.19	.19	.42	.28	.22	-.19	.02	.53	.37	.49	.08	1.00	.22	.21	.70	.03
14	I slept very little last night	.13	.01	.21	.15	.62	.32	.02	.08	.20	.18	.34	.21	.22	1.00	.29	.14	-.00
15	I cannot sit still	.43	-.02	.20	.24	.22	.72	-.03	.21	.29	.23	.40	.33	.18	.27	1.00	.18	.05
16	I find people get on my nerves easily	.25	-.23	.11	.37	.19	.22	-.19	.02	.45	.32	.40	.15	.75	.20	.16	1.00	.01
17	I have been having lots of great ideas	-.03	.28	-.01	-.09	-.09	.06	.40	.26	-.05	.07	.02	.03	.02	.03	.04	-.04	1.00

Abbreviations: CAST-C = Concise Associated Symptoms Tracking Clinician Rating, CAST-SR = Concise Associated Symptoms Tracking Self-Rated.

Table 4. Agreement Between CAST-C and CAST-SR

Item No.	Item	Agreement, %	Weighted κ	95% CI
1	I feel anxious all the time	70	0.71	0.65–0.77
2	I have been feeling really good lately	76	0.67	0.59–0.75
3	I feel as if I'm going to have a heart attack	74	0.70	0.63–0.77
4	I wish people would just leave me alone	74	0.76	0.70–0.81
5	I have been having more trouble sleeping than usual	73	0.72	0.66–0.79
6	I am feeling restless; as if I have to move constantly	64	0.65	0.58–0.72
7	I suddenly feel very confident	70	0.59	0.50–0.69
8	I am more talkative than normal	66	0.59	0.50–0.67
9	I feel very uptight	68	0.66	0.58–0.73
10	I find myself saying or doing things without thinking	63	0.64	0.57–0.71
11	I feel very tense and I cannot relax	72	0.72	0.65–0.78
12	I can feel my heart racing	68	0.68	0.61–0.75
13	Lately everything seems to be annoying me	65	0.67	0.60–0.74
14	I slept very little last night	74	0.78	0.72–0.83
15	I cannot sit still	69	0.68	0.61–0.75
16	I find people get on my nerves easily	74	0.75	0.69–0.81
17	I have been having lots of great ideas	67	0.65	0.57–0.72

Abbreviations: CAST-C = Concise Associated Symptoms Tracking Clinician Rating, CAST-SR = Concise Associated Symptoms Tracking Self-Rated.

the CAST-C and CAST-SR indicated that the measures are valid and can reliably assess symptoms listed in the FDA warning.

For both the CAST-C and the CAST-SR, distribution data showed significant variation between subjects in the items endorsed, suggesting that the measures will be able to identify subgroups and that they are not simply another way to assess depressive symptom severity. The CAST may thus be able to provide additional information not available from measures of depression severity.

The CAST produces 5 independent symptom domains: irritability, anxiety, mania, insomnia, and panic. The 16-item

version (without item 11) appears to possess more preferential psychometric properties than the 17-item version, with the 5 independent symptom domains still intact and no item overlap. Thus, each of the 16 items provides some unique information. By design, the 5 symptom domains of the CAST are consistent with those that constitute the activation syndrome as outlined in the FDA warning.

The CAST-C and CAST-SR each showed high internal consistency in their 16-item and 17-item versions. In addition, there was high agreement between the corresponding items of the CAST-C and the CAST-SR. Thus, the CAST shows good reliability. The CAST also demonstrated

Table 5. Correlation Coefficients for Validity Analyses of 16-Item CAST-C and CAST-SR

	Irritability	Anxiety	Mania	Insomnia	Panic
CAST-C scale					
Irritability	1.00	0.41	-0.11	0.30	0.30
Anxiety		1.00	0.09	0.39	0.40
Mania			1.00	-0.01	0.06
Insomnia				1.00	0.22
Panic					1.00
Validity scale					
BAI	0.40	0.48	-0.07	0.23	0.53
CARS-M	0.21	0.29	0.20	0.13	0.12
CARS-M irritability item	0.30	0.11	0.02	0.05	0.09
HDRS ₁₇	0.26	0.34	-0.02	0.41	0.22
HDRS ₁₇ anxiety	0.23	0.33	0.05	0.17	0.31
Irritability Rating Scale	0.40	0.13	0.09	0.11	0.06
PDSQ generalized anxiety	0.33	0.41	0.07	0.17	0.27
PDSQ mania	0.03	0.15	0.20	0.12	0.16
PDSQ panic	0.27	0.50	0.03	0.23	0.63
QIDS-C ₁₆	0.27	0.27	-0.13	0.39	0.11
QIDS-C ₁₆ insomnia	0.07	0.18	0.06	0.53	0.13
CAST-SR scale					
Irritability	1.00	0.44	-0.10	0.31	0.30
Anxiety		1.00	0.08	0.34	0.41
Mania			1.00	0.02	0.11
Insomnia				1.00	0.26
Panic					1.00
Validity scale					
BAI	0.42	0.51	-0.10	0.32	0.59
CARS-M	0.20	0.27	0.05	0.13	0.05
CARS-M irritability item	0.30	0.07	-0.04	0.01	0.04
HRSD ₁₇	0.24	0.29	-0.07	0.39	0.21
HRSD ₁₇ anxiety subscale	0.23	0.31	0.06	0.17	0.30
Impulsivity Rating Scale	0.39	0.10	0.04	0.15	0.07
PDSQ generalized anxiety	0.33	0.41	0.02	0.18	0.30
PDSQ mania	0.01	0.14	0.28	0.06	0.07
PDSQ panic	0.28	0.52	0.09	0.28	0.65
QIDS-C ₁₆	0.23	0.22	-0.18	0.34	0.13
QIDS-C ₁₆ insomnia subscale	0.07	0.12	-0.00	0.51	0.13

Abbreviations: BAI = Beck Anxiety Inventory, CARS-M = Clinician-Administered Rating Scale for Mania, CAST-C = Concise Associated Symptoms Tracking Clinician Rating, CAST-SR = Concise Associated Symptoms Tracking Self-Rated, HDRS₁₇ = 17-item Hamilton Depression Rating Scale, PDSQ = Psychiatric Diagnostic Screening Questionnaire, QIDS-C₁₆ = 16-item Quick Inventory of Depressive Symptomatology—Clinician-rated.

good discriminant and concurrent validity in that well-established and validated measures of each of the symptom domains were highly correlated with measures of the corresponding domain on the CAST. Finally, the CAST is brief to administer in both the CAST-C and CAST-SR formats, thus making it useful for inclusion in clinical trials or practice.

A strength of this study was the sampling technique in which eligible, consecutive, care-seeking adult MDD outpatients were enrolled at 6 primary and 9 psychiatric care sites across the United States, which provided a representative sample of outpatients with MDD. The current study is limited by several factors: (1) the study employed measurement-based care guidelines for antidepressant treatment which, while being widely disseminated, have not been adopted globally and may therefore reduce the generalizability of the findings; (2) the psychometric properties of the CAST require replication; (3) while we were able to present data supporting the measures' content and construct validity, criterion and predictive validity requires a large epidemiologic sample to determine if scale scores predict the

“activation syndrome” as a precursor to suicidal behavior; and (4) the study sample size is modest.

In summary, the CAST provides information on 5 broad domains of treatment-emergent symptoms seen in SSRI treatment that could be precursor symptoms of serious adverse events such as suicide, the same domains as those included by the FDA in its labeling warning on SSRI products. Both the -C and -SR versions of the CAST possess good psychometric properties, and both versions appear to be easy to implement and utilize in clinical practice. The 16-item scale has the advantage of a slightly cleaner factor structure and a better Goodness-of-Fit Index. In general, the CAST-C and CAST-SR (1) are psychometrically acceptable, easy to administer, and easy to interpret; (2) perform equally well; (3) produce assessments that are able to identify different domains related to the activation syndrome; and (4) were found to have 5 valid factors. Since this simple but comprehensive measure can now identify what previously took multiple measures to collect, it can also fill an important gap in evaluating the association between these negative, treatment-emergent symptoms and suicidal ideation and behavior. Thus, the CAST is a potentially useful measure for monitoring treatment-emergent negative symptoms associated with antidepressants, as recommended by the FDA.

Drug names: citalopram (Celexa and others), escitalopram (Lexapro and others), fluoxetine (Prozac and others), paroxetine (Paxil, Pexeva, and others), sertraline (Zoloft and others).

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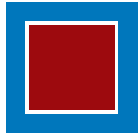
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See p 757 for a report by Trivedi et al on the Concise Health Risk Tracking Scale.

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Supplementary Material

Article Title: Concise Associated Symptoms Tracking Scale: A Brief Self-Report and Clinician Rating of Symptoms Associated With Suicidality

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List of Supplementary Material for the article

1. [eTable 1](#) Patient Baseline Characteristics

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This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

eTable 1. Patient Baseline Characteristics

Characteristic	N = 239
Age (years), mean (SD)	41.4 (13.7)
Female, no. (%)	169 (70.7)
Race, no. (%)	
White	155 (64.9)
Black	56 (23.4)
Other	28 (11.7)
Hispanic, no. (%)	29 (12.1)
Education (years), mean (SD)	13.4 (2.8)
Employment status, no. (%)	
Employed	139 (58.2)
Unemployed	88 (36.8)
Retired	12 (5.0)
Medical insurance, no. (%)	
Any private	106 (44.9)
Public	44 (18.6)
None	86 (36.4)
Marital status, no. (%)	
Never married	72 (30.1)
Married/cohabiting	93 (38.9)
Separated/divorced	64 (26.8)
Widowed	10 (4.2)
Age at first episode <18, no. (%)	87 (36.9)
At least 1 prior episode, no. (%)	138 (65.1)
Family history of, no. (%)	
Alcohol	92 (38.5)
Suicide	7 (2.9)
Current episode \geq 24 months, no. (%)	81 (34.0)
Psychiatric care, no. (%)	160 (66.9)
HRSD ₁₇ ^a , mean (SD)	20.9 (4.1)
QIDS-C ₁₆ ^a , mean (SD)	14.3 (3.0)
Anxious features	162 (67.8)
PDSQ, no. (%)	
Agoraphobia	21 (8.8)
Alcohol abuse	13 (5.5)
Bulimia	29 (12.1)
Drug abuse	17 (7.1)
Generalized anxiety	41 (17.2)
Hypochondriasis	5 (2.1)
Obsessive-compulsive	45 (18.9)
Panic	27 (11.4)
Post-traumatic stress	44 (18.4)
Social phobia	56 (23.6)
Somatoform	3 (1.3)
SCQ, mean (SD)	3.4 (3.7)

Abbreviations HRSD₁₇ 17-item Hamilton Rating Scale for Depression; PDSQ Psychiatric Diagnostic Screening Questionnaire; QIDS-C₁₆ 16-item Quick Inventory of Depressive Symptomatology; SCQ Self-administered Comorbidity Questionnaire.

^aTotal score less suicide item.