## **Original Research**

# It is illegal to post this copyrighted PDF on any website. Psychometrics of the Self-Report Concise Associated Symptoms Tracking Scale (CAST-SR): Results From the STRIDE (CTN-0037) Study

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## ABSTRACT

**Objective:** The self-report Concise Associated Symptoms Tracking Scale (CAST-SR) was developed to track mania, irritability, anxiety, panic, and insomnia symptoms among depressed outpatients receiving antidepressant medication. Given the overlap between these domains, depression, and stimulant use disorders, we reexamined CAST-SR psychometrics in a novel sample: individuals with stimulant use disorder receiving aerobic exercise or health education interventions.

**Methods:** Using the subsample of stimulant-dependent (following DSM-IV criteria) individuals prescribed antidepressants (N = 124) from the multisite Stimulant Reduction Intervention Using Dosed Exercise (CTN-0037) trial (total sample N = 302), conducted July 2010 to February 2013, we analyzed CAST-SR data collected at the first assessment after participant's discharge from residential treatment. We also evaluated the convergent/discriminant validity of the CAST-SR with several self-report questionnaires.

**Results:** Confirmatory factor analysis revealed a 12-item measure composed of 4 factors: irritability, anxiety, panic, and insomnia. This factor structure loaded only in participants prescribed antidepressant medication, not in those who were not prescribed antidepressants. These results replicate the original CAST-SR factor structure, except for the mania factor, which failed to load. Internal consistency was high ( $\alpha$ =0.92 for total scale and  $\alpha$ =0.78–0.89 for the 4 factors), and convergent validity was established, especially for the insomnia and irritability factors, alongside the total score with depressive symptoms, insomnia, quality of life, suicide risk, and physical health measures.

**Conclusions:** These results demonstrate the factor structure, reliability, and validity of the CAST-SR in a novel population of only individuals with stimulant use disorders receiving both exercise/ health education interventions and antidepressant medication.

Trial Registration: ClinicalTrials.gov identifier: NCT01141608

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<sup>d</sup>Current affiliation: Harbor-UCLA Medical Center, Los Angeles, California \**Corresponding author:* Madhukar H. Trivedi, MD, Department of Psychiatry, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390-9119 (madhukar.trivedi@utsouthwestern.edu). Data associating antidepressant use with increased suicidal thoughts and behavior in some individuals created a need for monitoring potential symptoms that come after beginning antidepressant medication. The US Food and Drug Administration warned that treatment-emergent "behaviorally activating" symptoms of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, and mania may represent precursors to emerging suicidality.<sup>1</sup> These symptoms have been linked to increased suicide risk<sup>2,3</sup> and are thus important in monitoring patient safety.

The concern about activating symptoms led to the development of the Concise Associated Symptoms Tracking Scale (CAST),<sup>4</sup> a brief instrument, easily implementable in clinical practice, to track a broad spectrum of symptoms in patients beginning antidepressant medication. Two versions of the CAST, clinician-rated (CAST-C) and selfrated (CAST-SR), were developed; both contain 17 items that measure 5 broad domains of activating symptoms: (1) anxiety (anxiety, akathisia), (2) panic (panic attacks), (3) insomnia, (4) irritability (irritability, hostility, aggressiveness), and (5) mania (hypomania, mania, impulsivity). The irritability subscale of the CAST-SR has also been previously associated with hopelessness, a component of suicide risk, and full information about this measure's development, reliability, and validity among a sample of depressed outpatients has been previously described.<sup>4</sup>

Originally designed to monitor symptoms among depressed outpatients, the CAST symptom domains may also be useful in monitoring commonly associated symptoms in other psychiatric conditions that are highly comorbid with depression, like substance use disorders, and are therefore likely to have patients receiving antidepressants as part of their treatment. Indeed, depressive symptoms and disorders, including major depressive disorder and dysthymia, are highly comorbid with substance use disorders.<sup>5-9</sup> Major depressive disorder has been associated with poorer substance use treatment outcomes,<sup>10</sup> while antidepressant treatment as a concurrent treatment for both comorbid depressive and substance use disorders has shown clinical efficacy.<sup>11</sup> Following this research, the clinical utility of the CAST-SR is likely to be enhanced by applying this instrument to a sample of stimulant-dependent individuals who are also receiving antidepressant medication to treat their depression.

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**Clinical Points** 

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- The self-report Concise Associated Symptoms Tracking Scale (CAST-SR) has been validated as a reliable instrument to track symptoms across the domains of irritability, mania, anxiety, panic, and insomnia in depressed outpatients after beginning antidepressant medication. However, its factor structure, validity, and reliability have not yet been tested in other treatmentseeking populations.
- The CAST-SR loaded only in individuals with primary stimulant use disorders who were prescribed antidepressant medications, not in all individuals with primary stimulant use disorders.
- Clinicians treating antidepressant-receiving individuals with comorbid stimulant use disorders may use the CAST-SR to examine changes in symptoms of anxiety, insomnia, irritability, and panic throughout treatment, thereby optimizing treatment outcomes.

Furthermore, the 5 domains of the CAST map on closely to substance use–related symptoms, further indicating the application of the CAST to this population. For example, substance use disorders impact sleep nature and quality, with negative ramifications on circadian rhythm, REM cycle, the sleep-wake cycle,<sup>12–14</sup> and insomnia.<sup>15,16</sup> Similarly, substance use disorders are highly comorbid with anxiety disorders including generalized anxiety disorder.<sup>17</sup> The comorbidity between anxiety disorders, bipolar disorders, and substance use disorders has also been well established.<sup>18</sup> Taken together, mania, irritability, insomnia, anxiety, and panic are comorbid with stimulant use disorders, suggesting the utility of applying the CAST-SR to this population.

The current study extends prior psychometric research on the CAST-SR by applying this measure to a sample of antidepressant-medicated individuals with stimulant use disorders receiving health education or aerobic exercise as part of their participation in a clinical trial. Our work demonstrates its novelty and importance by extending prior research on the CAST-SR, evaluating this measure in a separate population. This research is important in individuals with stimulant use disorders, because these disorders confer substantial economic costs related to treatment and reduced work productivity<sup>19</sup> and are generally difficult to treat and chronic.<sup>20</sup> To conform to the population for which the measure was originally designed, tested, and validated (ie, outpatients receiving antidepressant medication) and to capitalize on literature indicating the high degree of comorbidity between depression and substance use disorders, we restricted our sample for analysis to only those participants who, at study baseline, endorsed currently being prescribed antidepressant medication to treat their depression.

### METHODS

#### **Participants and Procedure**

The multisite Stimulant Reduction Intervention Using Dosed Exercise (STRIDE, CTN-0037) trial was implemented

within the National Drug Abuse Treatment Clinical Trials Network. Participants were recruited from 9 communitybased residential substance abuse treatment programs located in geographically diverse regions of the United States. The study was approved by the institutional review boards of all participating sites, all participants provided written informed consent, and the study was registered at Clinical Trials.gov (identifier: NCT01141608). The trial was conducted from July 2010 to February 2013.

Full study procedures have previously been described.<sup>21,22</sup> Briefly, eligible participants had a stimulant (cocaine, methamphetamine, amphetamine, or other stimulant, excluding nicotine and caffeine) abuse or dependence diagnosis over the past 12 months that met DSM-IV-TR criteria. Eligible participants must also have reported stimulant use within 30 days prior to their admission to the residential treatment program and had received medical clearance to engage in aerobic exercise. Exclusion criteria included individuals with a general medical condition that prevented exercise or individuals who had previously engaged in significant aerobic exercise over the prior 3 months; individuals with a current psychotic disorder or opiate dependence; and individuals who were pregnant or considered a high suicide risk. Participants were randomized to receive either health education (3 weekly sessions of one-on-one psychoeducation) or high-dose aerobic exercise (defined as a dosage of 12 kcal/kg/wk, ie, 30-50 minutes, 3-5 times per week) for 12 weeks.

Participants (N = 302) aged 18–65 years were enrolled in the STRIDE study and were transferred from residential treatment into the trial. Participants began the study while in residential treatment and continued throughout their transition to outpatient/community treatment, with weekly study assessment and intervention visits. The current analysis uses a subsample of participants who reported being prescribed antidepressant medication at study entry (N = 124).

#### Measures

The self-report Concise Associated Symptoms Tracking scale<sup>4</sup> originally consisted of 17 items. Participants were instructed to rate the extent to which each item "describes how you have been feeling or acting in the past 24 hours." All items were rated on a 5-point scale (from "strongly disagree" to "strongly agree"). Trivedi and colleagues subsequently determined that the 16-item version fit slightly better than the 17-item version, due to 1 item that cross-loaded. The original measure demonstrated an appropriate level of reliability and validity ( $\alpha$ =0.81 for 17-item and 0.78 for 16-item) in a sample of outpatients with depression receiving antidepressant medication. Five factors were determined: mania, irritability, anxiety, panic, and insomnia.<sup>4</sup>

Stimulant use disorders using *DSM-IV* criteria were assessed with the clinician-administered World Health Organization (WHO) Composite International Diagnostic Interview (CIDI), Version 2.1.<sup>23,24</sup>

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Table 1. Confirmatory Factor Analysis (N = 124)								
Model	Factors and Items	χ² ( <i>df</i> )	χ²/df	RMSEA	90% CI	CFI	TLI	WRMR
1	5 factors, 17 items	463.68*** (109)	4.25	0.162	0.147-0.177	0.906	0.883	1.357
2	5 factors, 16 items	434.23*** (94)	4.62	0.171	0.155–0.187	0.892	0.862	1.377
3	4 factors, 13 items	123.62*** (59)	2.10	0.094	0.071-0.117	0.981	0.975	0.712
4	4 factors, 12 items	90.91*** (48)	1.89	0.085	0.058-0.111	0.985	0.979	0.632

\*\*\*P<.001.

Abbreviations: CFI = comparative fit index, RMSEA = root mean square error of approximation, TLI = Tucker-Lewis index, WRMR = weighted root-mean-square residual values.

Current depressive symptoms were assessed with the 16-item clinician-rated version of the Quick Inventory of Depressive Symptomatology (QIDS-C).<sup>25</sup> Adequate levels of reliability ( $\alpha$ =0.85) and validity have been determined among depressed patients.<sup>25</sup>

Participants completed the 14-item version of the Concise Health Risk Tracking—Self-Report (CHRT-SR).<sup>26</sup> Questions focus on hopelessness, pessimism, perceived lack of social support, passive suicidality, impulsivity, and active suicidal planning and intentions. A total CHRT-SR score was calculated, with higher scores signifying greater overall suicidal risk.

The General Activities subscale of the Short-Form Quality of Life Enjoyment and Satisfaction Questionnaire  $(Q-LES-Q-SF)^{27}$  assessed participants' overall level of past-week satisfaction with various life domains, including physical health, work, and social relationships. Closely related, the self-report Short Form Health Survey (SF-36)<sup>28,29</sup> measured 8 domains of health-related quality of life. Reliability statistics for all SF-36 scales are regularly above  $\alpha = 0.70$ ,<sup>30</sup> demonstrating adequate reliability.

The 14-item Snaith-Hamilton Pleasure Scale,<sup>31</sup> a measure of the ability to experience pleasure, was also administered; this scale assessed for anhedonia, a core symptom of major depressive disorder. The measure's reliability ( $\alpha$ =0.91) and validity have been well established among depressed outpatients.<sup>32,33</sup>

## **Statistical Analyses**

Confirmatory factor analysis (CFA) assessed CAST-SR model fit. Further modifications were made if items did not significantly load on a latent variable or if a latent variable was found not to be supported. The model  $\chi^2$  value,<sup>34</sup> model  $\chi^2$  value per degrees of freedom  $(\chi^2/df)$ ,<sup>35</sup> and root mean square error of approximation (RMSEA)<sup>36</sup> with a 90% confidence interval were used to assess model fit. Good model fit was indicated by a lower and nonsignificant  $\chi^2$ value,  $\chi^2/df$  value < 3.0, and RMSEA scores < 0.08 or 0.10. Additional fit indices included the Bentler comparative fit index (CFI), Tucker-Lewis index (TLI), and weighted rootmean-square residual values (WRMR).<sup>37</sup> CFI and TLI scores <0.95 and a WRMR near 1.0 indicate model fit. CFA was conducted using Mplus 7.4<sup>38</sup> with weighted least squares means and variance adjusted (WLSMV) estimation.<sup>39</sup> The WLSMV robust model estimator does not assume normally distributed data and is well suited for skewed data.

SPSS 24.0 (IBM; Armonk, New York) was used for all other statistical analyses. Cronbach  $\alpha$  was calculated for

the CAST-SR total and the 4 subscale scores. Convergent construct validity<sup>40</sup> was tested by comparing scores on the total scale and subscales with other similar self-reported measures, such as depression, mental and physical health, and perceptions of life satisfaction. Spearman  $\rho$  rank order correlations were used to test the association between the CAST-SR total and subscale scores and scores from the QIDS, QIDS sleep items (3-item insomnia total and maximum score on the 3 insomnia items), Q-LES-Q-SF, Snaith-Hamilton Pleasure Scale, and the SF-36 Mental Component and Physical Component scores. As validity analyses were exploratory, no multiple comparison correction was made; in fact, methods such as the Bonferroni correction generally create additional problems, including increasing type II errors.<sup>41</sup>

## RESULTS

## **Descriptive Statistics**

The age of participants in this subsample (N = 124) ranged from 19 to 64 years, with a mean of 39.22 years (SD = 11.12). A majority were women (n = 71, 57.3%), Caucasian/non-Hispanic (n = 72, 58.1%), and never married (n = 64, 51.6%). The sample included 11 Hispanic participants (8.9%) and 41 black participants (33.1%). The mean educational level was 12.46 years (SD = 2.33), with 25.0% of the participants currently employed (n = 31).

## **Factor Validity**

Confirmatory factor analysis indicated that both the 17and 16-item CAST-SR versions reported by Trivedi and colleagues<sup>4</sup> fit poorly (Table 1, models 1 and 2). These 2 models were then both retested after the removal of the 4 items in the mania factor (Table 1, models 3 and 4). Both models then demonstrated excellent fit. Model 4, containing 4 factors and 12 items, had marginally improved fit compared to the other models and was used in all subsequent analyses (Figure 1). The proportion of variance explained in each item by the model ranged from 59.5% to 91.5%.

Separately, an additional CFA analysis was conducted with those participants not on medication (n = 156) using the same 12-item model. Results from the analysis indicated worse model fit ( $\chi^2_{48}$  = 123.38, *P* < .001). RMSEA scores were also beyond the recognized values indicating good fit (RMSEA = 0.100; 90% confidence interval, 0.079–0.122). These poor-fit findings are expected and further validate our decision to restrict the analyzed sample to only those prescribed antidepressant medication.

It is <u>illegal to post this copyrighted PDF on any webs</u>ite. Figure 1. CAST-SR Factor Model, 12 Items (N = 124)

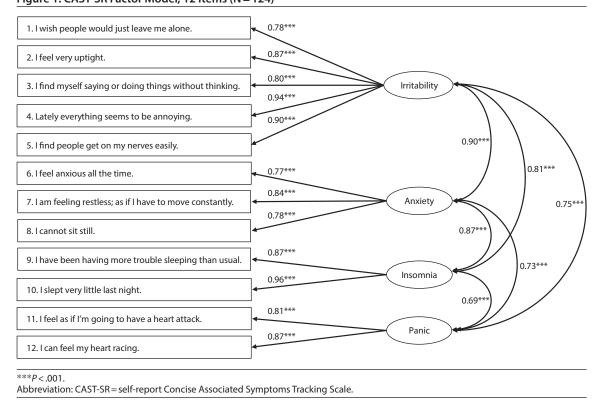


Table 2. CAST-SR Measure and Internal Consistency Reliability (N = 124)

Measure	$Mean \pm SD$	Cronbach α
CAST-SR-12		
Total	$22.51 \pm 8.85$	0.916
Irritability	$9.53 \pm 4.15$	0.886
Anxiety	$5.95 \pm 2.67$	0.785
Insomnia	$4.01 \pm 2.17$	0.778
Panic	$3.02 \pm 1.50$	0.794
QIDS		
Total score	$3.77 \pm 3.00$	0.566
Sum of sleep items	$1.91 \pm 2.00$	0.489
Max of sleep items	$1.31 \pm 1.09$	
Q-LES-Q-SF	65.73±18.89	0.891
Snaith-Hamilton Pleasure Scale	$1.63 \pm 2.02$	0.818
SF-36		
Mental Component score	45.42±12.06	0.831
Physical Component score	$51.54 \pm 8.45$	0.812
CHRT-SR-14	21.16±8.01	0.909

Abbreviations: CAST-SR-12 = self-report Concise Associated Symptoms Tracking Scale; CHRT-SR-14 = Concise Health Risk Tracking—Self-Report, 14-item version; QIDS = Quick Inventory of Depressive Symptomatology; Q-LES-Q-SF = Short-Form Quality of Life Enjoyment and Satisfaction Questionnaire; SF-36 = Short Form Health Survey.

## **Internal Consistency**

Internal consistency for the CAST-SR total and subscale scores ranged from good to excellent (Table 2). The subscale scores obtained Cronbach  $\alpha$  values ranging from 0.78 to 0.89. Although Anxiety, Insomnia, and Panic subscales had Cronbach  $\alpha$  below 0.80, each of these subscales have 2 or 3 items, which limits these reliability scores. The CAST-SR total score's internal consistency was excellent ( $\alpha$ =0.92). Cronbach  $\alpha$  values for all other included measures were

high, with the exception of the QIDS (most likely due to low mean values and skewness). Intercorrelations between each CAST-SR subscale, items from each subscale, and the total scores are provided in Table 3. The significant intercorrelations among these factors are to be expected, given the substantial comorbidity between substance use, anxiety, panic, irritability, and insomnia.

## **Convergent Construct Validity**

The association between the CAST-SR total and subscale scores with the QIDS scores and the QIDS sleep problems (ie, insomnia items) scores are provided in Table 4. The correlations between the CAST-SR scores and the QIDS total scores were modest, though significant, ranging from 0.18 to 0.33 (each P<.05). The QIDS sleep items—both the sum and maximum sleep problems scores—were significantly correlated with the CAST-SR Total, Irritability, Anxiety, and Insomnia subscale scores ( $\rho$  ranging from 0.19 to 0.34, each P<.05). In each case, increases in reported CAST-SR scores were associated with increased depression and insomnia.

CAST-SR total and subscale scores were significantly correlated with Q-LES-Q-SF ( $\rho$  ranging from -0.30 to -0.49, each *P*<.001), total CHRT-SR-14 scores ( $\rho$  ranging from 0.471 to 0.732, each *P*<.001), and the SF-36 Physical Health Component scores ( $\rho$  ranging from -0.26 to -0.43, each *P*<.01). SF-36 Mental Health Component scores were significantly correlated with CAST-SR total ( $\rho$ =-0.19, *P*=.048) and Irritability subscale scores ( $\rho$ =-0.20, *P*=.035), although at a small effect size. In each case, CAST-SR scores were correlated with health-related quality of life measures,

#### It is illea htod any weh nn Table 3. Intersubscale and Item Correlations for CAST-SR-12 (Spearman ρ rank order coefficient test) (N - 124)

CAST-SR-12 Total, Subscales, and Item Scores	Total	Irritability	Anxiety	Insomnia	Panic
Total	1.00				
Subscale					
Irritability	0.936***	1.00			
Anxiety	0.898***	0.749***	1.00		
Insomnia	0.828***	0.680***	0.698***	1.00	
Panic	0.707***	0.625***	0.560***	0.532***	1.00
Item					
1. I wish people would just leave me alone	0.739***	0.810***			
2. I feel very uptight	0.795***	0.880***			
3. I find myself saying or doing things without thinking	0.772***	0.835***			
<ol><li>Lately everything seems to be annoying</li></ol>	0.857***	0.887***			
5. I find people get on my nerves easily	0.814***	0.843***			
6. I feel anxious all the time	0.705***		0.794***		
7. I am feeling restless; as if I have to move constantly	0.821***		0.871***		
8. I cannot sit still	0.727***		0.813***		
9. I have been having more trouble sleeping than usual	0.755***			0.866***	
10. I slept very little last night	0.778***			0.928***	
11. I feel as if I'm going to have a heart attack	0.527***				0.761***
12. I can feel my heart racing	0.698***				0.971***

<sup>a</sup>Spearman p rank order coefficients were not provided when redundant or when items did not belong to a subscale of the CAST-SR-12.

\*\*\*P<.001.

Abbreviation: CAST-SR-12 = self-report Concise Associated Symptoms Tracking Scale.

## Table 4. Construct Validity for CAST-SR-12 (Spearman o rank order coefficient test)

CAST-SR-12		QIDS	QIDS		Snaith-Hamilton	SF-36 Mental	SF-36 Physical	
Measure	QIDS Total	Sum of Sleep Items	Max of Sleep Items	Q-LES-Q-SF	Pleasure Scale	Component Score	Component Score	CHRT-SR-14
Total	0.328***	0.248**	0.258**	-0.436***	0.178	-0.185*	-0.419***	0.705***
Irritability	0.296**	0.186*	0.188*	-0.492***	0.236*	-0.195*	-0.432***	0.732***
Anxiety	0.289**	0.185*	0.225*	-0.326***	0.073	-0.149	-0.352***	0.559***
Insomnia	0.289**	0.340***	0.325***	-0.332***	0.156†	-0.183†	-0.261**	0.471***
Panic	0.182*	0.140	0.132	-0.296***	0.091	-0.090	-0.387***	0.628***
†P<.10.								
*P< 05								

\*\*P<.01.

\*\*\*P<.001.

Abbreviations: CHRT-SR-14 = 14-item Self-Report Concise Health Risk Tracking Scale: OIDS = Ouick Inventory of Depressive Symptoms: O-LES-O-SF = Ouality of Life Enjoyment and Satisfaction Questionnaire—Short Form; SF-36=36-item Short Form Survey.

with higher CAST-SR scores associated with lower life satisfaction and lower reported physical and mental health scores. CHRT-SR-14 scores demonstrated the strongest correlation with CAST-SR scores, indicating that higher CAST-SR scores were associated with increased reported suicide risk. As expected, the CAST-SR mainly failed to correlate with the Snaith-Hamilton Pleasure Scale, a measure of anhedonia, with the exception of the irritability factor.

## DISCUSSION

The current project investigated the extent to which the 5 original factors of the self-report Concise Associated Symptoms Tracking Scale, developed for use in outpatients receiving antidepressant medication-based depression treatment, would hold when extended to a sample of participants currently prescribed antidepressant medication who were also receiving behavioral interventions for their primary stimulant use disorder. Results confirmed a model that was fairly similar to the original one. Four of the 5 factors (irritability, anxiety, insomnia, and panic) loaded nearly

identically to the original study using the better-performing 16-item scale,<sup>4</sup> while the fifth factor, mania, failed to load and was dropped. Internal consistency was high, and the total score plus many of its factors correlated significantly with total depressive symptoms, suicide risk, the sleep-specific QIDS items, and measures of physical health and quality of life. These results mostly replicate prior research establishing the reliability and validity of the CAST-SR, with the exception of the mania factor. These results also extend this research into a new population (individuals with stimulant use disorder) receiving a different primary treatment modality (health education or cardiovascular exercise). Our findings therefore further confirm this measure's reliable factor structure around irritability, insomnia, anxiety, and panic symptoms in a different population—individuals with primary stimulant use disorders receiving study-intervention to treat their stimulant use, and prescribed antidepressants as part of outside clinical care—from the original research.

It is important to note, however, that our findings suggest that the measure does not fit (and therefore should not be used) among all individuals with stimulant or substance use

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**It is illegal to post** disorders but rather only in participants with depressive symptoms (through a proxy of antidepressant medication prescription). Clarifying the scope of use of the CAST-SR in a new population represents an important contribution to understanding the utility of this measure.

In spite of the similarities between our findings and the original psychometric data,<sup>4</sup> there are some noteworthy differences. First, items failed to load into a mania factor. In contrast with the unipolar depressed sample in the original study, most likely characterized by low selfesteem/self-worth and ruminative, depressogenic cognitions, participants with a current stimulant use disorder may have a different perception of questions tapping into "feeling really good lately" or "suddenly feel[ing] very confident." The current sample's participants may therefore interpret the questions tapping mania as instead being reflective of generally highfunctioning mental and/or physical health. Alternatively, outpatients in a current depressive episode are unlikely to endorse such items. One other possibility is that the participants in our sample were comparing mania items to the sensations experienced while using stimulants, which are likely to engender these euphoric mood states, in contrast to the original sample who could not have been making this comparison (as current substance use or dependence was an explicit exclusion criterion).

Second, the 4 factors were more highly correlated (r values ranging from r = 0.53 to r = 0.75) in this study compared to the original one, which may be due in part to overlap between pharmacologic effects of stimulants and

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Potential conflicts of interest: Dr Trombello owns stocks in Merck and Gilead Sciences. Dr Greer has received research funding from NARSAD and has received honoraria and consulting fees from H. Lundbeck A/S and Takeda. Dr Rethorst has received research funding from the National Institute of Mental Health, the American Cancer Society, and the Cancer Prevention Research Institute of Texas. Dr Trivedi is or has been an advisor/consultant and received fee from (lifetime disclosure) Abbott, Akzo (Organon), Allergan Sales, Alkermes, Arcadia, AstraZeneca,

total and maximum sleep disturbance scores on the 3 QIDS insomnia items correlated with many of the CAST factors beyond the insomnia factor. This result is not surprising, given the associations between sleep disturbances and anxiety<sup>42</sup> and irritability.<sup>43</sup>

Study strengths included a regionally and ethnically diverse sample representing a cross-section of the United States, clinician-rated instruments for Axis I and substance use disorders, the extension of the CAST-SR to a new sample, and the application of a wide variety of self-report measures to test reliability and validity. The CAST-SR demonstrates advantages when compared to other measures of treatment-emergent activating symptoms, such as the Treatment-Emergent Activation and Suicidality Assessment Profile,44 as it is shorter and therefore less burdensome. Limitations included the limited variability of many of the measures (especially the QIDS) and the sometimes modest (although statistically significant) correlations with convergent measures. These may affect the generalization of the findings in the current study and suggest the need for additional psychometric validation of the CAST, especially in additional psychiatric populations. Furthermore, the fact that 2 factors were supported by only 2 indicators represents a measure limitation, as it increases the possibility of model misspecification and underidentification. Finally, we did not collect data as to when participants began antidepressant medication, only that, at study entry, participants reported currently being prescribed at least 1 antidepressant medication. We are therefore unable

Axon Advisors, Brintellix, Bristol-Myers Squibb Company, Cephalon, Cerecor, Eli Lilly, Evotec, Fabre Kramer, Forest, GlaxoSmithKline, Global Medical Education Inc., Health Research Associates, Johnson & Johnson, Lundbeck, MedAvante Medscape, Medtronic, Merck, Mitsubishi Tanabe Pharma Development America, MSI Methylation Sciences, Nestle Health Science-PamLab, Naurex, Neuronetics, One Carbon Therapeutics, Otsuka, Pamlab, Parke-Davis, Pfizer, PgxHealth, Phoenix Marketing Solutions, Rexahn, Ridge Diagnostics, Roche Products, Sepracor, Shire Development, Sierra, SK Life and Science, Sunovion, Takeda, Tal Medical/Puretech Venture, Targacept, Transcept, VantagePoint, Vivus, and Wyeth-Ayerst; has

the measured symptoms. Third, the to test treatment-emergent effects after beginning antidepressant medication, as in the original article. Nonetheless, we successfully demonstrate that a 12-item CAST-SR scale is composed of 4 statistically reliable factors among participants currently prescribed antidepressants who also received study intervention to treat their stimulant use disorder.

> In conclusion, our study investigated the psychometric properties of the CAST-SR, a measure of treatmentemergent symptoms after beginning antidepressant treatment, in a novel population of individuals prescribed antidepressants and receiving health education or aerobic exercise as a potential intervention for primary stimulant use disorders. We determined that the CAST-SR did not load in participants with primary stimulant use disorders who were not currently prescribed antidepressant medication. Among the subsample of participants for whom this measure fit, results confirmed much of the original factor structure of the CAST-SR. Furthermore, these results suggest that the CAST-SR reliably measures irritability, insomnia, panic, and anxiety not only in depressed outpatients but also in individuals prescribed antidepressant medications who are also receiving study-based intervention for stimulant use disorders. Pending replication and further investigation, the CAST-SR may also be of use to clinicians treating antidepressant-receiving individuals with substance use disorders to monitor changes in associated symptoms of anxiety, insomnia, irritability, and panic as treatment persists, which can be used to help optimize substance use treatment and prevent relapse.

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the design, analysis, interpretation, or publication of this study.

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## REFERENCES

- Culpepper L, Davidson JR, Dietrich AJ, et al. Suicidality as a possible side effect of antidepressant treatment. *Prim Care Companion J Clin Psychiatry*. 2004;6(2):79–86.
- Akiskal HS, Benazzi F, Perugi G, et al. Agitated "unipolar" depression re-conceptualized as a depressive mixed state: implications for the antidepressant-suicide controversy. J Affect Disord. 2005;85(3):245–258.
- Chu C, Klein KM, Buchman-Schmitt JM, et al. Routinized assessment of suicide risk in clinical practice: an empirically informed update. J Clin Psychol. 2015;71(12):1186–1200.
- Trivedi MH, Wisniewski SR, Morris DW, et al. Concise Associated Symptoms Tracking scale: a brief self-report and clinician rating of symptoms associated with suicidality. J Clin Psychiatry. 2011;72(6):765–774.
- Conway KP, Compton W, Stinson FS, et al. Lifetime comorbidity of DSM-IV mood and anxiety disorders and specific drug use disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry. 2006;67(2):247–257.
- Kessler RC, Berglund P, Demler O, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA. 2003;289(23):3095–3105.
- Sanchez K, Chartier KG, Greer TL, et al. Comorbidities and race/ethnicity among adults with stimulant use disorders in residential treatment. *J Ethn Subst Abuse*. 2015;14(1):79–95.
- Sanchez K, Walker R, Campbell AN, et al. Depressive symptoms and associated clinical characteristics in outpatients seeking community-based treatment for alcohol and drug problems. Subst Abus. 2015;36(3):297–303.
- Warden D, Sanchez K, Greer T, et al. Demographic and clinical characteristics of current comorbid psychiatric disorders in a randomized clinical trial for adults with stimulant use disorders. *Psychiatry Res.* 2016;246:136–141.
- Compton WM 3rd, Cottler LB, Jacobs JL, et al. The role of psychiatric disorders in predicting drug dependence treatment outcomes. Am J

- Nunes EV, Levin FR. Treatment of depression in patients with alcohol or other drug dependence: a meta-analysis. *JAMA*. 2004;291(15):1887–1896.
- 12. Angarita GA, Emadi N, Hodges S, et al. Sleep abnormalities associated with alcohol, cannabis, cocaine, and opiate use: a comprehensive review. *Addict Sci Clin Pract*. 2016;11(1):9.
- Conroy DA, Arnedt JT. Sleep and substance use disorders: an update. *Curr Psychiatry Rep.* 2014;16(10):487.
- Hasler BP, Smith LJ, Cousins JC, et al. Circadian rhythms, sleep, and substance abuse. *Sleep Med Rev.* 2012;16(1):67–81.
- Hartwell EE, Pfeifer JG, McCauley JL, et al. Sleep disturbances and pain among individuals with prescription opioid dependence. *Addict Behav.* 2014;39(10):1537–1542.
- Teplin D, Raz B, Daiter J, et al. Screening for substance use patterns among patients referred for a variety of sleep complaints. *Am J Drug Alcohol Abuse*. 2006;32(1):111–120.
- Alegría AA, Hasin DS, Nunes EV, et al. Comorbidity of generalized anxiety disorder and substance use disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry. 2010;71(9):1187–1195.
- Goldstein BI, Levitt AJ. The specific burden of comorbid anxiety disorders and of substance use disorders in bipolar I disorder. *Bipolar Disord*. 2008;10(1):67–78.
- Office of National Drug Control Policy. The Economic Costs of Drug Abuse in the United States, 1992–2002. (Publication No. 207303). Washington, DC: Executive Office of the President; 2004.
- Dutra L, Stathopoulou G, Basden SL, et al. A meta-analytic review of psychosocial interventions for substance use disorders. Am J Psychiatry. 2008;165(2):179–187.
- Trivedi MH, Greer TL, Grannemann BD, et al. Stimulant Reduction Intervention Using Dosed Exercise (STRIDE)—CTN 0037: study protocol for a randomized controlled trial. *Trials.* 2011;12(1):206.
- Trivedi MH, Greer TL, Potter JS, et al. Determining the primary endpoint for a stimulant abuse trial: lessons learned from STRIDE (CTN 0037). *Am J Drug Alcohol Abuse*. 2011;37(5):339–349.
- World Health Organization. Composite International Diagnostic Interview, Version 2.1. Geneva, Switzerland: World Health Organization; 1997.
- Robins LN, Wing J, Wittchen HU, et al. The Composite International Diagnostic Interview: an epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. Arch Gen Psychiatry. 1988;45(12):1069–1077.
- 25. Trivedi MH, Rush AJ, Ibrahim HM, et al. The Inventory of Depressive Symptomatology, Clinician Rating (IDS-C) and Self-Report (IDS-SR), and the Quick Inventory of Depressive Symptomatology, Clinician Rating (QIDS-C) and Self-Report (QIDS-SR) in public sector patients with mood disorders: a psychometric evaluation. *Psychol Med.* 2004;34(1):73–82.

- 5. Trivedi MH, Wisniewski SR, Morris DW, et al. Concise Health Risk Tracking scale: a brief self-report and clinician rating of suicidal risk. J Clin Psychiatry. 2011;72(6):757–764.
- Endicott J, Nee J, Harrison W, et al. Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. *Psychopharmacol Bull*. 1993;29(2):321–326.
- Ware JE Jr. Conceptualization and measurement of health-related quality of life: comments on an evolving field. Arch Phys Med Rehabil. 2003;84(suppl 2):S43–S51.
- Ware JE Jr. SF-36 Physical and Mental Health Summary Scales: A User's Guide. Version 2. Montreal, Canada: Quality Metrics, Inc; 1997.
- Tsai C, Bayliss MS, Ware JÉ. SF-36 Health Survey Annotated Bibliography. 2nd ed. Boston, MA: Health Assessment Lab, New England Medical Center; 1997:1988–1996.
- Snaith RP, Hamilton M, Morley S, et al. A scale for the assessment of hedonic tone: the Snaith-Hamilton Pleasure Scale. Br J Psychiatry. 1995;167(1):99–103.
- Nakonezny PA, Carmody TJ, Morris DW, et al. Psychometric evaluation of the Snaith-Hamilton Pleasure Scale in adult outpatients with major depressive disorder. Int Clin Psychopharmacol. 2010;25(6):328–333.
- Nakonezny PA, Morris DW, Greer TL, et al. Evaluation of anhedonia with the Snaith-Hamilton Pleasure Scale (SHAPS) in adult outpatients with major depressive disorder. J Psychiatr Res. 2015;65:124–130.
- Kline RB. Principles and Practice of Structural Equation Modeling. 3rd ed. New York, NY: Guilford Press; 2011.
- Bollen KA. Structural Equations With Latent Variables. New York, NY: Wiley; 1989.
- Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. *Struct Equ Modeling*. 1999;6(1):1–55.
- Yu C. Evaluating Cutoff Criteria of Model Fit Indices for Latent Variable Models With Binary and Continuous Outcomes. Los Angeles, CA: University of California; 2002.
- Múthen LK, Múthen BO. Mplus User's Guide. 7th ed. Los Angeles, CA: Múthen & Múthen; 2012.
- Brown T. Confirmatory Factor Analysis for Applied Research. New York, NY: Guilford Press; 2006.
- 40. DeVellis RF. Scale Development: Theory and Applications. 4th ed. Los Angeles, CA: Sage; 2016.
- 41. Perneger TV. What's wrong with Bonferroni adjustments. *BMJ*. 1998;316(7139):1236–1238.
- 42. Uhde TW, Cortese BM, Vedeniapin A. Anxiety and sleep problems: emerging concepts and theoretical treatment implications. *Curr Psychiatry Rep.* 2009;11(4):269–276.
- Dinges DF, Pack F, Williams K, et al. Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 hours per night. *Sleep*. 1997;20(4):267–277.
- Reid JM, Storch EA, Murphy TK, et al. Development and psychometric evaluation of the treatment-emergent activation and suicidality assessment profile. *Child Youth Care Forum*. 2010;39(2):113–124.