

# Becoming the Center of Attention in Social Anxiety Disorder: Startle Reactivity to a Virtual Audience During Speech Anticipation

Brian R. Cornwell, PhD; Randi Heller, BA; Arter Biggs, BA;  
Daniel S. Pine, MD; and Christian Grillon, PhD

**Objective:** A detailed understanding of how individuals diagnosed with social anxiety disorder (SAD) respond physiologically under social-evaluative threat is lacking. Our aim was to isolate the specific components of public speaking that trigger fear in vulnerable individuals and best discriminate between SAD and healthy individuals.

**Method:** Sixteen individuals diagnosed with SAD (*DSM-IV-TR* criteria) and 16 healthy individuals were enrolled in the study from December 2005 to March 2008. Subjects were asked to prepare and deliver a short speech in a virtual reality (VR) environment. The VR environment simulated standing center stage before a live audience and allowed us to gradually introduce social cues during speech anticipation. Startle eye-blink responses were elicited periodically by white noise bursts presented during anticipation, speech delivery, and recovery in VR, as well as outside VR during an initial habituation phase, and startle reactivity was measured by electromyography. Subjects rated their distress at 4 time-points in VR using a 0–10 scale, with anchors being “not distressed” to “highly distressed.” State anxiety was measured before and after VR with the Spielberger State-Trait Anxiety Inventory.

**Results:** Individuals with SAD reported greater distress and state anxiety than healthy individuals across the entire procedure ( $P$  values  $< .005$ ). Analyses of startle reactivity revealed a robust group difference during speech anticipation in VR, specifically as audience members directed their eye gaze and turned their attention toward participants ( $P < .05$ , Bonferroni-corrected).

**Conclusions:** The VR environment is sufficiently realistic to provoke fear and anxiety in individuals highly vulnerable to socially threatening situations. Individuals with SAD showed potentiated startle, indicative of a strong phasic fear response, specifically when they perceived themselves as occupying the focus of others’ attention as speech time approached. Potentiated startle under social-evaluative threat indexes SAD-related fear of negative evaluation.

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**Corresponding author:** Brian R. Cornwell, PhD, Mood and Anxiety Disorders Program, National Institute of Mental Health, 15K North Dr, MSC 2670, Bethesda, MD 20892 (cornwellb@mail.nih.gov).

Social anxiety disorder (SAD) is a common, impairing psychiatric illness with lifetime prevalence between 10% and 15%.<sup>1,2</sup> It involves persistent fear of situations in which the individual is scrutinized.<sup>3</sup> We assessed startle reactivity in a virtual reality (VR) context to demonstrate heightened physiologic reactivity in SAD and to identify specific

components of social-evaluative contexts that discriminate between healthy individuals and those with SAD.

Clinical neuroimaging work, much of which has studied neural responses to facial emotional expressions, has demonstrated that patients with SAD as well as other anxiety disorders exhibit hyperactivity of structures mediating conditioned fear responses and attention allocation to salient cues.<sup>4</sup> For instance, amygdala reactivity, which indexes functioning of the brain’s so-called fear circuit, is abnormally high in individuals with SAD, particularly for faces conveying fear, anger, and contempt,<sup>5–7</sup> but also emotionally neutral ones.<sup>8</sup> These findings are complemented by evidence of heightened amygdala activity when SAD patients anticipate giving a speech while undergoing functional imaging scans.<sup>9–11</sup>

Surprisingly, psychophysiological studies that have measured autonomic reactivity (eg, heart rate, electrodermal activity) in individuals with SAD present mixed results that are difficult to reconcile with evidence of hyperactivity in fear/anxiety-related brain structures in SAD. In one comprehensive study,<sup>12</sup> no associations emerged between trait indices of social anxiety and an array of physiologic measures collected during speech anticipation, corroborating previous studies<sup>13–15</sup> that failed to find the hypothesized relationships. Despite some positive evidence,<sup>16–19</sup> these inconsistencies among physiologic and brain imaging raise important questions regarding how social anxiety manifests physiologically and what features of social situations are especially potent to trigger SAD-related physiologic hyperactivity.

Few studies have explored SAD-related modulation of the startle reflex, a defensive reflex that is highly relevant to translational research approaches. Fear-potentiated startle refers to increased startle reactivity (ie, larger eye-blinks) under fear/anxiety-provoking conditions,<sup>20</sup> which, in rodents, is mediated by the amygdala and related structures.<sup>21</sup> Larsen et al<sup>22</sup> reported that individuals with SAD showed greater startle reactivity when exposed to social threat words compared to healthy individuals. Greater startle reactivity was also found in patients imagining socially threatening situations<sup>23</sup> and in high-trait socially anxious participants during self-focus compared to non-self-focus conditions.<sup>24</sup> However, Blumenthal et al<sup>25</sup> reported diminished startle responses in introverted individuals during a social encounter relative to baseline conditions. The authors argued that an inward shift of attention elicited by the social encounter<sup>26</sup> might reduce startle reactivity. The relevance of the latter finding to SAD is not clear, however, given that the dimensional constructs of introversion and social anxiety are distinct.

**Table 1. Sample Characteristics for Healthy Participants and Participants With Social Anxiety Disorder (SAD)**

Demographic Characteristic	Healthy (n = 16)	SAD (n = 16)	P (test of group difference)
Age, mean $\pm$ SD, y	31 $\pm$ 8	35 $\pm$ 12	.30 <sup>a</sup>
Gender, women:men, n	7:9	6:10	.72 <sup>b</sup>
Ethnicity, n			.30 <sup>b</sup>
African-American	2	6	
Asian Pacific	2	0	
Caucasian/non-Hispanic	10	7	
Hispanic	1	1	
Other	1	2	
Other Axis I diagnoses, n			.06 <sup>b</sup>
None	16	10	
Generalized anxiety disorder	0	2	
Panic disorder	0	1	
Past major depressive disorder	0	3	

<sup>a</sup>Based on a Student *t* test.<sup>b</sup>Based on a  $\chi^2$  test of independence.

Using VR, we found a positive association in healthy individuals between startle reactivity under social-evaluative threat and trait social anxiety as measured by fear of negative evaluation.<sup>27</sup> Participants in that study performed a speech in VR, which simulated being center stage before a live audience. Greater fear of negative evaluation correlated with larger startle reactivity during speech anticipation but not during anticipation of a counting task without an audience. Schulz et al<sup>28</sup> recently replicated this result. While none of these subjects in either study met criteria for SAD, fear of negative evaluation is a core cognitive component of social anxiety that relates to symptom severity<sup>29</sup> and may be partly heritable.<sup>30</sup>

We extend these findings by measuring startle reactivity under social-evaluative conditions simulated in VR in individuals diagnosed with SAD. The speech anticipation period in VR was modified to include a phase in which the audience is visible but not attentive, followed by a period in which the audience directs its attention to the participant and silently awaits speech delivery. We hypothesized that individuals with SAD would be particularly fearful of being the focus of others' attention and would thus show heightened startle during the latter part of anticipation. This hypothesis is based on evidence that socially anxious individuals show greater amygdala reactivity to faces<sup>5-8</sup> and defensive responding (ie, heart-rate acceleration) to faces with direct eye gaze than low socially anxious individuals.<sup>31</sup> We also predicted that SAD patients would report more distress and anxiety than healthy individuals across all phases of the experiment, including at baseline before entering virtual reality. This last prediction was based on the hypothesis that vulnerable individuals experience sustained anxiety in experimental contexts that contain personally relevant threats.<sup>32,33</sup>

## METHOD

### Participants

Individuals with generalized SAD (n = 16) and healthy individuals (n = 16) were recruited and were enrolled in the study from December 2005 to March 2008. Two additional participants, 1 from each group, were excluded due to equipment

**Table 2. Social Anxiety, General Anxiety, and Depressive Symptoms Among Healthy Participants and Participants With Social Anxiety Disorder (SAD)<sup>a</sup>**

Instrument	Healthy	SAD	Student <i>t</i>
Liebowitz Social Anxiety Scale			
Anxiety	15.7 $\pm$ 9.8	42.9 $\pm$ 11.8	-6.96**
Avoidance	13.1 $\pm$ 10.3	42.4 $\pm$ 16.7	-5.83**
Fear of Negative Evaluation scale	8.9 $\pm$ 5.3	23.6 $\pm$ 5.1	-7.88**
Self-Statements during Public Speaking Scale			
Positive subscale	17.6 $\pm$ 4.1	8.5 $\pm$ 5.2	5.48**
Negative subscale	2.8 $\pm$ 2.8	13.8 $\pm$ 6.0	-6.57**
Spielberger State-Trait Inventory			
Trait	31.4 $\pm$ 9.3	46.8 $\pm$ 8.6	-4.88**
State (before speech)	29.4 $\pm$ 12.1	43.4 $\pm$ 10.7	-3.46*
State (after speech)	28.8 $\pm$ 9.4	41.4 $\pm$ 11.8	-3.34*
Penn State Worry Questionnaire	38.8 $\pm$ 11.2	52.3 $\pm$ 11.3	-3.35*
Beck Depression Inventory	3.7 $\pm$ 3.4	7.2 $\pm$ 6.7	-1.86†

<sup>a</sup>Values shown as mean  $\pm$  SD unless otherwise stated. Statistical tests are adjusted for unequal variances.†*P* < .10.\**P* < .005.\*\**P* < .001.

failure. Demographics appear in Table 1. All individuals with SAD met diagnostic criteria based on a Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders, Research Version, Patient Edition (SCID-I/P),<sup>34</sup> administered by one of 4 staff psychologists with high interrater reliability ( $\kappa = 0.76$ ). All SAD diagnoses were confirmed through in-person evaluations by a board-certified psychiatrist (D.S.P.).

Individuals were excluded if they exhibited current major depressive disorder symptoms or suicidal ideation, a history of substance or alcohol abuse or dependence, or a current or past history of bipolar depression or psychosis. Healthy individuals did not meet criteria for current or past Axis I disorders based on a SCID. Additional exclusion criteria for all participants were (1) use of psychopharmacologic medication within 2 weeks of testing or use of fluoxetine within 6 weeks, (2) current use of illicit drugs or pregnancy per urine tests, or (3) any medical condition determined by physical examination by a staff physician that may interfere with the study's objectives. All procedures were approved by the Combined Neuroscience Institutional Review Board of the National Institutes of Health. We obtained informed consent from all participants after procedures were fully explained.

### Measures

Participants completed the Liebowitz Social Anxiety Scale (LSAS)<sup>35</sup> and Fear of Negative Evaluation scale (FNE)<sup>36</sup> to assess social anxiety symptoms. The Spielberger State-Trait Anxiety Inventory (STAI-State, STAI-Trait)<sup>37</sup> was administered to measure both general trait and state anxiety. The Self-Statements during Public Speaking scale (SSPS),<sup>38</sup> a 10-question Likert-based (0-5) instrument, measured the extent of positive thoughts (eg, "I can handle everything") and negative thoughts (eg, "I'm a loser") one has about oneself during public speaking. Depressive and general worry symptoms were measured with the Beck Depression Inventory (BDI)<sup>39</sup> and Penn State Worry Questionnaire (PSWQ),<sup>40</sup> respectively. Table 2 presents group statistics for each of

these instruments. One SAD participant was missing LSAS, FNE, and BDI scores. One healthy participant was missing a PSWQ score.

Finally, we also asked participants at several time points, inside and outside VR, their levels of distress on a 0–10 scale, with anchors being “not distressed” to “highly distressed.”

### Apparatus

The virtual reality (VR) used to simulate the public speaking experience was part of a commercial package (Virtually Better, Inc, Decatur, Georgia). This package contains several audiences exhibiting different behaviors: positive, neutral, and hostile. We chose the emotionally neutral audience. VR was experienced through a lightweight head-mounted 3dVisor (eMagin, Bellevue, Washington). Separate stereo headphones were used to deliver acoustic probes for eliciting startle responses.

### Procedure

After informed written consent procedures, participants completed the questionnaires and donned the 3dVisor to get acclimated to the VR system. A VR environment different from that used for the speech was presented. Participants doffed the 3dVisor, and electrodes were attached for electromyographic (EMG) measurement. Participants provided a subjective distress rating, after which 9 startle probes were administered via headphones to habituate startle reactivity. Startle probes were 40-millisecond white noise bursts (105 dB, near-instantaneous rise/fall times), delivered every 17–23 seconds. Participants were then given the topic of the speech (eg, favorite movie) and prepared for 5 minutes. A second distress rating was obtained before entering VR.

Participants stood during the entire VR procedure in a darkened room. Inside VR, participants initially found themselves onstage, behind a podium with curtains closed. After 4 minutes, the audience was heard entering the room. The curtains were then drawn, revealing the audience of approximately 30 members talking among themselves. Approximately 30 seconds later, the audience turned their heads, applauded, and maintained attention to the participant (Figure 1). Participants then began their 3-minute speech. Following the speech, the curtains were closed, and participants spent 2 minutes in recovery before exiting VR. Participants rated their distress 4 times inside VR: (1) 2 minutes into baseline with curtains closed, (2) just before beginning the speech with the audience looking at them, (3) after the speech as the curtains were closing, and (4) at the end of recovery before exiting VR. The virtual podium was used to display text messages, prompting participants to provide distress ratings at these times and to begin and end speaking. Startle probes were delivered every 17–23 seconds, beginning 2 minutes after entering VR. Startle probe delivery did not coincide with subjective distress reports.

After VR, participants provided a final distress rating and completed 3 more questionnaires. One was a 10-item yes-or-no recognition memory questionnaire designed to determine whether they could recollect specific features

Figure 1. Static View of Virtual Reality Depicting the Silent, Attentive Audience From the Perspective of the Participants



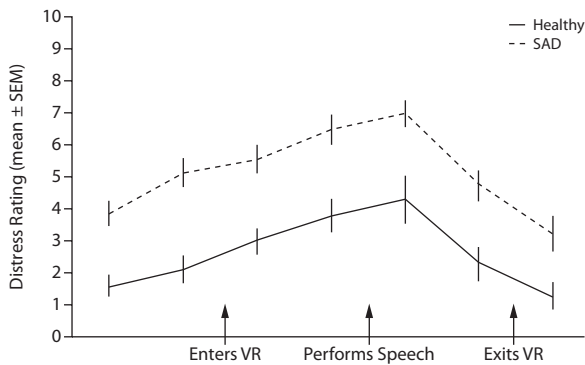
of the environment (eg, “Were you standing on a wooden floor?”), as well as specific social aspects of the audience (eg, “Was the white man in the front row wearing a sweater?”). Although participants’ subsequent memory may be influenced by multiple factors, the absence of a group difference would be consistent with similar levels of attention to the VR environment among healthy participants and those with SAD. We presented 2 additional items that asked them to appraise their own performance and the audience behavior. Both questions were answered on a scale from –10 to +10, with anchors being “very bad” to “very good” and “very negatively” to “very positively,” respectively. We administered the STAI-State again to determine changes in state anxiety following the speech.

### Psychophysiologic Recording and Analysis

Commercial hardware and software were used for measurement and analysis of startle reactivity (Contact Precision Instruments, London, United Kingdom). Continuous EMG recordings were made during VR (and habituation) with two 2-mm tin-cup electrodes placed beneath the left eye with a bandwidth of 30–500 Hz and sampling rate of 1,000 Hz. Electrodes were filled with a 0.5% saline/neutral base electrode gel (BioPac Systems, Inc., Goleta, California). A third electrode was attached to the forearm for electrical grounding. EMG data were rectified and smoothed offline with a 20-millisecond time constant for startle response analysis. Startle response amplitude was determined by subtracting average EMG activity in the 50-millisecond preprobe baseline window from the peak response in the 20- to 100-millisecond window following probe onset.

We divided 26 startle trials during VR into 6 phases and averaged them for analysis. These phases included (1) baseline with curtains closed and no audience sounds (5 startle probes), (2) audience entering with curtains closed (2 probes), (3) audience visible but not attentive (2 probes), (4) audience looking at participants (2 probes), (5) speech delivery (9 probes), and (6) recovery with curtains closed and no audience (6 probes). In consideration of differences in number of startle trials between phases, we performed

**Figure 2. Subjective Distress Ratings<sup>a</sup> for Healthy Participants and Participants With SAD During Anticipation of, Delivery of, and Recovery From the Speech in Virtual Reality (VR)**



<sup>a</sup>Levels of distress rated on a 0–10 scale, with anchors of “not distressed” to “highly distressed.”  
Abbreviation: SAD = social anxiety disorder.

**Table 3. Raw Startle Reactivity (mean ± SD μV) and Standardized Differences (Cohen *d*) Between Healthy Participants and Participants With Social Anxiety Disorder (SAD) Across Each Phase of the Virtual Reality (VR) Public Speaking Procedure**

Phase	Healthy (n = 16)	SAD (n = 16)	Cohen <i>d</i>
Habituation, outside VR	45.29 ± 44.14	64.16 ± 58.11	0.37
Baseline, inside VR	31.29 ± 26.55	53.25 ± 57.42	0.49
Audience enters, curtains closed	26.01 ± 27.06	52.67 ± 61.03	0.56
Audience visible, curtains drawn	19.02 ± 22.02	44.88 ± 58.77	0.58
Audience looks at participant	17.65 ± 17.96	50.47 ± 58.69	0.76
Speech delivery	16.21 ± 15.72	31.04 ± 31.96	0.59
Recovery, curtains closed	16.59 ± 18.62	32.52 ± 34.51	0.57
Overall	24.58 ± 23.19	47.00 ± 46.20	0.61

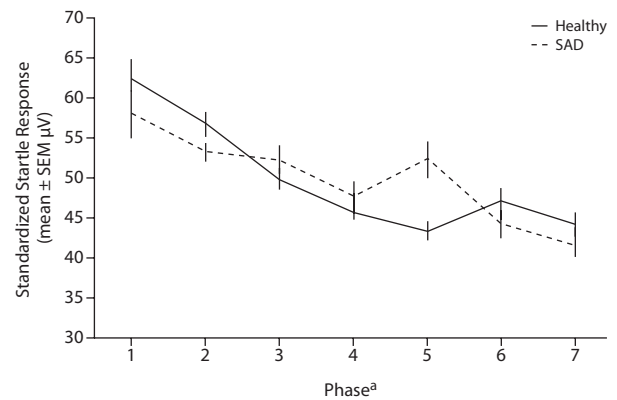
an alternative analysis based on averages of the first 2 startle responses in each phase. Results were very similar between the 2 approaches, and thus we report the outcome of the first one. Distress ratings and startle data, including the habituation phase, were analyzed by 2 (group) by 7 (phase) mixed-factorial analyses of variance (ANOVAs). Preliminary analyses revealed no evidence of any main or interactive effects of gender on these dependent measures.

**RESULTS**

**Self-Reported Distress and State Anxiety**

Individuals with SAD reported greater distress across the entire procedure relative to healthy individuals ( $F_{1,30} = 22.08, P < .001, \eta_p^2 = 0.42$ ) (Figure 2). There was also a main effect of phase, with levels of distress across both groups increasing as the speech approached, peaking during speech delivery, and returning to baseline during postspeech recovery ( $F_{6,180} = 31.58, P < .001, \eta_p^2 = 0.51$ ), but no group-by-phase interaction was observed ( $F < 1$ ). There was a significant group difference in state anxiety measured by the STAI ( $F_{1,30} = 14.59, P < .005, \eta_p^2 = 0.33$ ), but no effect of phase or group-by-phase interaction ( $F$  values  $< 1$ ) (Table 2).

**Figure 3. Standardized Startle Reactivity for Healthy Participants and Participants With SAD at Habituation Outside Virtual Reality and Across Each Phase Inside Virtual Reality (VR)**



<sup>a</sup>Phases were as follows:  
1. Habituation, outside VR  
2. Baseline, inside VR  
3. Audience enters, curtains closed  
4. Audience visible, curtains drawn  
5. Audience looks at participant  
6. Speech performance  
7. Recovery, curtains closed  
Abbreviation: SAD = social anxiety disorder.

**Startle Reactivity**

Raw startle means are presented in Table 3. To determine whether there was a baseline difference in raw startle reactivity between groups, a between-subjects ANOVA on overall startle means was performed and resulted in a statistical trend toward greater baseline startle reactivity in individuals with SAD relative to the healthy individuals ( $F_{1,30} = 3.01, P < .10$ ). Given a potential baseline startle reactivity difference between groups and substantial variance heterogeneity, raw startle means were within-subject standardized by conversion to *T* scores (mean = 50, SD = 10) to explore specificity of potentiated startle in individuals with SAD at different VR phases.

A 2 × 7 mixed-factorial ANOVA revealed a significant interaction between group and phase on standardized startle reactivity ( $F_{6,180} = 2.92, P < .05, \eta_p^2 = 0.09$ ). Bonferroni-corrected post hoc analyses revealed that individuals with SAD showed greater mean standardized startle responses compared to healthy individuals during anticipation when the audience directed its attention to the participant (“audience looks at participant” in Figure 3) ( $F_{1,30} = 12.56, P < .05, \eta_p^2 = 0.30$ ). There were no other group differences at other phases (all  $P$  values  $> .10$ ). Across both groups, there was a main effect of phase ( $F_{6,180} = 18.58, P < .001, \eta_p^2 = 0.38$ ), with a strong linear decrease in standardized startle reactivity across phase ( $F_{1,30}$  linear = 86.42,  $P < .001, \eta_p^2 = 0.74$ ). This linear decrease reflects habituation of startle reactivity.

**Recognition of Virtual Reality Environment Features**

Percentage error rates were computed over the 10-item memory test and for subsets of items directly related to social aspects or nonsocial aspects, 4 versus 6 items, respectively.

There were no group differences in overall mean error rate (SAD group,  $35\% \pm 18\%$ ; healthy group,  $26\% \pm 13\%$ ;  $t_{30} = 1.57$ , NS); similarly, no difference was found in mean error rates for the social and nonsocial subsets (for the social subset: SAD,  $39\% \pm 26\%$ ; healthy,  $25\% \pm 24\%$ ; for the nonsocial subset: SAD,  $33\% \pm 23\%$ ; healthy,  $28\% \pm 14\%$ ). There was a statistical trend toward individuals with SAD appraising their own performances more negatively ( $-3.0 \pm 6.0$ ), on average, than healthy individuals ( $0.8 \pm 6.0$ ) ( $t_{30} = -2.25$ ,  $P < .10$ ). There was no group difference in their appraisals of the emotional behavior of the audience (SAD,  $2.3 \pm 3.8$ ; healthy,  $2.0 \pm 3.0$ ;  $t_{30} = 0.26$ , NS).

## DISCUSSION

We compared startle reactivity and subjective distress among individuals with and without SAD. Participants were exposed to naturalistic public speaking conditions by a VR system with sequential phases of increasing social salience during anticipation, followed by speech delivery and recovery. We observed 2 critical differences between healthy individuals and those with SAD: (1) individuals with SAD reported consistently greater distress and anxiety relative to healthy individuals throughout the procedure and (2) individuals with SAD showed a robust increase in startle reactivity when the virtual audience became silent and members directed their eye gaze toward them.

Individuals with SAD were considerably more distressed than healthy individuals during anticipation outside and inside VR and during and after delivering the speech. Both groups also showed increased distress as speech time approached, peaking during speech delivery. State anxiety was also higher in individuals with SAD before and after the VR procedure, but there were no between-group differences in appraisal of audience behavior. These results suggest that VR is sufficiently realistic to provoke clinically meaningful differences in fear and anxiety. Subjective reports of distress and state anxiety, however, did not illuminate the precise aspects of the VR situation that generated such differences. In this respect, differential patterns of startle reactivity were more informative.

Compared to healthy individuals, individuals with SAD showed a robust increase in startle reactivity when the audience members directed their eyes at the participant. These results suggest that individuals with SAD may be threatened most by perceiving themselves as being the object of others' attention, exhibiting a strong phasic fear response. Moreover, unlike prior findings in SAD, which do not consistently link observations of increased physiologic and subjective-state reports, the current findings demonstrate parallels between the physiologic response to threat in SAD and in animal models of phasic fear. Given prior findings documenting lack of specificity in heightened responses to social cues in SAD, this is an important finding that is in line with previous findings of SAD-related potentiated startle,<sup>22,23,28</sup> including our report<sup>27</sup> showing that startle reactivity during speech anticipation was positively associated with trait

social anxiety (ie, FNE) in healthy individuals. There was also a trend toward significantly greater baseline startle responding in individuals with SAD compared to healthy individuals, which was maintained across the entire experiment (Table 3). Vulnerable individuals may experience sustained anxiety from the outset of any experimental procedure involving confrontation with a personally relevant threat or stressor. In these cases, it is thought that the laboratory acts as a threatening context that gives rise to sustained anxiety.<sup>32,33</sup> This SAD-related increase in baseline startle will need further substantiation in a larger sample.

In line with findings of Panayiotou and Vrana,<sup>24</sup> we found no evidence that self-focus necessarily entails diversion of attentional resources away from the environment. First, individuals with SAD showed heightened startle reactivity and not diminished startle reactivity during the social situation, which runs counter to the conjecture that self-focused attention may limit resources to process the environment including startle probes.<sup>25</sup> Second, individuals with SAD scored as well as their healthy counterparts on a surprise recognition memory questionnaire that required encoding various features of the environment, including specific aspects of the audience. It could be that the questionnaire lacked the necessary sensitivity to reveal subtle impairments in individuals with SAD that have been successfully captured by other researchers.<sup>41</sup> Moreover, there may have been sufficient time to encode details of the environment before the audience directed its attention to the participant, and perhaps before individuals with SAD engaged in extensive self-monitoring. In any event, it does not appear as though individuals with SAD showed outright attentional avoidance of the VR when social-evaluative threat was anticipated and then confronted.

Given the approach we took of simulating a realistic public speaking situation, we did not counterbalance the order of phases, which raises interpretational difficulties for startle reactivity. That is, because the audience always turned its attention to participants immediately before speech delivery, group differences in startle reactivity may be related to the specific behavior of the audience, the imminence of the speech, or a combination of both. Thus, we cannot definitively conclude that direct eye gaze and the potential inferences drawn from this social stimulus by participants (ie, being attended to by others) were the primary driving force of potentiated startle in individuals with SAD. Nevertheless, because both groups were exposed to identical stimuli, this limitation does not affect our conclusions concerning the presence of between-group differences in both subjective and physiologic responding in a realistic social-evaluative context. In addition, because startle reactivity was measured in a social context only, we cannot determine the specificity of potentiated startle reactivity in SAD patients. It is plausible that the social-evaluative nature of the context was the critical factor underlying group differences insofar as fear of negative evaluation was not correlated with startle reactivity in a nonsocial condition (ie, counting in VR without an audience) in our previous study.<sup>27</sup> Finally, we should

acknowledge that we tested a small sample of patients with generalized SAD and that further work will need to extend these findings to a broader sample of SAD patients, including those with circumscribed fears.

Building on previous work, we extended the use of a VR procedure to study how individuals diagnosed with SAD respond psychophysiological during anticipation of, delivery of, and recovery from a speech in an effort to identify biologic markers of the disorder. Social-evaluative contexts are no doubt complex and multifaceted, and to gain insight into what components of these contexts trigger fear and anxiety in socially anxious individuals requires their proper simulation under well-controlled laboratory conditions. We have taken a first step in this direction by measuring startle reactivity in VR and showing that one particularly potent trigger for fear elicitation in individuals with SAD is the recognition of being the focus of others' attention, signaled by direct eye gaze, as speech time arrives. Startle reflex elicitation may prove extremely useful in further studying how fear and anxiety unfold across a social situation in individuals with SAD as it affords an online and relatively unobtrusive method to measure these negative affective states. As a translational tool for measuring fear/anxiety, novel SAD therapies might be developed through work in rodents and nonhuman primates that targets underlying fear-circuit abnormalities implicated in SAD.<sup>42</sup> Work in other areas of translational medicine shows that such attempts to develop such novel therapies benefit greatly when close parallels have been demonstrated between physiologic parameters in humans and other species.<sup>43</sup>

By the same token, we could consider the value of combining startle measurement and VR in clinical settings. Although VR has been demonstrated to be useful in exposure-based treatment protocols for SAD,<sup>44</sup> among other anxiety disorders,<sup>45,46</sup> self-report measures are still the standard way of assessing outcomes. Startle reactivity provides a biologically based measure, free of social desirability influences, that may inform a more complete assessment of treatment outcome. To the extent that startle reactivity indirectly reflects activity of fear and anxiety circuits in the brain, it offers a practical way to quantify the level of fear and anxiety experienced under diagnostically and personally relevant conditions for the patient. Startle measures taken under these anxiety-provoking conditions, before and then intermittently over the course of treatment, could perhaps provide a valuable metric of symptom change. Similar to other psychophysiological variables, however, startle reactivity is influenced by a range of cognitive (eg, attention) and physiologic factors (eg, skin impedance) as well as affective ones. Uncontrolled, these factors will contribute to measurement noise and weaken measurement reliability. Thus, the clinical applicability of startle measurement must await technical refinement and further basic human research. The present results should nevertheless provoke more work with startle reactivity in clinically anxious populations under diagnostically relevant conditions to establish the specificity and distinctness of fear and anxiety among anxiety disorder subtypes in a biologically based manner.

**Author affiliation:** Mood and Anxiety Disorders Program, National Institute of Mental Health, National Institutes of Health, Bethesda, Maryland.

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