

Published in final edited form as:

J Clin Psychiatry. 2011 July ; 72(7): 942–948. doi:10.4088/JCP.09m05731blu.

Becoming the center of attention in social anxiety disorder: Startle reactivity to a virtual audience during speech anticipation

Brian R. Cornwell, Randi Heller, Arter Biggs, Daniel S. Pine, and Christian Grillon

Mood and Anxiety Disorders Program, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, USA

Abstract

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

Method—Sixteen individuals diagnosed with SAD and 16 healthy individuals 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.

Results—SAD individuals reported greater distress and state anxiety than healthy individuals across the entire procedure ($p < .005$). 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. SAD individuals 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.

Social anxiety disorder (SAD) is a common, impairing psychiatric illness with lifetime prevalence between 10 and 15%^{1,2}. It involves persistent fear of situations in which the individual is scrutinized³. We assessed startle reactivity in a virtual reality (VR) context in an effort to demonstrate heightened physiological reactivity in SAD and to potentially isolate specific components of social-evaluative contexts that discriminate among healthy and SAD individuals.

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

Brian R Cornwell Mood and Anxiety Disorders Program National Institute of Mental Health 15K North Drive, MSC 2670 Bethesda, MD 20892 Phone: 301-402-8992 Fax: 301-594-9959 cornwellb@mail.nih.gov.

Financial Disclosures Daniel S. Pine has received income from clinical practice, editorship duties, and teaching through continuing medical education activities. Beyond these instances, the authors declare that, except for income received from our primary employer, no financial support or compensation has been received from any individual or corporate entity over the past three years for research or professional service and there are no personal financial holdings that could be perceived as constituting a potential conflict of interest.

allocation to salient cues⁴. For instance, amygdala reactivity is abnormally high in SAD individuals, particularly for faces conveying fear, anger and contempt⁵⁻⁷, but also emotionally-neutral ones⁸. These findings are complemented by evidence of heightened amygdala activity when SAD patients anticipate giving a speech while undergoing functional imaging scans⁹⁻¹¹.

Surprisingly, psychophysiological studies that have measured autonomic reactivity (e.g., heart rate, electrodermal activity) in SAD individuals present mixed results that are difficult to reconcile with evidence of hyperactivity in fear/ anxiety-related brain structures in SAD. In one comprehensive study, no associations emerged between trait indices of social anxiety and an array of physiological measures collected during speech anticipation¹², corroborating previous studies that failed to find the hypothesized relationships¹³⁻¹⁵. Despite some positive evidence¹⁶⁻¹⁹, this inconsistency raises important questions regarding how social anxiety manifests physiologically and what features of social situations are especially potent to trigger potential SAD-related physiological hyperactivity.

Few studies have explored SAD-related modulation of the startle reflex – a cross-species defensive reflex sensitive to valence-specific emotional arousal. Fear-potentiated startle refers to increased startle reactivity (i.e., larger eyeblinks) under fear/anxiety-provoking conditions²⁰, which, in rodents, is mediated by the amygdala and related structures²¹. Larsen et al.²² reported that SAD individuals 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 situations²³ and in high-trait socially-anxious participants during self focus compared to non-self focus conditions²⁴. However, Blumenthal et al.²⁵ 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, proposed by Clark and Wells²⁶, 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.

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 evaluation²⁷. Participants in this 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; this was not found for startle reactivity during anticipation of a counting task without an audience, nor did we find any relationships between general trait anxiety and startle reactivity. Schultz et al.²⁸ 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 clinical symptom severity²⁹ and may be partly heritable³⁰.

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 period in which the audience directs its attention to the participant and silently awaits speech delivery. We hypothesized that SAD individuals would be particularly fearful of being the focus of others' attention, and would thus show heightened startle reactivity during the latter part of anticipation. This hypothesis is based on evidence that socially anxious individuals show greater amygdala reactivity to faces⁵⁻⁸ and defensive responding (i.e., heart-rate acceleration) to faces with direct eye gaze than low socially anxious individuals³¹. 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^{32–33}.

Method

Participants

Individuals with generalized SAD ($N = 16$) and healthy individuals ($N = 16$) were recruited. Two additional participants, one from each group, were excluded due to equipment 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/P³⁴), administered by one of four staff psychologists with high interrater reliability ($\kappa = .76$). All SAD diagnoses were confirmed through in-person evaluations by a Board-Certified psychiatrist (DSP). Individuals were excluded if they exhibited current major depressive disorder symptoms or suicidal ideation, a history of substance or alcohol abuse or dependence, and 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 psychopharmacological medication within 2 weeks of testing or use of fluoxetine within 6 weeks, (2) current use of illicit drugs or pregnancy per urine tests, (3) or any medical condition determined by physical exam 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 (LSAS³⁵) and Fear of Negative evaluation scale (FNE³⁶) to assess social anxiety symptoms. The Spielberger State-Trait Anxiety Inventory (STAI-State, STAI-Trait³⁷) was administered to measure both general trait and state anxiety. The Self-Statements during Public Speaking Scale (SSPS³⁸), a 10-question Likert-based (0–5) instrument, measured the extent of positive (e.g., “I can handle everything.”) and negative thoughts (e.g., “I’m a loser.”) one has about oneself during public speaking. Depressive and general worry symptoms were measured with the Beck Depression Inventory (BDI³⁹) and Penn-State Worry Questionnaire, respectively (PSWQ⁴⁰). 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.” 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.

Apparatus

The virtual reality (VR) used to simulate the public speaking experience was part of a commercial package (Virtually Better, Inc., <http://www.virtuallybetter.com>). This package contains several audiences exhibiting different behaviors: positive, neutral and hostile. We choose the emotionally-neutral audience. VR was experienced through a lightweight head-mounted 3dVisor (eMagin, Bellevue, WA). 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 nine startle probes were administered via headphones to habituate startle reactivity. Startle probes were 40-msec white noise bursts (105dB, near instantaneous rise/fall times), delivered every 17–23 sec. Participants were then given the topic of the speech (e.g., favorite movie), and prepared for 5 min. 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 on stage, behind a podium with curtains closed. After 4 min, the audience was heard entering the room. The curtains were then drawn, revealing the audience of approximately 30 members talking among themselves. Approximately 30 sec later, the audience turned their heads, applauded, and maintained attention to the participant (Figure 1). Participants then began his/her 3 min speech. Following the speech, the curtains were closed, and participants spent 2 min in recovery before exiting VR. Participants rated their distress four times inside VR: (1) two min 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 17–23s, beginning 2 min after entering VR. Startle probe delivery did not coincide with subjective distress reports.

After VR, participants provided a final distress rating and completed three more questionnaires. One was a 10-item yes-or-no recognition memory questionnaire designed to determine whether they could recollect specific features of the environment (e.g., “Were you standing on a wooden floor?”), as well as specific social aspects of the audience (e.g., “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 and SAD participants. We presented two 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.

Psychophysiological recording and analysis

Commercial hardware and software were used for measurement and analysis of startle reactivity (Contact Precision Instruments, London, UK). Continuous electromyographic (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 1000 Hz. Electrodes were filled with a 0.5% saline/neutral base electrode gel (BioPac Systems, Inc., Goleta, CA). A third electrode was attached to the forearm for electrical grounding. EMG data were rectified and smoothed offline with a 20-msec time constant for startle response analysis. Startle response amplitude was determined by subtracting average EMG activity in the 50 msec preprobe baseline window from the peak response in the 20–100 msec window following probe onset.

We binned 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 (BA, 5 startle probes), (2) audience entering with curtains closed (AE, 2 probes), (3), audience visible but not attentive (AV, 2 probes), (4) audience looking at participants (AL, 2 probes), (5) speech delivery (SP, 9 probes) and (6) recovery with curtains closed and no audience (RE, 6 probes). In consideration of differences in number of startle trials between phases, we performed an alternative analysis based on averages of the first two startle responses in each

phase. Results were very similar between the two 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 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, $F(1, 30) = 22.08, p < .001, \eta_p^2 = .42$ (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 post-speech recovery, $F(6, 180) = 31.58, p < .001, \eta_p^2 = .51$; but no Group by Phase interaction was observed, $F < 1$. There was a significant Group difference in state anxiety measured by the STAI, $F(1, 30) = 14.59, p < .005, \eta_p^2 = .33$, but no effect of Phase nor Group-by-Phase interaction, $F_s < 1$ (Table 2).

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 resulted in a statistical trend toward greater baseline startle reactivity in SAD individuals 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 SAD individuals at differences VR phases.

A 2×7 mixed-factorial ANOVA revealed a significant interaction between Group and Phase on standardized startle reactivity, $F(6, 180) = 2.92, p < .05, \eta_p^2 = .09$. 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), $F(1, 30) = 12.56, p < .05, \eta_p^2 = .30$. There were no other group differences at other phases, all $p_s > .10$. Across both groups, there was a main effect of Phase, $F(6, 180) = 18.58, p < .001, \eta_p^2 = .38$, with a strong linear decrease in standardized startle reactivity across Phase, $F_{linear}(1, 30) = 86.42, p < .001, \eta_p^2 = .74$. This linear decrease reflects habituation of startle reactivity.

Recognition of VR 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 SAD individuals appraising their own performances more negatively (-3.0 ± 6.0), on average, than healthy individuals (0.8 ± 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 ± 3.8 , Healthy, 2.0 ± 3.0), $t(30) = .26, ns$.

Discussion

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

SAD individuals 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 levels as speech time approached, peaking as they delivered the speech, followed by complete recovery afterwards. State anxiety was also higher in SAD individuals before and after the VR procedure, and there was a trend toward SAD individuals giving more negative appraisals of their performance. They did not appraise the audience's behavior more negatively than healthy individuals. 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, SAD individuals showed a robust increase in startle reactivity when the audience members directed their eyes at the participant. These results suggest that SAD individuals may be threatened most by perceiving themselves being the object of others' attention, exhibiting a strong phasic fear response. Given prior findings documenting lack of specificity in heightened responses to social cues in SAD, this is an important finding and line with previous findings of SAD-related potentiated startle in SAD^{22–23,28}, including our report showing that startle reactivity during speech anticipation was positively associated with trait social anxiety (i.e., FNE) in healthy individuals²⁷. There was also a trend toward significantly greater baseline startle responding in SAD individuals 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^{32–33}. This SAD-related increase in baseline startle will need further substantiation in a larger sample.

In line with findings of Panayiotou and Vrana²⁴, we found no evidence that self-focus necessarily entails diversion of attentional resources away from the environment. First, SAD individuals 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 probes²⁵. Second, SAD individuals 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 SAD individuals that have been successfully captured by other researchers⁴¹. 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 SAD individuals engaged in extensive self-monitoring. In any event, it does not appear as though SAD individuals 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 (i.e., being attended to by others) was the primary driving force of potentiated startle in SAD individuals. This limitation notwithstanding, it is promising that startle reactivity differentiates SAD individuals from healthy individuals 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, though, given that in our previous study fear of negative evaluation was not correlated with startle reactivity in a non-social condition (i.e., counting in VR without an audience). 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, delivery and recovery of a speech in an effort to identify biological 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 SAD individuals 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 SAD individuals as it affords an online and relatively unobtrusive method to measure these negative affective states.

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 SAD⁴², among other anxiety disorders⁴³⁻⁴⁴, self-report measures are still the standard way of assessing outcomes. Startle reactivity provides a biologically-based measure, free of social desirability influences, which 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 (e.g., attention) and physiological factors (e.g., 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.

Acknowledgments

This research was supported by the Intramural Research Program of the National Institute of Mental Health, NIH.

References

1. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005; 62:593–602. [PubMed: 15939837]
2. Lochner C, Mogotsi M, du Toit PL, Kaminer D, Niehaus DJ, Stein DJ. Quality of life in anxiety disorders: A comparison of obsessive-compulsive disorder, social anxiety disorder, and panic disorder. *Psychopathology*. 2003; 36:255–262. [PubMed: 14571055]
3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. American Psychiatric Association; Washington, DC: 1994. DSM-IV
4. Etkin A, Wager TD. Functional neuroimaging of anxiety: A meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. *Am J Psychiatry*. 2007; 164:1476–1488. [PubMed: 17898336]
5. Blair K, Shaywitz J, Smith BW, et al. Response to emotional expressions in generalized social phobia and generalized anxiety disorder: Evidence for separate disorders. *Am J Psychiatry*. 2008; 165:1193–1202. [PubMed: 18483136]
6. Phan KL, Fitzgerald DA, Nathan PJ, Tancer ME. Association between amygdala hyperactivity to harsh faces and severity of social anxiety in generalized social phobia. *Biol Psychiatry*. 2006; 59:424–429. [PubMed: 16256956]
7. Stein MB, Goldin PR, Sareen J, Zorilla LT, Brown GG. Increased amygdala activation to angry and contemptuous faces in generalized social phobia. *Arch Gen Psychiatry*. 2002; 59:1027–1034. [PubMed: 12418936]
8. Cooney RE, Atlas LY, Joormann J, Eugene F, Gotlib IH. Amygdala activation in the processing of neutral faces in social anxiety disorder: Is neutral really neutral? *Psychiatry Res: Neuroimaging*. 2006; 148(1):55–59.
9. Lorberbaum JP, Kose S, Johnson MR, Arana GW, Sullivan LK, Hamner MB, Ballenger JC, Lydiard RB, Brodrick PS, Bohning DE, George MS. Neural correlates of speech anticipatory anxiety in generalized social phobia. *Neuroreport*. 2004; 15(18):2701–2705. [PubMed: 15597038]
10. Tillfors M, Furmark T, Marteinsdottir I, Fischer H, Pissiota A, Langstrom B, Fredrikson M. Cerebral blood flow in subjects with social phobia during stressful speaking tasks: a PET study. *Am J Psychiatry*. 2001; 158:1220–1226. [PubMed: 11481154]
11. Tillfors M, Furmark T, Marteinsdottir I, Fredrikson M. Cerebral blood flow during anticipation of public speaking in social phobia: A PET study. *Biol Psychiatry*. 2002; 52:1113–1119. [PubMed: 12460694]
12. Mauss IB, Wilhelm FH, Gross JJ. Is there less to social anxiety than meets the eye? Emotion experience, expression, and bodily responding. *Cogn Emot*. 2004; 18(5):631–662.
13. Heimberg RG, Hope DA, Dodge CS, Becker RE. DSM-III-R subtypes of social phobia. Comparison of generalized social phobics and public speaking phobics. *J Nerv Ment Dis*. 1990; 178(3):172–179. [PubMed: 2307969]
14. Hofmann SG, Newman MG, Ehlers A, Roth WT. Psychophysiological differences between subgroups of social phobia. *J Abnorm Psychol*. 1995; 104(1):224–231. [PubMed: 7897046]
15. Puigcerver A, Martinez-Selva JM, Garcia-Sanchez FA, Gomez-Amor J. Individual differences in psychophysiological and subjective correlates of speech anxiety. *J Psychophysiol*. 1989; 3:75–81. 1989.
16. Davidson RJ, Marshall JR, Tomarken AJ, Henriques JB. While a phobic waits: Regional brain electrical and autonomic activity in social phobias during anticipation of public speaking. *Biol Psychiatry*. 2000; 47:85–95. [PubMed: 10664824]
17. Feldman PJC, Cohen SC, Hamrick NC, Lepore SJC. Psychological stress, appraisal, emotion and cardiovascular response in a public speaking task. *Psychol Health*. 2004; 19(3):353–368.

18. Gonzales-Bono E, Moya-Albiol L, Salvador A, Carrillo E, Ricarte J, Gomez-Amor J. Anticipatory autonomic response to a public speaking task in women: The role of trait anxiety. *Biol Psychology*. 2002; 60:37–49.
19. Levin AP, Saoud JB, Strauman T, Gorman JM, Fyer AJ, Crawford R, Liebowitz MR. Responses of 'generalized' and 'discrete' social phobics during public speaking. *J Anxiety Disord*. 1993; 7:207–221.
20. Grillon C. Startle reactivity and anxiety disorders: Aversive conditioning, context, and neurobiology. *Biol Psychiatry*. 2002; 52:958–975. [PubMed: 12437937]
21. Davis M. Are different parts of the extended amygdala involved in fear versus anxiety? *Biol Psychiatry*. 1998; 44(12):1239–1247. [PubMed: 9861467]
22. Larsen DK, Norton GR, Walker JR, Stein MB. Analysis of startle responses in patients with panic disorder and social phobia. *Cogn Behav Ther*. 2002; 31(4):156–169.
23. McTeague LM, Lang PJ, Laplante M, Cuthbert BN, Strauss CC, Bradley MM. Fearful imagery in social phobia: Generalization, comorbidity, and physiological reactivity. *Biol Psychiatry*. 2009; 65:374–382. [PubMed: 18996510]
24. Panayiotou G, Vrana SR. Effects of self-focused attention on the startle reflex, heart rate, and memory performance among socially anxious and nonanxious individuals. *Psychophysiol*. 1998; 35:328–336.
25. Blumenthal TD, Chapman JG, Muse KB. Effects of social anxiety, attention, and extraversion on the acoustic startle eyeblink response. *Pers Individual Differences*. 1995; 19(6):797–807.
26. Clark, DM.; Wells, A. A cognitive model of social phobia. In: Heimberg, R.; Liebowitz, M.; Hope, DA.; Schneier, FR., editors. *Social phobia: Diagnosis, assessment, and treatment*. Guilford Press; New York: 1995. p. 69-83.
27. Cornwell BR, Johnson L, Berardi L, Grillon C. Anticipation of public speaking in virtual reality reveals a relationship between trait social anxiety and startle reactivity. *Biol Psychiatry*. 2006; 59:664–666. [PubMed: 16325155]
28. Schultz SM, Alpers GW, Hofmann SG. Negative self-focused cognitions mediate the effect of trait social anxiety on state anxiety. *Behav Res Ther*. 2008; 46:438–449. [PubMed: 18321469]
29. Stein MB, Chavira DA. Subtypes of social phobia and comorbidity with depression and other anxiety disorders. *J Affect Disord*. 1998; 50:S11–S16. [PubMed: 9851573]
30. Stein MB, Jang KL, Livesley WJ. Heritability of social anxiety-related concerns and personality characteristics: A twin study. *J Nerv Ment Dis*. 2002; 190(4):219–224. [PubMed: 11960082]
31. Wieser MJ, Pauli P, Alpers GW, Muhlberger A. Is eye to eye contact really threatening and avoided in social anxiety? An eye-tracking and psychophysiology study. *J Anxiety Disord*. 2009; 23(1):93–103. [PubMed: 18534814]
32. Grillon C. Models and mechanisms of anxiety: evidence from startle studies. *Psychopharmacol*. 2008; 199(3):421–437.
33. Grillon C, Morgan CA, Davis M, Southwick SM. Effects of experimental context and explicit threat cues on acoustic startle in Vietnam veterans with posttraumatic stress disorder. *Biol Psychiatry*. 1998; 44:1027–1036. [PubMed: 9821567]
34. First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition (SCID-I/P)*. New York State Psychiatric Institute, Biometrics Research; New York: 2002.
35. Liebowitz MR. Social phobia. *Mod Probl Pharmacopsychiatry*. 1987; 22:141–173. [PubMed: 2885745]
36. Watson D, Friend R. Measurement of social-evaluative anxiety. *J Consult Clin Psychol*. 1969; 33(4):448–457. [PubMed: 5810590]
37. Spielberger, CD.; Gorsuch, RC.; Lushene, RE. *Manual for the State Trait Anxiety Inventory*. Consulting Psychologists Press; Palo Alto, CA: 1970.
38. Hofmann SG, DiBartolo PM. An instrument to assess self-statements during public speaking: Scale development and preliminary psychometric properties. *Behav Ther*. 2000; 31(3):499–515. [PubMed: 16763666]
39. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961; 4:561–571. [PubMed: 13688369]

40. Meyer TJ, Miller ML, Metzger RL, Borkovec TD. Development and validation of the Penn State Worry Questionnaire. *Behav Res Ther.* 1990; 28:487–495. [PubMed: 2076086]
41. Mellings TMB, Alden LE. Cognitive processes in social anxiety: The effects of self-focus, rumination and anticipatory processing. *Behav Res Ther.* 2000; 38:243–257. [PubMed: 10665158]
42. Anderson PL, Zimand E, Hodges LF, Rothbaum BO. Cognitive behavioral therapy for public-speaking anxiety using virtual reality for exposure. *Depression Anxiety.* 2005; 22:156–158.
43. Ressler KJ, Rothbaum BO, Tannenbaum L, Anderson P, Graap K, Zimand E, Hodges L, Davis M. Cognitive enhancers as adjuncts to psychotherapy. *Arch Gen Psychiatry.* 2004; 61:1136–1144. [PubMed: 15520361]
44. Rothbaum BO, Hodges L, Ready D, Graap K, Alarcon R. Virtual reality exposure therapy for Vietnam veterans with posttraumatic stress disorder. *J Clin Psychiatry.* 2001; 62:617–622. [PubMed: 11561934]



Figure 1. Static view of virtual reality depicting the silent, attentive audience from the perspective of the participants.

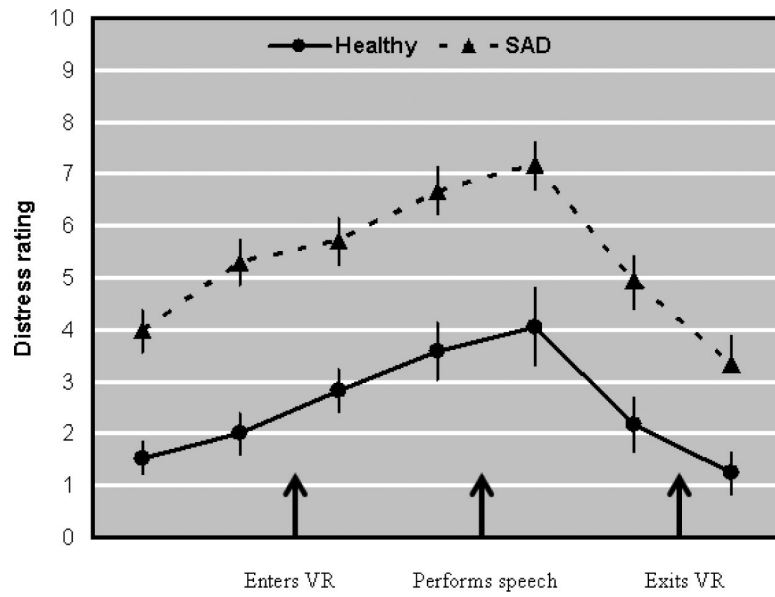


Figure 2. Mean (\pm SEM) subjective distress ratings for healthy and SAD participants during anticipation, delivery and recovery from the speech in virtual reality.

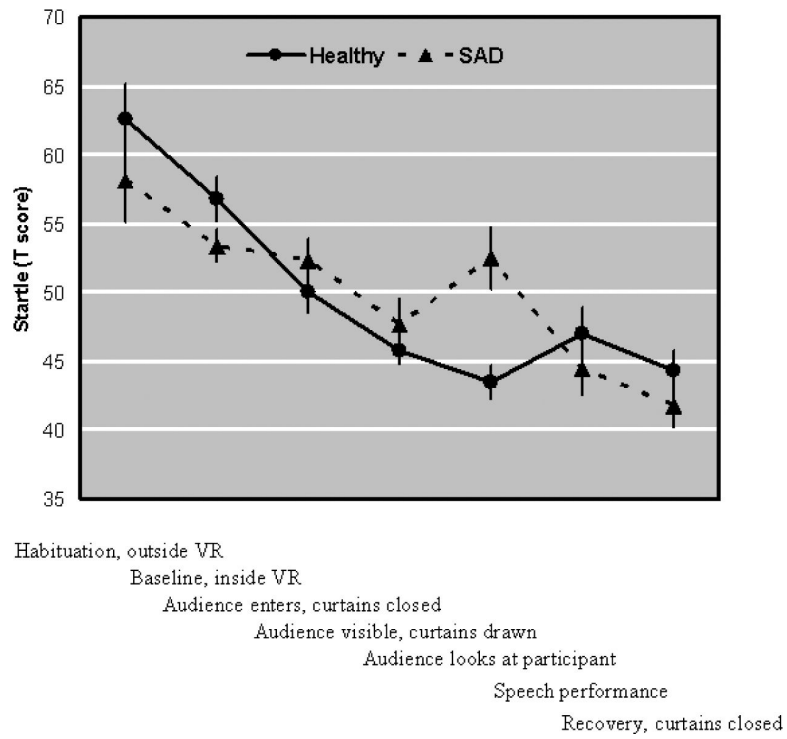


Figure 3. Mean (\pm SEM) standardized startle reactivity for healthy and SAD participants at habituation outside virtual reality and across each phase inside virtual reality.