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Niacin biological challenge: A paradigm to evaluate social concerns

Nicholas P. Allan[a,*], Kevin G. Saulnier[a], Danielle Cooper[a], Mary E. Oglesby[b], Norman B. Schmidt[b]

[a] Department of Psychology, Ohio University, Athens, OH, 45701, USA
[b] Department of Psychology, Florida State University, Tallahassee, FL, 32306, USA

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ABSTRACT

Background and objectives: Anxiety sensitivity (AS) social concerns, the fear of observable anxiety symptoms is posited as a risk factor for social anxiety by increasing fear reactivity in social situations when observable anxiety symptoms are present. Experimental evaluation of AS social concerns is limited. The current study utilized several manipulations designed to be relevant to AS social concerns or fear of negative evaluation (FNE), a distinct social anxiety risk factor. The effects of these manipulations on fear reactivity to a speech were examined.

Methods: Participants (N = 124 students; M *age* = 19.44, SD = 2.45; 64.5% female) were randomized to one of four conditions in a 2 (100 mg niacin vs 100 mg sugar pill) X 2 (instructional set) design. For the instructional set manipulation, participants were told their speech performance would be evaluated by a judge based on their performance (i.e., FNE-relevant) or their observable anxiety symptoms (i.e., AS social concerns-relevant).

Results: There was a main effect for vitamin condition with participants in the niacin condition reporting higher panic symptoms post-speech relative to those in the placebo condition. There was no main effect for speech instructions. As hypothesized, these effects were qualified by an interaction indicating that AS social concerns significantly predicted panic symptoms for those receiving niacin.

Limitations: Limitations include the reliance on self-reports of outcome variables and the use of an undergraduate student sample.

Conclusions: These findings highlight a distinct role of AS social concerns in fear responding to socially evaluative situations in the context of physically observable arousal.

1. Introduction

Social anxiety disorder (SAD) is characterized by maladaptive distress, anxiety, and avoidance in social situations (American Psychiatric Association, 2013; Olatunji & Wolitzky-Taylor, 2009). SAD is one of the most prevalent anxiety disorders (Kessler, Petukhova, Sampson, Zaslavsky, & Wittchen, 2012) and is associated with significant impairment in occupational, social, and familial domains (Merikangas, Avenevoli, Acharyya, Zhang, & Angst, 2002; Olatunji, Cisler, & Tolin, 2007). Further, untreated social anxiety tends to follow a chronic and increasingly debilitating trajectory (Hayward et al., 2008). Given the prevalence and impact of SAD, identifying factors contributing to the etiology of this disorder is an important avenue for research.

1.1. Anxiety sensitivity social concerns and theoretical models of social anxiety

Cognitive theories of SAD posit that people with elevated social anxiety form a mental representation of the self in social situations (Clark & Wells, 1995; Heimberg, Brozovich, & Rapee, 2010; Rapee & Heimberg, 1997). This “loosely based amalgam” (Rapee & Heimberg, 1997, p. 742) consists of information obtained from long-term memory about prior social experiences, internal cues, including physical symptoms of anxiety, and external cues, including audience feedback. Biased monitoring of *internal and external* threat cues serves to update the amalgam over time. Much of the research on social anxiety has focused on delineating the role of a cognitive bias toward external threat cues, fear of negative evaluation (FNE), in the development and maintenance of social anxiety (e.g., Collins, Westra, Dozois, & Stewart, 2005; Heinrichs & Hofmann, 2001). In fact, the most prominent treatments for SAD focus on remediating maladaptive cognitive biases regarding negative interpretations of external cues (Beck, Emery, & Greenberg, 1985; Heimberg & Becker, 2002). However, these treatments tend to neglect internal threat cues, which may account for limitations in efficacy (e.g., Hofmann, 2007).

Reiss’ (1991; 1997) expectancy theory is a general theory of anxiety,

* Corresponding author.
E-mail address: allan@ohio.edu (N.P. Allan).

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for which FNE, and another risk factor, anxiety sensitivity (AS), are considered fundamental fears for anxiety psychopathology. AS is the fear that anxious arousal can have harmful consequences; Thus, AS can serve as an amplifier of responses to stress and anxiety (Reiss, 1991). More specifically, this construct is considered a trait-like cognitive vulnerability that serves to compound preexisting anxiety levels such that individuals with elevated AS might misinterpret sensations of anxiety as being harmful, thus resulting in a greater experience of anxiety (Olatunji & Wolitzky-Taylor, 2009). AS is a hierarchical construct with three lower-order dimensions (Allan, Albanese, Short, Raines, & Schmidt, 2015a; Taylor et al., 2007); fear of physiological sensations of anxiety (AS physical concerns), fear of mental incapacitation or cognitive dyscontrol due to anxiety (AS cognitive concerns), and fear of publicly observable manifestations of anxiety (AS social concerns). These lower-order dimensions are differentially related to particular anxiety disorders (Kemper, Lutz, Bahr, Ruddel, & Hock, 2011; Raines, Short, Allan, Oglesby, & Schmidt, 2015; Zinbarg, Barlow, & Brown, 1997) with AS social concerns most closely related to social anxiety disorder (SAD; Allan, Capron, Raines, & Schmidt, 2014a; Olatunji & Wolitzky-Taylor, 2009). Although expectancy theory posits a unique role for AS social concerns in relation to social anxiety very little research has been conducted to explore this position.

According to expectancy theory, AS social concerns should operate by exacerbating physiological arousal (i.e., an internal cue) in the context of a social setting, resulting in a maladaptive feedback loop. For example, an individual high in AS social concerns who noticed blushing, sweating, or an elevated heart rate would be more likely to believe these symptoms were harmful, causing an increase in these and other anxiety symptoms. Building on this idea that AS social concerns is a central and distinct risk factor for SAD, this construct should predict fear reactivity in response to internal physiological cues that are potentially observable by others in social evaluative situations. Further, although AS social concerns may capture fear of internal cues due to the likelihood of these cues being observed by others, the impact of AS social concerns should be distinct from the impact of FNE in social evaluative situations given that FNE is focused on the possibility of external evaluation more generally and AS social concerns captures a more circumscribed fear of evaluation as well as a more general fear of physically observable anxiety sensations.

Several studies have demonstrated that AS social concerns is related to social anxiety and that this relation is distinct from the relation between FNE and social anxiety (e.g., Allan et al., 2014a, b, 2017). However, nearly all of this research has been cross-sectional and non-experimental, limiting the ability to make causal implications. Further, studies have typically measured social anxiety using retrospective recall of symptoms. This approach does not address how AS social concerns and FNE impact anxiety reported directly after a socially evaluative situation. However, there is some experimental evidence that individuals high in social anxiety exhibit a greater bias toward internal cues than they do toward external threat cues (e.g., Ashbaugh & Radomsky, 2011; Mansell, Clark, & Ehlers, 2003). For example, Mansell et al. (2003) found that high speech anxious people, compared to low speech anxious people, showed a bias toward an internal stimulus (a pulse on the finger meant to reflect significant physiological changes) during social-evaluative threat conditions. To better understand the impact of AS social concerns and FNE in social anxiety, additional experimental approaches in the context of social evaluation, for which internal cues can be manipulated, are needed.

1.2. Biological challenge paradigms as experimental manipulations of anxiety

Biological challenge paradigms offer one approach for studying the manipulation of internal physiological anxiety. These paradigms involve eliciting and evaluating fear reactivity, or elevated anxious sensations (often measured as changes in subjective units of distress [SUDs] and/or increased panic-like symptoms) in response to anxiety-inducing agents. Most prior work on AS has focused on the global construct or the AS physical concerns facet (e.g., Brown, Smits, Powers, & Telch, 2003; Schmidt, 1999; Schmidt & Mallott, 2006; Zinbarg, Brown, Barlow, & Rapee, 2001). Elevated fear reactivity is typically found in participants undergoing these challenges, such as inhaling high concentrations of CO_2, and the AS physical concerns lower-order dimension is uniquely related with fear reactivity (Schmidt, 1999; Zinbarg et al., 2001).

Other biological challenge manipulations have been developed focusing on AS cognitive concerns. These challenge tasks are designed to elicit sensations more relevant to AS cognitive concerns, such as depersonalization and derealization (Capron, Norr, Albanese, & Schmidt, 2017; Leonard, Telch, & Owen, 2000; Lickel, Nelson, Lickel, & Deacon, 2008; Petkova & Ehrsson, 2008). For example, Capron et al. (2017) used a perceptual illusion paradigm utilizing a head-mounted display to induce feelings of depersonalization and derealization. Participants with elevated AS cognitive concerns showed greater fear reactivity to this challenge compared to those with lower AS cognitive concerns. Together, these studies suggest the biological challenge is a useful framework for manipulating internal anxiety sensations relevant to the lower-order AS dimensions.

Few studies have attempted to target internal anxiety sensations relevant to AS social concerns in socially evaluative situations. Studies such as these are needed because theories of social anxiety posit that internal and external cues, *in socially evaluative situations*, exacerbate fear reactivity. Dixon, Kemp, Farrell, Blakey, and Deacon (2015) conducted the only study we are aware of that expressly manipulated internal anxiety cues with the goal of examining AS social concerns in the context of social evaluation. In this study, 58 college students (M age = 20.35 years, SD = 4.34) endorsing "much" or "very much" fear of blushing, trembling, or sweating first completed a series of interoceptive exposure (IE) exercises as well as a control task in a random order. IE exercises included participants placing their head between their legs, holding weights, drinking hot liquids, doing push-ups, placing a heat pack across their cheeks, drinking hot sauce, jogging in place, and hyperventilating. The control task involved breathing at a slow, comfortable pace for 1 min. Participants then identified the IE task that elicited anxiety symptoms similar to the symptoms they would fear in social situations. Participants were then randomized to one of two conditions: 1) completing a 3-min speech or 2) completing the chosen IE exercise followed by the speech. In contrast to their hypothesis, Dixon et al. did not find differences in self-reported fear between these two conditions. There are several possibilities for these null findings including the completion of so many challenge exercises might have habituated participants to their anxiety symptoms, as well as the fact that participants were able to select the challenge task to be completed prior to the speech, which may have led to the selection of less anxiogenic interoceptive exercises.

Blushing is one of the central fears of AS social concerns (Taylor et al., 2007) such that a viable manipulation for AS social concerns could be one that induces sensations similar to blushing, such as facial flushing. A dose of niacin (i.e., vitamin B_3 or nicotinic acid; an over-the-counter vitamin) will typically induce facial flushing and thereby might prove an effective manipulation in the context of social evaluation. Blushing is somewhat distinct from flushing in that blushing occurs in response to social evaluation (Leary, Britt, Cutlip II, W. D., & Templeton, 1992). However, niacin-induced flushing can mimic or exacerbate actual and perceived blushing (Drummond et al., 2007; Drummond, Minosora, Little, & Keay, 2013). In prior studies, participants given niacin reported enhanced facial flushing and demonstrated greater physiologically-measured flushing compared to participants given a placebo pill (Drummond & Lazaroo, 2012b). This effect was amplified when participants completed an embarrassing task (singing a children's song; Drummond & Lazaroo, 2012a). These findings suggest that experimentally-induced flushing, especially in the presence of

social evaluation, could serve as a potent experimental manipulation to test the role of AS social concerns in social anxiety.

To date, most studies examining the fear of blushing have done so in relation to FNE (Bögels, 2006; Drummond et al., 2013; Drummond & Lazaroo, 2012a). FNE has been posited to act as a modulator of facial flushing, with higher FNE scores relating to increased flushing (Dijk, de Jong, & Peters, 2009). For example, Drummond and Lazaroo (2012b) reported enhanced facial flushing in participants with higher FNE when they consumed niacin and had to sing a children's song to induce embarrassment. Although FNE enhances blushing responses to socially stressful tasks, no study has examined whether AS social concerns might better explain fear reactivity to blushing. As niacin induces an observable physiological reaction similar to a symptom of anxiety (blushing), it is anticipated that for participants consuming niacin, fear reactivity will be uniquely associated with AS social concerns.

1.3. The current study

The current study was designed to experimentally evaluate the role of AS social concerns as a unique risk factor for increased fear response to niacin-induced flushing during a social evaluative task. In the current study, niacin was used as a biological agent to induce facial flushing. In addition, pre-speech instructions were manipulated to focus participants on their flushing symptoms versus external judgment to make the threat more specific to AS social concerns versus FNE. The primary aim of the current study was to examine fear reactivity in a 2 × 2 design, involving vitamin condition (100 mg niacin vs. 100 mg placebo) and speech instructions (AS social concerns relevant vs. FNE relevant). Based on prior studies indicating increased fear reactivity for people who consume niacin prior to engaging in a socially stressful task (e.g., Drummond & Lazaroo, 2012a) and expectations that focusing people's attention on their anxiety sensations would evoke increased fear reactivity (e.g., Dickerson & Kemeny, 2004), significant main effects of both vitamin condition and speech instructions were expected. Further, a significant interaction was expected such that the highest levels of fear reactivity would be found in participants receiving niacin and receiving the AS social concerns speech instructions. A second aim of the current study was to determine whether AS social concerns uniquely predicted fear reactivity in the context of the study manipulations and relevant covariates. It was hypothesized that AS social concerns, controlling for FNE, the other AS dimensions, social anxiety symptoms, age, and gender would predict fear reactivity, in the niacin condition but not in the placebo condition (i.e., a significant vitamin condition by AS social concerns interaction).

2. Methods

2.1. Participants

Study participants included 124 undergraduate students (*M age* = 19.44, *SD* = 2.45; 64.5% female) recruited from a large southern university. Most of the sample identified as White (75.2%), followed by Black (16%), Asian (1.6%), and American Indian (0.8%), with 6.4% declining to respond. All participants were 18 years of age or older. All participants were given course credit for participation. The Internal Review Board at Florida State University approved the study (Human Subjects Committee # 2017.22666).

2.2. Procedure

Upon arrival to the lab, participants provided informed consent. During the informed consent process, all participants were informed that they may consume a vitamin B_3 supplement and that this supplement could cause slight facial flushing. Participants were then randomly assigned to one of four conditions in a 2 × 2 design (see Fig. 1). The research assistant administering the protocol and all participants were blind to condition. Participants were randomly assigned to receive 100 mg niacin or 100 mg sugar pill placebo in identical gelatin capsules. Participants were also randomly assigned to receive instructions prior to their speech relevant to AS social concerns or FNE. For the AS social concerns instructions, participants were told “You will be rated on how anxious you appear. Criteria include trembling, sweating, blushing, other observable signs of anxiety.” For the FNE instructions, participants were told “You will be rated on the impression you make on the judge. Criteria include speech content, impression made on the judge, and opinion of you as a speaker.” Once participants consumed the niacin, they completed a battery of self-report measures assessing various anxiety-related variables in a private experiment room. The battery of questionnaires took approximately 20–30 min to complete, allowing enough time for the niacin to be absorbed. Following completion of the battery of self-report measures, participants were read the speech instructions, which included a reminder that their speech would be recorded and of the criteria they would be judged on. Participants were recorded using an I-Pad mounted on a tripod. Participants then gave a 3-min speech selecting between one of three controversial topics (abortion, health care reform, death penalty). If participants were silent for more than 10s, they were prompted to continue their speech until their time was up. Following completion of the speech, participants completed a brief battery of outcome measures and were debriefed.

2.3. Measures

2.3.1. Demographics and medical screening questionnaire

A questionnaire containing demographic information was created for this study. In addition, questions pertaining to kidney disorder, diabetes, liver disease, or peptic ulcer disease were included as taking niacin with these conditions is contraindicated.

2.3.2. Acute Panic Inventory (API)

The API is a 24-item self-report questionnaire designed to measure symptoms of arousal associated with panic (Liebowitz et al., 1984). Participants were asked to rate the severity of each symptom on a Likert-type scale ranging from 0 (*absent*) to 3 (*severe*). Higher API total scores represent increased panic-related symptoms. In addition to a total score, the API includes a SUDS rating of current fear/anxiety (0 = *no* anxiety; 100 = *extreme* anxiety). The API is a widely used measure of panic symptoms and has been used extensively in fear provocation studies (Fyer et al., 1987; Schmidt & Zvolensky, 2007). In the current study, the API total score and SUDs ratings were collected before (pre-API) and after (post-API) the experimental manipulation to index fear reactivity. The pre-API panic symptoms (α = 0.75) and post-API panic symptoms (α = 0.89) demonstrated adequate internal consistency in the present investigation. These variables were operationalized as measures of fear reactivity.

2.3.3. Anxiety Sensitivity Index-3 (ASI-3)

The ASI-3 (Taylor et al., 2007), derived from the original ASI (Reiss, Peterson, Gursky, & McNally, 1986), is an 18-item self-report questionnaire designed to measure the feared physical, cognitive, and social consequences associated with anxious arousal. Participants were asked to rate how much they agreed with each item on a 5-point Likert-type scale ranging from 0 (*very little*) to 4 (*very much*). The ASI-3 yields three subscale scores representing physical concerns, cognitive concerns, and social concerns. Higher scores represent a greater fear of anxiety-related symptoms. In the current study, the ASI-3 was administered at baseline (i.e., before experimental manipulation) and subdimension scores (physical α = .83, cognitive α = 0.90, and social α = 0.74) demonstrated adequate internal consistency.

2.3.4. Brief Fear of Negative Evaluation-II (BFNE-II)

The BFNE-II is a 12-item self-report measure used to index an individual's fear of being negatively evaluated by others (Carleton,

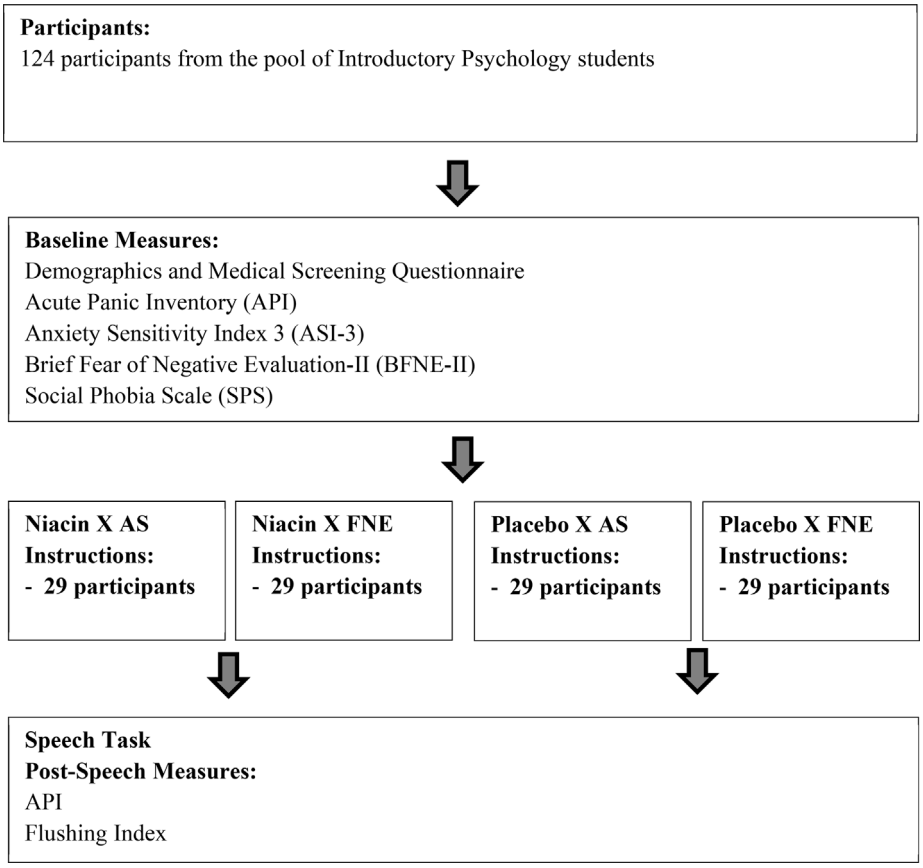

Fig. 1. Study flow chart.

Collimore, & Asmundson, 2007). Participants were asked to select the answer choice that best corresponds to how much they agree with each item on scale ranging from 1 (*not characteristic of me*) to 5 (*entirely characteristic of me*). In the current study, the BFNE-II was administered at baseline and demonstrated adequate internal consistency ($\alpha = 0.71$).

2.3.5. Social Phobia Scale (SPS)

The SPS is a 20-item self-report measure used to index social anxiety symptoms (Mattick & Clarke, 1998). Participants were asked to select the answer choice that best corresponds to how much they agree with each item on scale ranging from 0 (*not characteristic of me*) to 4 (*extremely characteristic of me*). In the current study, the SPS was administered at baseline and demonstrated excellent internal consistency ($\alpha = 0.92$).

2.3.6. Flushing index

A flushing reactivity index was created for the study. Participants were asked to rate their level of current flushing, itchiness, and facial heat as mild, moderate, or severe. This index was given following the speech task. For data analysis and interpretation, responses were dichotomized as "yes" (39.2%) and "no" (60.8%), depending on whether participants endorsed at least one of these sensations.

3. Results

3.1. Preliminary analyses

Descriptive statistics, by condition, for all baseline variables and for the post-experiment variables are provided in Table 1 and correlations between all study variables are provided in Table 2. Comparisons across groups revealed a significant overall difference in baseline SUDs ratings, $F(3, 120) = 2.81$, $p = .04$. However, this difference was minimal as no Benjamini-Hochberg corrected differences between conditions emerged. There were no other significant baseline differences. Significant skew, as determined by skew divided by standard error > 1.96 (Tabachnick & Fidell, 2007) was detected for most baseline and post-intervention variables. Square root transformations resulted in non-significant skew values for most variables, except for baseline AS cognitive concerns and API difference scores. Logarithmic transformations were conducted for these variables, resulting in skew values approaching nonsignificance. All models were conducted with and without the transformed variables and no differences in significance were found. Therefore, all analyses were reported using the untransformed variables. There were eight participants missing data on the ASI-3 at baseline (this measure was omitted due to a clerical error). There were no differences in other baseline variables for these participants as compared to participants who received the ASI-3 at baseline. However, given that the primary analyses included ASI-3 scores as predictors, all analyses were conducted on the 116 people who received the ASI-3. Examination of Mahalanobis Distance revealed one outlier. However, exclusion of this participant did not substantively alter the results. Therefore, this person was included in the analyses.

In prior studies including the SPS, a clinical cutoff ≥ 24, reflecting a score 1 *SD* above the community mean, has been used (Heimberg, Mueller, Holt, Hope, & Liebowitz, 1992). The mean of this sample ($M = 13.75$, $SD = 12.46$) was thus more in line with a community sample on levels of social anxiety. However, approximately 23 participants had SPS scores above the clinical cutoff (6 in Niacin + AS condition, 8 in Niacin + Evaluation, 3 in Placebo + AS, and 6 in Placebo + Evaluation).

3.2. Manipulation check

To ensure that niacin caused greater rates of flushing than did the

Table 1
Descriptive Statistics for Baseline Variables, Demographics, and Outcomes by Condition.

	Niacin + AS Instructions		Niacin + Evaluation Instructions		Placebo + AS Instructions		Placebo + Evaluation Instructions		*F*
	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*	
ASI-3 Social	7.48	4.82	6.90	5.35	5.69	3.37	5.68	4.44	1.13
ASI-3 Physical	4.48	4.84	4.53	4.92	3.48	5.03	2.93	2.67	.88
ASI-3 Cognitive	3.21	4.20	2.83	5.17	2.28	3.32	1.79	2.94	.69
BFNE	29.00	8.14	26.84	6.81	26.38	6.48	28.93	5.82	1.19
API Panic	3.87	4.33	4.65	4.61	3.38	2.73	4.07	3.91	.67
API SUDS	5.16	11.51	6.13	9.89	14.14	18.42	11.72	15.60	2.81*
SPS Anxiety	15.24	14.77	15.07	13.15	11.10	9.42	14.71	12.47	.52
Age	19.23	1.26	19.68	4.26	19.41	1.57	19.34	1.59	.18
Post API Panic	7.29	8.61	6.77	8.83	3.14	3.23	3.21	3.82	3.31*
Post API SUDS	33.87	25.26	28.06	23.72	34.83	26.13	40.00	23.60	1.18
χ^2 (3 *df*)									
% Male	32.26%		25.81%		51.72%		31.03%		.34

Note. ASI-3 = Anxiety Sensitivity Index-3. BFNE = Brief Fear of Negative Evaluation. API = Acute Panic Inventory. SUDS = Subjective Units of Distress. SPS = Social Phobia Scale.
*$p < .05$.

Table 2
Bivariate Correlations between Baseline Variables and Post-Experiment Distress and Panic Response.

Variables	1	2	3	4	5	6	7	8
1. BL API SUDS	–							
2. BL API Panic	.48***	–						
3. BL SPS Anxiety	.19*	.21*	–					
4. BL ASI-3 Social	.03	.19*	.56***	–				
5. BL ASI-3 Physical	.22*	.24**	.37***	.42***	–			
6. BL ASI-3 Cognitive	.20*	.32***	.47***	.49***	.62***	–		
7. BL BFNE	.19*	.21*	.60***	.47***	.33***	.35***	–	
8. Post API SUDS	.42***	.32***	.44***	.23*	.13	.21*	.29***	–
9. Post API Panic	.25**	.57***	.29***	.33***	.20*	.24**	.14	.43***

Note. BL = Baseline. API = Acute Panic Inventory. SUDS = Subjective Units of Distress. SPS = Social Phobia Scale. ASI-3 = Anxiety Sensitivity Index-3. BFNE = Brief Fear of Negative Evaluation. Post = Post-experiment.
***$p < .001$, **$p < .01$, *$p < .05$.

placebo pill, participants' responses to a post-experiment question about whether they experienced facial flushing, itching or heat were compared across the niacin and placebo conditions using a logistic regression model. The overall model was significant ($\chi^2 = 13.59$, $df = 1$, $p < .001$) and results indicated that participants assigned to the niacin condition were significantly more likely to report facial flushing, itching, or heat (54.8%) than were participants in the placebo condition (28.9%; $p < .001$).

3.3. Regression models examining treatment condition, AS social concerns, fear of negative evaluation and baseline covariates predicting fear reactivity

Hierarchical multiple regression was conducted to examine post-experiment API SUDs and panic symptoms scores across vitamin condition (niacin [coded as 0] vs. placebo), speech instructions condition (AS social concerns instructions [coded as 0] vs. standard speech instructions), the interaction between conditions, baseline AS social concerns scores, and baseline BFNE scores. Interaction terms between conditions and baseline AS social concerns and baseline BFNE scores were also examined. Baseline AS social concerns and BFNE scores were mean-centered to aid in interpretation of the lower-order effects in the presence of an interaction term. Control variables, including gender, age, baseline API SUDs and panic symptoms, baseline social anxiety symptoms, and baseline AS physical and cognitive concerns were entered in the first step, followed by baseline AS social concerns and BFNE scores, the vitamin and speech conditions, and the vitamin and speech condition interaction in step two, and finally interactions between vitamin and speech conditions and AS social concerns and BFNE were included in step 3.

Model output was examined to determine whether multicollinearity was impacting these results. Variables with a reported variance inflation factor (VIF) greater than 2.5 (indicating greater than 60% of variance overlapping with additional predictor variables) were considered for removal with the goal to optimize inclusion of predictors relevant to the study hypotheses. There were several variables that exceeded this threshold across both models, including AS social concerns and BFNE scores and all the interaction terms with the exception of the BFNE by vitamin condition interaction term. Probing these potential suppression effects revealed these effects appeared to be driven by statistical suppression. Recentering the variables by some other metric such as mean-centering the dichotomous variables prior to creation of the interaction terms led to all VIF values below the 2.5 threshold. Given that reporting the results of the mean-centered results produces the same interaction term but outcome coefficients for any continuous outcome centered on an artificial participant midway between conditions, results are reported when the condition is not centered but rather has a meaningful zero point.

Results of the analysis on post-experiment API SUDs are provided in Table 3. The R^2 value did not improve from step one to step two ($\Delta R^2 = 0.02$, $p = .69$) or from step two to step three ($\Delta R^2 = 0.02$, $p = .66$). Further, there were no significant main or interaction effects of vitamin condition, speech condition, baseline AS social concerns, or baseline BFNE. The overall model was significant at step three, $F(16, 98) = 3.58$, $p < .001$. Significant effects of baseline API SUDs ($B = 0.54$, $p = .01$) and baseline SPS social anxiety ($B = 0.69$, $p = .01$) were detected.

Results of the analyses on post-experiment API panic symptoms are provided in Table 3. The R^2 value improved from step one to step two ($\Delta R^2 = 0.11$, $p < .001$) but not from step two to step three ($\Delta R^2 = 0.03$, $p = .22$). The overall model was significant at step three, $F(16, 98) = 6.18$, $p < .001$. Further, there were significant effects of the vitamin condition ($B = -3.30$, $p = .03$) and AS social concerns ($B = 0.60$, $p = .02$), qualified by a significant vitamin condition by AS social concerns interaction term ($B = -0.61$, $p < .05$). This interaction was probed by examining the effect of AS social concerns in the niacin and placebo pill conditions, separately (see Fig. 2). Probing this interaction using the Johnson-Neyman technique revealed significant group differences emerging at AS social concerns scores greater than 5.94. Further, AS social concerns was significantly predictive of API

Table 3
Hierarchical Linear Regression Models Predicting Fear Reactivity from Anxiety Sensitivity and Fear of Negative Evaluation.

	API SUDS			API Panic Symptoms		
	B	*p*	ΔR^2	*B*	*p*	ΔR^2
						.36
Step One			.33			
Gender	1.21	.78		.10	.93	
Age	-.64	.44		-.29	.20	
API SUDs	.56	< .001		-.02	.61	
API Panic Symptoms	.75	.21		.96	< .001	
SPS Social Anxiety	.80	< .001		.10	.05	
AS Physical Concerns	-.51	.39		.10	.55	
AS Cognitive Concerns	-.10	.89		-.07	.72	
Step Two			.02			.11
Gender	2.24	.63		.00	1.00	
Age	-.71	.42		-.46	.04	
API SUDs	.53	.003		.04	.36	
API Panic Symptoms	.82	.19		.87	< .001	
SPS Social Anxiety	.78	< .001		.09	.14	
AS Physical Concerns	-.45	.47		.05	.74	
AS Cognitive Concerns	-.18	.80		-.22	.24	
Vitamin Condition	9.06	.13		−2.67	.08	
Speech Condition	7.12	.21		1.62	.26	
Vitamin by Speech	−9.50	.25		−1.22	.56	
AS Social Concerns	.36	.56		.43	.01	
BFNE	-.13	.74		-.20	.04	
Step Three			.02			.03
Gender	2.74	.57		-.30	.80	
Age	-.24	.80		-.55	.03	
API SUDs	.54	.004		.06	.24	
API Panic Symptoms	.66	.31		.80	< .001	
SPS Social Anxiety	.69	.01		.08	.18	
AS Physical Concerns	-.49	.44		.01	.93	
AS Cognitive Concerns	.05	.94		-.25	.18	
Vitamin Condition	7.64	.21		−3.30	.03	
Speech Condition	5.36	.36		1.31	.37	
Vitamin by Speech	−7.73	.36		-.59	.78	
AS Social Concerns	-.52	.61		.60	.02	
BFNE	.54	.42		-.22	.20	
ASI-3 Social X Vitamin	.36	.76		-.61	.05	
ASI-3 Social X Speech	1.58	.17		.22	.44	
BFNE X Vitamin	-.53	.47		.11	.54	
BFNE X Speech	-.68	.35		-.02	.90	

Note. ASI-3 = Anxiety Sensitivity Index-3. BFNE = Brief Fear of Negative Evaluation. API = Acute Panic Inventory. SUDS = Subjective Units of Distress.

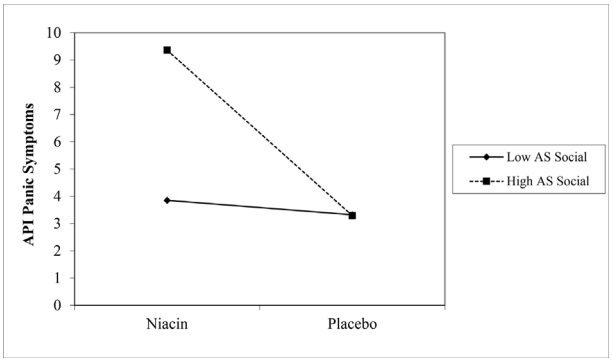

Fig. 2. Effect of ASI-3 social concerns on API panic symptoms in the niacin and placebo conditions. AS Social = Baseline AS social concerns. API panic symptoms scale ranges from 0 to 69. The effects are presented at −1 standard deviation (Low AS Social) and +1 standard deviations (High AS Social) from the mean of AS Social Concerns.

panic symptoms in the niacin condition ($B = 0.60$, $p = .02$) and not in the placebo condition ($B = 0.00$, $p = .99$). Several of the covariates also significantly predicted post-experiment API panic symptoms, including baseline API panic symptoms ($B = 0.80$, $p < .001$) and age ($B = -0.55$, $p = .03$).

4. Discussion

As hypothesized, fear reactivity, as indexed by panic symptoms, was significantly elevated in the niacin condition as compared to the placebo condition following a brief social stressor. Further, AS social concerns uniquely predicted this increased fear reactivity, controlling for relevant covariates, including social anxiety, FNE, and the other AS dimensions. In contrast to hypotheses, API SUDS-indexed fear reactivity was not significantly elevated in the niacin condition or predicted by AS social concerns. In contrast to hypotheses, no significant effects of speech condition or speech condition by vitamin condition were found across either outcome variable.

In contrast to the finding of a significant vitamin condition by AS social concerns interaction predicting fear reactivity (as measured by panic symptoms), Dixon et al. (2015) did not find significant differences in post-speech anxiety levels between participants who did or did not complete IE exercises that were designed to elicit AS social concerns prior to giving a speech. There are several possible explanations for these discrepant findings. First, as Dixon et al. suggest, it is possible that people who knew they were about to complete a speech task did not fully engage in the IE exercise. In contrast, the use of niacin does not allow participants to attenuate sensations induced by the challenge. Second, Dixon and colleagues allowed participants to select the IE exercise they would engage in. Most participants selected hyperventilation, which is less associated with blushing and other physically observable anxiety sensations. Finally, the use of niacin is also likely more anxiety-provoking to participants given that it can yield unpredictable, uncontrollable sensations that last longer than the more predictable IE exercises used by Dixon and colleagues. Thus, the current study provides preliminary evidence that ingesting niacin prior to engaging in a social stressor is a useful biological challenge exercise for AS social concerns.

When controlling for AS social concerns, FNE was not a unique predictor of fear reactivity for participants ingesting niacin. These findings qualify prior studies suggesting that FNE predicts fear reactivity to blushing in social evaluative situations following niacin ingestion (Dijk et al., 2009; Drummond & Lazaroo, 2012b). Of note, these other studies did not consider AS social concerns as a potential explanatory variable. In sum, results of the current study as well as other studies examining AS social concerns and FNE together (e.g., Allan, Oglesby, Uhl, & Schmidt, 2016) indicate that these constructs are distinct risk factors of social anxiety.

These findings are in line with suggestions that social anxiety risk factors need to be considered together (Heimberg et al., 2010; Hirsch, Clark, & Mathews, 2006). In the current study, including AS social concerns and FNE allowed us to determine which risk factor was associated with increased fear reactivity. However, it is possible that if a potent manipulation related to FNE were included in addition to a manipulation relevant to AS social concerns, a synergistic AS by FNE effect might be found. It is also possible that AS social concerns and FNE serve as antagonistic risk factors for social anxiety, in line with several recent self-report studies that found AS was a stronger risk factor for anxiety at lower levels of other risk factors (Allan, Macatee, Norr, & Schmidt, 2014b; Allan, Norr, Macatee, Gajewska, & Schmidt, 2015b). Future studies are needed to establish whether AS social concerns and FNE operate synergistically, antagonistically, or in an additive manner as these findings would highlight whether these risk factors should be targeted individually or in tandem to reduce social anxiety symptoms.

Unexpectedly, API SUDs ratings were not significantly different between niacin and placebo conditions in the current study. There are

several explanations for the lack of significant API SUDs ratings post-speech. A recent meta-analysis examining relations between self-reported, visual analog scale (VAS) measures of stress and anxiety and physiological response during the Trier Social Stress Task (TSST; Campbell & Ehlert, 2012) revealed generally nonsignificant relations between self-reported and physiological response to the TSST. The authors posited several possible explanations for these findings, including weak construct validity for VAS measures, minimal emotional involvement in the laboratory task compared to how participants might respond in real-world situations, and the possibility that physiological responses are likely attributed to the task itself. This last suggestion is particularly compelling in the context of how participants responded in the current study. Whereas elevated physiological arousal was self-reported, this physiological arousal did not correspond highly to SUDs ratings ($r = 0.34$). Thus, participants may have noticed these panic symptoms but attributed them to the potential ingestion of niacin and/or the speech task, resulting in lower self-reported fear. This may be partially attributable to the inclusion of participants with normative levels of AS social concerns. Indeed, theories of AS would suggest that, for participants with elevated levels of AS, self-reported fear response would align more closely with panic symptom reporting. Thus, future studies are needed that focus on samples of participants with more elevated levels of AS.

From a clinical perspective, these findings highlight the prominence of AS social concerns as a risk factor for social anxiety. This finding is especially important given that the most common treatments for SAD neglect internal threat cues, instead focusing on cognitive biases regarding negative interpretations of external cues (e.g., Hofmann, 2007). One possible solution to this is to add brief interventions targeting AS adjunctively to existing SAD treatments. Given that brief interventions targeting AS reduce mood and anxiety symptoms through reductions in AS, (e.g., Schmidt, Capron, Raines, & Allan, 2014; Schmidt, Norr, Allan, Raines, & Capron, 2017), it is possible that these same interventions could also reduce social anxiety. Current AS interventions target either AS globally or the AS cognitive concerns dimension despite impacting AS social concerns (e.g., Schmidt et al., 2014). The use of such interventions as well as the development of similar interventions that targeting AS social concerns is likely to enhance existing treatments for social anxiety.

Despite the promising results of the present study, several limitations and opportunities for future research should be noted. First, the present study used a predominantly female undergraduate student sample, which may limit the generalizability of the present findings. Given prior research suggesting the role of culture and various demographic characteristics on the presentation, prevalence, and treatment of social anxiety (e.g., Hofmann, Anu Asnaani, & Hinton, 2010), future research should include a more diverse and representative sample of participants. In addition, undergraduate students are higher functioning with lower severity of anxiety-related symptoms than treatment-seeking individuals within the community. Thus, stronger responses to the challenge might be found in clinical samples. Moreover, consistent with prior research focusing on biological challenge tasks (e.g., Schmidt & Zvolensky, 2007), the present study examined fear reactivity using self-report methodology (i.e., API). Consistent with psychobiological approaches toward understanding psychopathology (e.g., Insel et al., 2010), integrating additional methodologies such as physiological measures, including photoplesmyography to measure facial blood flow would increase our understanding of the impact of this challenge on fear reactivity. The current study used a between-subjects design instead of a within-subjects design. Whereas within-subject to the vitamin and speech condition might have advanced understanding further, it is also possible that habituation would have attenuated findings. Finally, although a post-experimental manipulation check was conducted for the niacin versus placebo groups, no post-experimental manipulation check was conducted for the speech conditions.

Despite these limitations, there were several notable strengths of the current study. This was the first study to demonstrate that niacin can be used as a biological challenge relevant to AS social concerns. This paradigm can thus be integrated with existing paradigms used to study FNE and other risk factors related to social anxiety within a laboratory setting. Additionally, this study suggests that AS social concerns are highly relevant to levels of anxiety present during social evaluation. Whereas the relevance of internal anxiety sensations is mentioned in theories of social anxiety (e.g., Clark & Wells, 1995; Heimberg et al., 2010), these sensations, and the role of risk factors like AS social concerns on these sensations, are rarely considered in research and treatment. This study suggests that AS social concerns may be a useful construct in better understanding the etiology, maintenance, and treatment of social anxiety.

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