ORIGINAL ARTICLE

Physiological Inflexibility in Generalized Anxiety Disorder: Modulation by Trait Worry

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ABSTRACT

Generalized anxiety disorder (GAD) is associated with pathological worry and somatic symptoms including autonomic arousal and muscle tension. Individuals with GAD tend to engage in worry as an attempt to control feelings of uncertainty and avoid unwanted emotional experience. As a result, GAD patients may exhibit diminished physiological flexibility. Furthermore, there have been research attempts to examine psychophysiological correlates of GAD, but the findings are often mixed. Preliminary studies suggest that GAD is separable into cognitive and somatic domains, and individuals with GAD present different psychophysiological profiles depending on levels of worry tendency. Ninety-five undergraduate students (75 females and 20 males) were instructed to worry in a laboratory while electrodermal activity (EDA), electrocardiography, respiration rate, and electromyography (EMG) over a corrugator supercilii muscle were being continuously monitored. We found that during worry induction, the range of EDA reactivity was more restricted for GAD participants than non-GAD participants. Among GAD participants, respiratory sinus arrhythmia (RSA) decreased for individuals with high trait worry whereas an increase in RSA was observed for those with low trait worry. These findings provide support for physiological inflexibility in GAD and have clinical implications for the assessment and treatment of individuals with GAD.

Key words: Electrodermal activity, Electromyography, Generalized anxiety disorder, Muscle tension, Physiological inflexibility, Respiratory sinus arrhythmia

INTRODUCTION

When we anticipate a serious adverse event in the future, we often worry to prepare ourselves for the upcoming event and avoid any negative consequences. Worry is a common human experience and is considered an adaptive response to impending danger. However, chronic, excessive, and uncontrollable worry that causes significant distress and functional impairment establishes cardinal diagnostic feature of generalized anxiety disorder (GAD).[1] According to the national comorbidity survey replication[29] and the national comorbidity survey replication-adolescent supplement,[36] life-time prevalence of GAD was estimated to be 4.3%.[30] Despite its relatively low prevalence rate in the general population, GAD is the most common anxiety disorder treated in the primary care setting and is linked to a high degree of disability comparable to that of depression.[51] These findings indicate that patients with GAD are high utilizes of health-care resources, and as a result, GADs economic burden to the society is considerably high.[25] Thus, further investigation on etiology and the development of effective treatment approaches for GAD are warranted.

Pathological worry has been conceptualized as an avoidance strategy.[11] Individuals with pathological worry attempt to replace the vivid mental imagery and emotional experience of facing a fearful event with a verbal, abstract, and preservative cognitive activity.[21] Inhibition of somatic and emotional experience may preclude effective information processing that is necessary for adaptive habituation, and

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therefore, chronic worry is developed and maintained through negative reinforcement.[11,21] This avoidance model predicts dampened somatic arousal among individuals with GAD, and preliminary evidence supports that GAD patients do not exhibit much variability in psychophysiological parameters in response to psychological stress.[24,48] For example, Hoehn-Saric *et al*.[24] found that change in skin conductance level (SCL) during divided attention and risk-taking conditions was weaker for the GAD patients compared with the non-anxious controls. Further examination of daily fluctuations in electrodermal activity (EDA) revealed diminished EDA variability for GAD patients compared with individuals without any psychiatric disorder.[23] However, these studies are limited in that they did not examine how worry, the cardinal feature of GAD, affects the relationship between physiological reactivity and GAD symptomatology.

Despite reduced physiological reactivity, GAD patients often complain about somatic symptoms such as heart palpitation and sweating.[1,24] Since somatic symptoms of GAD resemble physiological responses to an acute stressor, GAD patients have been assumed to be in a chronically heightened state of sympathetic nervous system (SNS) activity.[24] A high correlation between the amplitude of SNS activity and SCL renders EDA a reliable index of SNS activity,[13] but baseline EDA was not found to differ between patients with GAD and controls.[24] One explanation for this contrary finding might be dissociation between objectively measured physiological activities and subjectively experienced somatic symptoms.[9] Investigated whether EDA could reliably discriminate between individuals with any of the four DSM-III anxiety disorders and healthy controls and concluded that EDA was not adequate to separate GAD patients from non-anxious controls. Similarly, Fisher *et al*.[19] demonstrated that baseline SCL and non-specific skin conductance responses were not different among GAD, comorbid GAD, and non-anxious control groups. Taken together, these findings indicate that somatic symptoms of GAD are not closely associated with objectively measured EDA.

Another documented biomarker of GAD is vagal control that is often indexed by heart rate variability or respiratory sinus arrhythmia (RSA). Vagal control has been proposed to represent physiological flexibility in modulating emotional processes.[40,49] Vagal control mediates parasympathetic nervous system (PNS) activity and promotes rest and restoration by slowing heart rate and inhibiting SNS activity (e.g., fight-or-flight response) and stress response.[41] While sympathetic influences on cardiac control are slow (e.g., about 4 s to reach the peak effect), faster parasympathetic control (e.g., about 0.5 s to reach the peak effect) allows for the nuanced modulation of internal state including emotional reactions.[8,42] Thayer *et al*.[50] suggest that deregulated vagal control contributes to disinherited SNS activity, which in turn may lead to the manifestation of somatic symptoms in GAD. There are a few empirical studies investigating vagal control in GAD, but the findings are unclear. For example, Tan *et al*.[48] reported that participants diagnosed with GAD showed diminished vagal activity (e.g., shorter inter-beat interval (IBI) and lower high-frequency spectral power in electrocardiography [ECG]) compared with non-anxious controls both at baseline and worry induction. Likewise, Grossman *et al*.[23] recorded tonic IBI and its variance over 4 days using an ambulatory monitoring device and found that individuals with GAD showed a significantly lower IBI variance than non-GAD controls although there was no group difference in mean IBI. However, Fisher *et al*.[20] found no group difference in RSA between GAD samples with high and low trait worry and healthy controls during baseline, worry, and relax conditions. These mixed results indicate the need for more controlled research on PNS activity in GAD, and one potential avenue is to search for possible moderators that may differentially affect PNS activity among GAD patients.

In addition to SNS and PNS activity, muscle tension has been found to play an important role in GAD. In a study examining the discriminate validity of the DSM-IV criteria for anxiety disorders, Brown *et al*.[12] demonstrated that motor tension and vigilance and scanning symptoms showed the maximal discriminative power to differentiate GAD from other anxiety disorders. Horvath *et al*.[27] further examined the relationship between worry and the six somatic symptoms of the DSM-IV GAD criteria and reported that muscle tension predicted self-reported pathological worry when depressive symptoms were controlled. Consistent with these results, psychological interventions often target muscle tension through techniques such as progressive muscle relaxation and diaphragmatic breathing.[4,10] Clinical trials showed that relaxation techniques that aim to reduce autonomic arousal and muscle tension were comparable to cognitive therapy in the treatment of GAD symptoms.[3,39] Thus, it is critical to understand how muscle tension relates to GAD symptomatology.

We have so far reviewed previous research on SNS and PNS activity and muscle tension as physiological parameters that may underlie GAD. However, the overall findings are unclear or mixed. One explanation for these inconsistent findings is that a moderating factor that yet needs to be identified differentially affects physiological state among individuals with GAD. A substantial body of research has suggested that anxiety is separable into two distinct symptom domains: A cognitive domain that involves preservative thought processes (e.g., worry and recurrent intrusive thoughts) and a somatic domain with physiological symptoms (e.g., muscle tension, heart palpitation, and sweating)[15,32,43] Thus, it is possible that subgroups of GAD may differ on levels of worry tendency and somatic symptomology. For example, Fisher and Newman (2013) found that heart rate and RSA did not differ among non-GAD participants with high trait

worry, GAD patients, and healthy controls. However, the interaction between GAD diagnosis and trait worry could have masked the existing group difference. The authors reported that the mean Penn State Worry Questionnaire (PSWQ) score was 62.42 for GAD participants. According to the previous psychometric research suggesting the PSWQ score of 62 as a clinical cutoff for pathological worry,[6] a considerable number of participants in the GAD group is expected to experience subclinical worry. Thus, additional research is needed to examine whether trait worry in GAD interacts with physiological variables among individuals with GAD. The current study aims to address two important issues in GAD literature. First, we sought to increase our understanding of physiological states within GAD, especially their changes in response to laboratory-induced worry. EDA, RSA, and facial electromyography (EMG) data were collected to provide a comprehensive picture of how psychophysiological parameters are associated with self-reported GAD symptomatology and worry tendency. We hypothesize that compared with non-GAD participants, GAD participants (i.e., those whose scores on the GAD 7[45] exceed the clinical cutoff of 10) will demonstrate diminished variability in the physiological indices. Second, we examined whether trait worry interacts with the relationship between GAD status and variance in EDA, RSA, and EMG activity. Since previous research on physiological measurement associated with GAD has produced inconsistent results, we attempt to test the moderating effect of trait worry. Thus, we hypothesize that GAD participants with high trait worry will show diminished physiological reactivity during worry induction compared with those with low trait worry.

MATERIALS AND METHODS

Participants

Ninety-five undergraduate students (75 female, 20 male) from the University of Nevada, Reno, participated in the study. Participants were 53% Caucasian, 19% Hispanic, 7% Asian American, 7% African American, 5% Native American or Pacific Islander, and 9% mixed or other. Ages ranged from 18 to 55 years (M = 22.59, SD = 6.00). All participants provided written informed consent and were compensated with extra course credit or a $15 gift card. The study was approved by the University of Nevada, Reno's Institutional Review Board.

Instruments

Self-report questionnaires

GAD-7

The GAD-7[45] is a brief questionnaire that assesses symptoms of GAD and consists of 7 items that are rated on a 4-point Likert scale ranging from 0 (not at all) to 3 (nearly every day). The scale has been validated in clinical and general community samples and has shown excellent psychometric properties, such as internal consistency (Cronbach's alpha = 0.92 and 0.89 in the current sample), test-retest reliability (intraclass correlation = 0.83), and diagnostic criterion validity.[14,45] Sample items include "Feeling nervous, anxious, or on edge," "Worrying too much about different things," and "Trouble relaxing." The GAD-7 has been widely used in studies targeting various clinical and non-clinical populations including college students.[5,14,34] Schienle *et al.* investigated the diagnostic criterion validity of the GAD-7 among GAD patients and recommended the optimal cutoff of 10 with its sensitivity and specificity being 89% and 82 %, respectively.[45] Using this criterion, participants were assigned to either a GAD group or a non-GAD group.

PSWQ

The PSWQ[37] is a self-report instrument that assesses the symptoms of pathological worry. The PSWQ consists of 16 items that are rated on a 5-point Likert scale ranging from 1 (not at all typical of me) to 5 (very typical of me). The PSWQ has been validated in clinical and college samples and has shown excellent internal consistency (Cranach's alpha = 0.86–0.95 and 0.94 in the current sample), test-retest reliability (intraclass correlation = 0.74–0.92), and construct validity.[37,38] Sample items include "My worries overwhelm me," "Many situations make me worry," and "I worry all the time." Using non-treatment-seeking college student samples, Behar *et al.*[6] examined the diagnostic utility of the PSWQ and reported that a cutoff point of 62 produced the specificity of 86% and the sensitivity of 75%. These results suggested that symptoms of pathological worry may predict GAD diagnosis, and thus, we identified participants with either high or low trait worry using this cutoff score.

Physiological measurements

EDA was assessed using two Ag-AgCl electrodes with a 6 mm diameter hole that was filled with isotonic paste, and the electrodes were attached to the volar surfaces of distal phalanges of the index and middle fingers of the using Velcro straps. To record ECG, three pre-gelled Ag-AgCl electrodes were placed on the left and right ankles and the right wrist (Lead II configuration). Breathing rate was measured through a respiration belt transducer strap placed around the chest. To record facial EMG, two small electrodes were filled with isotonic paste and attached over the right corrugator supercilii muscle with the intercensor space of 1.0 cm. Before sensor placement, the skin was prepared by gently rubbing skin preparation gel into the skin surface. All physiological signals were recorded on a BIOPAC MP30 monitoring system, and the sampling rate was set to 1000 Hz. The digitized physiological data were band-pass filtered (0.5–35 Hz for ECG, 0.05–0.5 Hz for respiration, and 20–500 Hz for EMG) and low-pass filtered (1 Hz for EDA) offline using Acknowledge 4.1 software. RSA was derived from the filtered ECG and respiration data using the RSA module in the Acknowledge software. This module follows the "peak-valley" method in which maximum heart period is subtracted from minimum heart

period per each breathing cycle after adjusting for the phase relationship between respiration and heart period.[22] We found that the embedded QRS detector missed or misidentified some R-peaks, so they were manually corrected by two independent research assistants. When any discrepancy between the two datasets was found after the R-peak correction, a third research assistant repeated the task until the third dataset matched either of the two others. The average rectified EMG amplitude was calculated digitally from the filtered EMG data. EDA, RSA, and EMG responses were then averaged over the baseline and worry induction periods (5 min per each condition).

Procedure

After providing written consent, participants were seated in a comfortable chair in a quiet room and completed the GAD-7 and PSWQ. Next, sensors were attached for psychophysiological recording, and participants were told to stay relaxed for 10 min. Physiological data were recorded during the latter half of the 10-min baseline period. Participants were then instructed to write down their three most worrisome topics and worry about them as they normally do for 5 min while physiological data were being continuously recorded. This worry induction paradigm was used in previous research, and results showed an increase in self-rated negative affect and anxiety and a decrease in self-rated positive affect and IBI after worry induction.[35,48]

RESULTS

Preliminary Analyses

Means and standard deviations for all study variables are presented in Table 1. Change scores were then computed for EDA, RSA, and EMG by subtracting the baseline scores from the measurements taken during the worry induction period. Data were screened for outliers using the SPSS 20.0 statistical package. Nine univariate outliers that exceeded the three standardized deviations from the mean were identified. Mahalanobis distances were examined for the detection of multivariate outliers, and one case was found to be above the critical value of 22.46.[46] Ten outliers were excluded from the dataset, with leaving a total sample of 85. When normality was assessed, EDA and EMG data were positively skewed (0.90 ≤ skewness ≤8.03). We ran parallel analyses using original and log-transformed data, but we did not find meaningful difference in the results. For the ease of interpretation, only the results with original data are reported here.

Baseline

Before we conducted the main analyses, we performed a 2 × 2 (GAD × Worry Tendency) multivariate analysis of variance (MANOVA) for gender and age. Results suggested that GAD and worry status did not differ with respect to gender and age (all F(1, 71)1), 2.60, all p's ≥0.111). A MANOVA was conducted for EDA, RSA, and EMG at baseline to evaluate the main effects of GAD and worry tendency and their interaction effect. Levine's test of equality of error variances and Box's test of equality of covariance matrices were non-significant (all p's >0.05). Results indicated no significant main effects for GAD status on EDA ($F(1, 74) = 0.07$, $p = 0.793$, $\eta2 < 0.01$), RSA ($F(1, 74) = 1.79$, $p = 0.185$, $\eta2 = 0.02$), and EMG ($F(1, 74) = 0.54$, $p = 0.465$, $\eta2 < 0.01$) and for worry tendency on EDA ($F(1, 74) = 0.11$, $p = 0.744$, $\eta2 < 0.01$), RSA ($F(1, 74) = 1.41$, $p = 0.239$, $\eta2 = 0.02$), and EMG ($F(1, 74) < 0.32$, $p = 0.577$, $\eta2 < 0.04$). There was no significant interaction effect between GAD status and worry tendency on EDA ($F(1, 74) < 0.04$, $p = 0.949$, $\eta2 < 0.01$), RSA ($F(1, 74) = 1.06$, $p = 0.306$, $\eta2 = 0.01$), and EMG ($F(1, 74) = 0.34$, $p = 0.563$, $\eta2 = 0.01$). Consistent with the previous

Table 1: Means and standard deviations of EDA, RSA, and electromyography by groups and conditions (*n*=85)

Physiological measures	GAD status	Worry tendency	Baseline Mean (SD)	Worry induction mean (SD)	Change Mean (SD)
EDA (μS)	GAD	High (*n*=17)	6.19 (2.49)	7.10 (2.81)	0.91 (0.91)
		Low (*n*=10)	6.08 (2.76)	7.04 (3.05)	0.95 (1.54)
		Total (*n*=27)	6.15 (2.53)	7.07 (2.83)	0.93 (1.15)
	Non-GAD	High (*n*=23)	6.46 (3.48)	8.53 (4.22)	2.07 (2.23)
		Low (*n*=35)	6.13 (3.45)	7.96 (3.63)	1.83 (1.83)
		Total (*n*=58)	6.26 (3.43)	8.17 (3.84)	1.92 (2.00)
RSA (ms)	GAD	High (*n*=17)	82.38 (30.65)	70.67 (31.99)	−11.71 (25.87)
		Low (*n*=10)	94.65 (28.82)	104.71 (40.74)	10.06 (20.27)
		Total (*n*=27)	87.05 (29.86)	83.64 (38.49)	−3.41 (25.74)
	Non-GAD	High (*n*=23)	79.85 (27.81)	81.85 (33.73)	2.00 (20.53)
		Low (*n*=35)	81.12 (34.47)	78.23 (33.40)	−2.89 (27.41)
		Total (*n*=58)	80.65 (31.88)	79.59 (33.27)	−1.06 (24.97)

GAD: Generalized anxiety disorder, RSA: Respiratory sinus arrhythmia, EDA: Electrodermal activity

research,[17,19] these results indicate that tonic levels of SNS activity and muscle tension did not differ based on GAD status and worry tendency.

Worry induction

To ensure the induction was successful, we asked participants, "How much are you experiencing somatic symptoms of anxiety (e.g., muscle tension, heart racing, sweating, etc.)?" and "How much are you experiencing cognitive symptoms of anxiety (e.g., think of the worst thing that could happen, attempt to avoid intrusive and unwanted thoughts)?" Then, participants were instructed to report somatic and cognitive anxiety on a 4-point Likert scale ranging from 1 (Not at all) to 4 (Very much). Results from the paired sample t-test indicated that levels of self-reported cognitive and somatic anxiety after the worry induction increased significantly compared with those at baseline ($t(82) = -8.27$, $p < 0.001$ and $t(82) = -8.89$, $p < 0.001$, respectively). Mean change scores of physiological data were examined with a one-sample *t*-test. Mean EDA during worry induction significantly increased compared with mean EDA measured at baseline (mean difference = 1.62, $t(78) = 7.94$, $p < 0.001$). However, mean RSA (mean difference = −2.40, $t(80) = -0.86$, $p = 0.390$) and EMG (mean difference = 0.03, $t(83) = 0.79$, $p = 0.429$) values did not change after worry induction. Although self-reported cognitive and somatic anxiety increased in response to the worry induction, physiological changes were observed only in EDA.

Physiological inflexibility in response to laboratory-induced worry

To evaluate the main effects of GAD and worry tendency and their interaction effects, a MANOVA was conducted for change scores of EDA, RSA, and EMG. Levine's test of equality of error variances and Box's test of equality of covariance matrices were non-significant (all p's > 0.05). As shown in Figure 1, the change scores of EDA were greater for individuals in the non-GAD group (mean difference = 1.92, SD = 1.15) than for individuals in the GAD group (mean difference = 0.93, SD = 0.22; $F(1, 73) = 4.53$, $p = 0.037$, $\eta 2 = 0.06$). However, no main effects of GAD status were found for change scores of RSA ($F(1, 73) < 0.01$, $p = 0.954$, $\eta 2 < 0.001$) and EMG ($F(1, 73) = 0.48$, $p = 0.493$, $\eta 2 = 0.06$). Taken together, these results suggest that GAD participants exhibited a dampened response of sympathetic activity when they worried, which provide support for the avoidance theory of worry. Likewise, no significant main effect of worry tendency was found for EDA ($F(1, 73) = 0.04$, $p = 0.835$, $\eta 2 = 0.01$), RSA ($F(1, 73) = 1.67$, $p = 0.201$, $\eta 2 = 0.02$), and EMG ($F(1, 73) = 0.31$, $p = 0.577$, $\eta 2 = 0.04$). As illustrated in Figure 2, there was an interaction effect for RSA ($F(1, 73) = 4.16$, $p = 0.045$, $\eta 2 = 0.05$). Specifically, RSA change scores increased for individuals with GAD and low worry tendency whereas these scores decreased for individual with GAD and high worry tendency. These results indicate that, when people with GAD engage in worry, parasympathetic activity or vagal control is suppressed for individuals with high trait worry but increases for those with low trait worry. No interaction effect was found for EDA ($F(1, 73) = 0.09$, $p = 0.762$, $\eta 2 < 0.01$) and EMG ($F(1, 73)$ 1.02, $p = 0.317$, $\eta 2 = 0.01$).

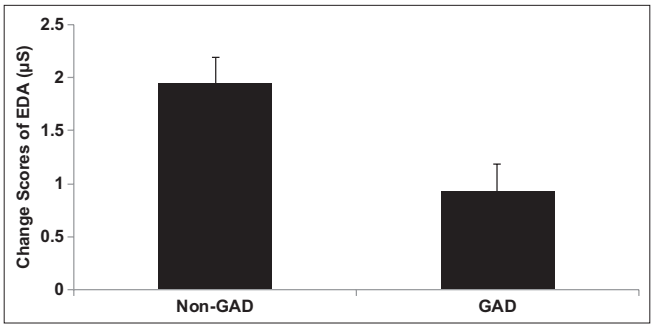

Figure 1: Change scores of electrodermal activity in response to worry induction. Error bars represent standard errors

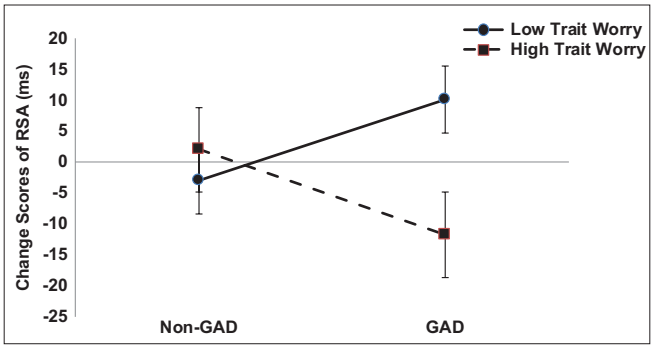

Figure 2: Interaction effects for change scores of respiratory sinus arrhythmia by generalized anxiety disorder and worry tendency. Error bars represent standard errors

DISCUSSION

The current study examined the effects of laboratory-induced worry on three physiological parameters: EDA, RSA, and facial EMG. We found that during worry induction, EDA reactivity was much diminished for individuals with GAD compared to non-GAD controls. These results provide support for diminished physiological reactivity of individuals with GAD and extend beyond the findings of existing research that investigated different psychophysiological markers (e.g., heart IBI) in GAD as well as other mental disorders such as specific phobia and post-traumatic stress disorder.[16,23,28] One could argue that individuals with GAD have heightened sensitivity to their physiological and emotional states. As their level of autonomic arousal increases in response to a threat, these individuals are more likely to engage in worry as a coping strategy to modulate ANS activation. Although no significant difference was observed in levels of basal autonomic arousal, individuals with GAD are more emotionally reactive to

negative events and sensitive to ensuing physiological changes than non-anxious controls.[2,19,47] Further support is provided by functional imaging studies demonstrating that greater amygdala reactivity to negatively balanced stimulus and larger amygdale volumes were associated with GAD diagnosis.[18,44] Such hypersensitivity to internal and external threats including physiological arousal may mediate worry tendency because the verbal-linguistic nature of worry serves to increase a sense of control, to hamper the effective processing of negative emotions, and as a result to dampen the magnitude of physiological responses.[7,11,33] The present study contributes to the literature by delineating the effect of worry on PNS activity in GAD, and it is the first study to date demonstrating that worry tendency moderates vagal control within GAD participants. We found among individuals with GAD that PNS activity indexed by RSA decreased for individuals with high trait worry during worry induction while an increase in PNS activity was observed for individuals with low trait worry. Considering that vagal control or "vagal brake" is responsible for modulating emotional responding and represents physiological flexibility to stressors,[41,50] reduced RSA in GAD participants with high trait worry indicates the dye regulation of such control mechanism, and therefore, worry appears to produce an iatrogenic effect when GAD participants with high trait engaged in worry. In other words, worry may help reduce physiological reactions (as shown in the diminished EDA reactivity above) but at the cost of undermining the ability to regulate emotion. As a result, such physiological inflexibility due to reduced vagal control may serve as an underlying mechanism of pathological worry. Furthermore, the current study provides a compelling explanation for inconsistent findings about the relationship between RSA and GAD status.[20,48] If RSA is moderated by worry tendency among GAD patients, the proportion of individuals with high trait worry within the GAD group may affect whether the study will yield a significant difference in RSA between GAD and non-GAD groups. These findings are in line with previous research suggesting multicomponent models of anxiety with discrete cognitive and somatic dimensions.[15,31,43] Our results provide support that a subgroup of GAD may exist depending on levels of worry tendency, and the role of worry in this subset of individuals with GAD carries a different functional relevance to the regulation of anxiety compared with individuals with GAD but low worry tendency. Despite these findings, it is worth noting several limitations of the study. First, we divided participants based on the scores of self-report questionnaires that assess GAD symptomology (GAD-7) and pathological worry (PSWQ). Although these questionnaires have been widely used in clinical research on GAD and demonstrated excellent diagnostic utility,[6,45] caution needs to be exercised in interpreting the study findings. Second, considering that the current sample primarily consists of non-treatment-seeking college students, a replication study is warranted where a diagnostic interview is conducted on diverse clinical samples. Third, there is a concern about the external validity of the present findings. Although previous studies using a similar worry induction paradigm[35,48] and our manipulation check data indicate that state worry was induced as intended, one may question to what degree laboratory-induced worry is analogous to pathological worry in GAD patients. On the one hand, since GAD patients often report that their worry is excessive and uncontrollable, worry in GAD appears to be under involuntary control. On the other hand, GAD participants were asked to voluntarily initiate worry in the current study. As a result, there might be a discrepancy in physiological profiles between experimentally induced and naturally occurring pathological worry. Finally, we did not assess state worry across conditions so that we could not evaluate whether the GAD participants worried "harder" during worry induction compared to controls. Thus, further research should seek to assess state worry using a more ecologically valid experimental paradigm. The current study has clinical implications for the assessment and treatment of GAD. Our study results suggest that individuals with GAD exhibit discrete physiological and cognitive profiles, which provides support for the heterogeneity of GAD. Hoffman *et al.*(26) argued for subgroups of anxiety patients who react with either muscle tension or autonomic arousal. On a similar account, Hoehn-Saric[24] maintained that GAD is characterized by muscle tension but not by ANS activity. Although counterevidence was later found that vagally mediated PSN also contributes to somatic symptoms of GAD,[39,48] we expanded these findings by demonstrating that PNS activity was moderated by the severity of worry tendency in the GAD sample. Thus, further research effort is needed to investigate whether the heterogeneity of GAD symptoms warrant different subcategories in GAD diagnosis. Moreover, the efficacy of GAD intervention can be enhanced by narrowing treatment target depending on the relative severity of each somatic and cognitive dimension. For example, biofeedback, progressive muscle relaxation, or pharmacological treatment can be applied to treat individuals presenting with severe somatic symptoms such as muscle tension and hyperarousal. On the other hand, a cognitive approach like Cognitive Behavior Therapy (CBT) can be utilized to address cognitive aspects of GAD (e.g., avoidance strategies and excessive worry).

CONCLUSIONS

To sum up, the current study aimed to provide comprehensive empirical coverage of physiological markers (i.e., EDA, RSA, and facial EMG) in GAD. Supporting evidence was found for physiological inflexibility in GAD. In response to worry induction, GAD participants showed a restricted range of SNS reactivity measured by EDA. Furthermore, the results suggest that vagally mediated PNS activity in GAD participants was moderated by levels of worry. Although these findings add to the exiting GAD literature, future

research needs to delineate the underlying mechanism by which pathological worry affects physiological states and the link between measured and experienced somatic symptoms in GAD patients.

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