



Published in final edited form as:

Psychosom Med. 2011 July ; 73(6): 498–503. doi:10.1097/PSY.0b013e3182223b28.

THE INTERPLAY BETWEEN PHYSICAL ACTIVITY AND ANXIETY SENSITIVITY IN FEARFUL RESPONDING TO CO₂ CHALLENGE

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Abstract

Objective—Physical activity may confer protective effects in terms of the development of anxiety and its disorders. These effects may be particularly strong among individuals who have elevated levels of anxiety sensitivity (i.e., the fear of somatic arousal; AS), an established cognitive-based risk factor for anxiety and its disorders. The present study performed a laboratory test of the interplay between physical activity and anxiety sensitivity.

Methods—Participants were adults free of Axis I psychopathology ($N = 145$) who completed measures of physical activity and AS prior to undergoing a recurrent 20% carbon dioxide-enriched air (CO₂) challenge.

Results—Consistent with hypothesis, physical activity was significantly related to CO₂ challenge reactivity among persons with elevated levels of AS, at high levels of physical activity ($p < .001$) but not at low levels of physical activity ($p = .90$). Also consistent with hypothesis, irrespective of the level of physical activity, physical activity did not relate significantly to CO₂ challenge reactivity among persons with normative levels of AS ($p = .28$).

Conclusions—These findings provide novel empirical insight into the role that physical activity may play in terms of resiliency for the development of anxiety disorders. Specifically, the protective effects of physical activity may only be evident at higher doses and among persons who are at increased risk of developing anxiety disorders because they have elevated anxiety sensitivity.

Keywords

physical activity; exercise; anxiety; anxiety sensitivity; biological challenge

INTRODUCTION

Growing evidence suggests that regular physical activity is a possible protective factor in terms of the development of anxiety and its disorders. For example, Goodwin (1) observed that regular physical activity predicted lower prevalence of panic attacks ($OR = 0.73$), social phobia ($OR = 0.65$), specific phobia ($OR = 0.78$), and agoraphobia ($OR = 0.64$) among a representative adult sample in the United States. These effects were evident after controlling for demographic variables and co-occurring physical and mental health conditions. In this same study, there also was evidence for a dose-response relationship between physical

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activity and mental health problems, such that the lowest prevalence rates of anxiety disorders were observed among persons who exercised regularly, followed by those who exercised occasionally, rarely and never, respectively (1). A recent prospective study has further found that physical activity is associated with a reduced incidence of anxiety disorders (2). Specifically, using a representative sample ($N = 2,548$) of adolescent and young adults (ages 14–24) from Munich, Germany, Ströhle and colleagues found that the incidence of any anxiety disorder during a 4-year follow-up was significantly lower among persons who reported engaging in regular physical activity versus those who reported no physical activity ($OR = 0.52$).

Extant work on the role of physical activity in the development of anxiety and its disorders has primarily focused on establishing the general overall effects of physical activity (1, 2). With any observed main effects, there is evidence of individual variability, which prompts research on identifying moderators. Determining whether the putative protective effects of physical activity with respect to anxiety vulnerability are equally applicable to all persons, or whether these effects are relevant to only a subset of the population has important implications for prevention. Accordingly, there is a need to empirically explore the interplay between physical activity and established risk factors for anxiety disorders.

Perhaps one of the most well-known cognitive-based risk factors for anxiety disorders is anxiety sensitivity (AS) (3). AS is defined as the extent to which individuals believe that anxiety and anxiety-related bodily sensations (i.e., somatic arousal) have harmful consequences (4, 5). AS is distinct from the temperament variables of trait anxiety (6) and negative affectivity (7); it reflects beliefs about internal sensations as opposed to frequency of (negative) mood symptoms. Laboratory (8–11) and prospective (12–16) studies consistently indicate that AS increases the risk for more intense anxiety symptoms and anxiety psychopathology.

Building upon previous work (1, 2), the present study sought to perform a test of the potential interplay between regular physical activity and AS with respect to anxiety vulnerability. We theorized that physical activity would interact with AS to significantly *decrease* vulnerability in anxiety-based emotional reactivity to bodily perturbation. This hypothesis was guided by extant work suggesting that the apparent protective effects of regular physical activity on the development of anxiety and its disorders may be centered upon reduced reactivity to anxiety-provoking stimuli (17). Indeed, a series of recent studies have shown that an *acute* bout of exercise reduces fearful responding to panicogenic agents such as carbon dioxide-enriched air (CO_2) (18, 19) and cholecystokinin tetrapeptide (20, 21). More importantly, results from both animal and human studies converge to indicate that *regular* physical activity reduces physiological and psychological reactivity to psychological stressors (17, 22–26). Accordingly, because it is associated with reduced reactivity to stressors, regular physical activity may buffer the effects of bodily perturbation on anxiety for persons who are prone to respond to such stressors with anxiety (i.e., persons with elevated levels of AS) but not for those who do not tend to respond to such stressors with anxiety (i.e., persons with non-elevated levels AS). In addition, there is some work to suggest that the buffering effects of PA on responses to bodily perturbation among individuals with elevated AS may vary across levels of physical activity. Indeed, Dishman and colleagues (27) reported that substantial reductions in trait anxiety become only evident when persons reach a certain threshold of physical activity (i.e., four to five months of exercise training). This observation coupled with the finding that reduced stress reactivity has been linked to *regular* physical activity may suggest that the PA-buffering effects for individuals with elevated AS may only be evident among individuals who engage in physical activity frequently.

We employed a CO₂ challenge laboratory paradigm for testing the present research questions. Inhalation of CO₂-enriched air is an ideal paradigm for the current test as it induces the somatic arousal characteristic of panic attacks (27) and CO₂ challenge reactivity has been found to significantly prospectively predict the onset of spontaneous panic attacks in the future (28, 29). In the current study, participants were young adults free of both Axis-I psychopathology and history of panic attacks who reported various levels of regular physical activity. Nonclinical healthy persons were sampled in order to rule out the possibility that any observed differences would be attributable to pre-existing psychological or health problems (30). We hypothesized that CO₂ challenge reactivity would vary as a function of the interaction between physical activity and AS. Specifically, we expected no relation between physical activity and CO₂ challenge reactivity among individuals with low or normative levels of AS. Further, we expected that, among individuals with elevated levels of AS, the relationship between physical activity and CO₂ challenge reactivity would be significant but discontinuous, such that greater physical activity would be related to lower CO₂ reactivity only for physical activity levels above a certain threshold.

METHODS

Participants

Participants were 145 adults (83 females) between the ages of 18 and 59 ($M_{\text{age}} = 21.6$ years; $SD = 7.43$) from the University of Vermont and the greater Burlington, Vermont community. Individuals were recruited through newspaper and other local advertisements posted in university and non-university settings. The racial distribution of the sample generally reflected that of the local population (31): 93.1% ($n = 135$) white; 2.8% ($n = 4$) African American; 1.4% ($n = 2$) Hispanic; 1.4% ($n = 2$) Asian; 0.7% ($n = 1$) “other;” and 0.7% ($n = 1$) did not specify race. The marital status for the vast majority of the sample was single ($n = 141$; 97.2%), and on average, participants had completed 13.2 years of education ($SD = 1.80$).

Participants were excluded for a history of Axis I psychiatric disorders, including nonclinical panic attacks, based upon their responses to the *Structured Clinical Interview for DSM-IV*, non-patient version (SCID-NP) (32). Inter-rater reliability for the SCID-NP for axis I diagnoses and sub-clinical panic attack history has been high in our group (33). Participants also were excluded from participation if they reported (a) current suicidal or homicidal ideation, (b) current use of psychotropic medication, (c) pregnancy, (d) current serious medical conditions (e.g., cancer), (e) serious breathing difficulties or respiratory-based illness (e.g., asthma, emphysema), or (f) limited mental competency or inability to give informed, written consent. As in past work (33), these additional exclusionary criteria were assessed within the context of the structured interview as an additional supplemental set of (standardized) interview-based medical screening questions. Finally, we excluded from our investigation participants who reported no physical activity. This exclusion criterion was used for three reasons. First, the present study was an investigation of the influence of the *amount* of physical activity and not the *occurrence* of physical activity. Second, those who *never* engage in physical activity tend to differ from those who do on numerous psychological and or physical health dimensions (27), which would make the interpretation of effects of physical activity difficult. Third, from a statistical perspective, calculating unbiased estimates of causal effects requires that the distributions of the effects must be completely overlapping (34). It is unlikely that the distributions of the effects of persons who report no physical activity and those who do engage in regular physical activity will be completely overlapping.

Procedures

A detailed description of the procedures has been provided elsewhere (35).¹ In short, interested participants responding to community-based advertisements for a laboratory study of anxiety were screened by a trained research assistant using the SCID-NP and scheduled by phone for an individual laboratory appointment. Eligible participants completed a self-report questionnaire packet before beginning the laboratory component of the study. Participants were instructed not to consume caffeine or engage in strenuous physical activity for 3 hours prior to their scheduled laboratory visit. During the laboratory component of the study, participants sat at a desk supporting a computer, which was programmed to administer the CO₂ administrations. After completing physiological hookup and listening to experimental instructions, participants were fitted with a positive-pressure C-pap mask. The experimenter observed participants from an adjacent control room containing a computer-operated apparatus designed to automatically provide participants with either room air or a mixture of 20% CO₂ - enriched room air. The apparatus (36) assured that all participants received 6 CO₂ inhalation trials and 18 room-air inhalation trials each lasting 90 seconds. Furthermore, all participants received the same trial order with CO₂ administrations occurring on trials 3, 6, 9, 14, 19, and 22. Lastly, because the original study (35) examined whether CO₂ challenge reactivity would vary as a function of the predictability of the biological stressor, each inhalation trial began with an instruction informing the participant of the trial type (room air or 20% CO₂).² Thus, participants received a total of 24 trials, of which 6 were CO₂ inhalations (3 predictable and 3 unpredictable) and 18 were room air inhalations (9 predictable and 9 unpredictable). After the laboratory component of the study, participants were debriefed and paid \$30 for their participation. All procedures were approved by the University of Vermont Institutional Review Board. Data were collected between September 2003 and August 2008.

Measures

Physical activity—The Exercise Health Survey (EHS) (37) is a self-report measure that includes questions pertaining to the weekly amount of time spent in physical activity and is comparable to that employed in previous work documenting physical activity-anxiety relations (1, 2, 38) as well as measures of physical activity used in large-scale epidemiological studies relating regular physical activity to morbidity and mortality (39–41). Specifically, the measure lists a variety of types of moderate- and vigorous-intensity activities and asks participants how many days per week on average they engage in these or other activities, and the duration of their exercise sessions per occasion. Using this information, we calculated the average minutes per week of physical activity.

Anxiety sensitivity—The Anxiety Sensitivity Index (ASI) is a 16-item questionnaire on which respondents indicate on a 5-point Likert-type scale (0 = *very little* to 4 = *very much*) the degree to which they fear anxiety symptoms and their negative consequences (42). The ASI is widely used and has demonstrated good psychometric properties (43). A large body of work suggests that AS is an important cognitive-based predictor of emotional response to biological challenge (8, 11, 44) and AS has been shown to affect estimations of

¹This study is based on an investigation from which other results have previously been reported (35). None of the predictors of outcome in the present study were investigated in the prior report.

²For unpredictable trials, the instruction “Unpredictable Trial: You will NOT be told whether or not you will receive CO₂ on this trial” appeared on the computer screen. For predictable trials, either the instruction “Predictable Trial: You will receive CO₂ on this trial” or “Predictable Trial: You will not receive CO₂ on this trial” appeared on the screen, depending on whether or not it would be a CO₂ trial. Participants were never misinformed. As reported by Yartz and colleagues (35), results indicated that equivalent levels of anxiety were experienced during predictable and unpredictable administrations of 20% carbon dioxide-enriched air. However, since predictability was significantly associated with anxiety for room air trials, this variable was included as a covariate in the present analysis.

cardiovascular fitness obtained by cycle ergometer testing (45). In the present investigation, we utilized the total ASI score, as it represents the global-order AS factor, and therefore takes into consideration different types of fears, including fears of anxiety-related somatic, cognitive, and social cues.

Challenge measures—Participants were asked to provide ratings of their current level of anxiety at baseline and at the end of each inhalation trial using an 11-point Likert-type rating scale, similar to those used in past work (e.g. Subjective Units of Distress Scale; SUDS) (46), ranging from ‘0’ (*no anxiety*) to ‘10’ (*extreme anxiety*). Specifically, participants provided a SUDS rating at the end of each of the 24 trials (regardless of whether or not CO₂ was delivered on that trial).

DATA ANALYSIS

In order to test whether AS moderated the effect of physical activity on CO₂ challenge reactivity, we employed a multi-level, within-subjects, mixed effects regression analysis (MLM) using the program *Hierarchical Linear and Nonlinear Modeling version 6.06* (HLM) (47). MLM was selected because of its flexibility in modeling complex relationships, its lack of restrictive assumptions, and its ability to include *all* of the observations of *all* subjects regardless of missing data. In addition, HLM 6.06 provides significance tests using “robust” standard errors, which are robust to violations of multivariate normality. The Level 1 portion of the MLM analysis modeled outcomes (SUDS) from each inhalation trial as a function of inhalation type (room air = 0; CO₂ = 1). Additionally, since previous findings with this sample (35) indicated that predictability was a significant determinant of SUDS, we included predictability (predictable = 0; unpredictable = 1) as a covariate. As such, the Level 1 portion of the MLM model was:

$$Y_{ij}(\text{SUDS}) = \beta_{0j} + \beta_{1j}(\text{inhalation type}) + \beta_{2j}(\text{predictability}) + e_{ij}.$$

Given this coding of the Level 1 predictors, β_{0j} represented average SUDS ratings for the predictable room air trials, β_{1j} represented the mean *difference* between SUDS reported for CO₂ versus room air inhalations (herein referred to as “CO₂ challenge reactivity”), and β_{2j} is the mean difference between the predictable and unpredictable trials.

The Level 2 portion of the MLM model allowed us to examine whether individual characteristics, such as physical activity and AS, predicted differences in mean SUDS ratings for the room air trials (β_{0j}) and for CO₂ challenge reactivity (β_{1j}). As noted above, we included “predictability” in the Level 1 model because predictability was significantly associated with SUDS for room air trials (35). Since we had no hypotheses regarding the effect of predictability on CO₂ challenge reactivity, we included it in the model to account for variance related to predictability, but did not include any Level 2 predictors for it.

Level 2 predictors of β_{0j} and β_{1j} included physical activity (PA) and AS. In order to test for discontinuous relations between PA and CO₂ challenge reactivity, we followed guidelines put forth by Singer and Willett (48). Specifically, we added an additional term to allow the relation between PA and CO₂ challenge reactivity to change at 1 SD above the mean of PA (the “threshold”). We selected this threshold of 1 SD above the mean following common practice when investigating interactions (49). The PA “slope difference” term was coded 0 for PA below threshold, and coded with the amount by which the participant’s PA exceeded the threshold for those with PA levels >1 SD above the mean (i.e., if PA was 1.55, the slope difference term would be coded 1.55–1 = 0.55) (48). Because we expected a “slope difference” only for those with high AS, we included a term for the interaction between AS

and the slope difference (i.e., AS \times PA Slope Difference). Although we did not expect that AS would moderate the relation between PA and CO₂ challenge reactivity among individuals below the PA threshold, we included the AS \times PA interaction in our initial model to examine this possibility. Further, we included gender (0 = male; 1 = female) as a covariate because females tend to report both higher AS (43) and lower levels of PA than men (50). Finally, because the age of our participants varied, we included age (log transformed to reduce skewness) as an additional covariate in the model. All predictors were converted to z-scores to enhance interpretation of the findings. Accordingly, the Level 2 equations were:

1. β_{0j} (mean SUDS, predictable air trials) = $\gamma_{00} + \gamma_{01}*(PA) + \gamma_{02}*(AS) + \gamma_{03}*(AS \times PA) + \gamma_{04}*(PA \text{ Slope Difference Term}) + \gamma_{05}*(AS \times PA \text{ Slope Difference Term}) + \gamma_{06}*(gender) + \gamma_{07}*(\ln(\text{age})) + r_{0j}$
2. β_{1j} (CO₂ challenge reactivity) = $\gamma_{10} + \gamma_{11}*(PA) + \gamma_{12}*(AS) + \gamma_{13}*(AS \times PA) + \gamma_{14}*(PA \text{ Slope Difference Term}) + \gamma_{15}*(AS \times PA \text{ Slope Difference Term}) + \gamma_{16}*(gender) + \gamma_{17}*(\ln(\text{age})) + r_{1j}$
3. β_{2j} (predictability) = $\gamma_{20} + r_{2j}$

RESULTS

Preliminary Analysis

On average participants were relatively active ($M_{PA} = 148.28$, $SD = 77.98$) and had AS levels similar to those observed in other community samples ($M_{AS} = 15.88$, $SD = 9.44$) (3). As expected, women reported higher AS levels than men (17.42 vs. 15.88; $F [1, 141] = 5.43$, $p < .05$) and men reported more weekly minutes of PA than women (169.28 vs. 132.60; $F [1, 143] = 8.25$, $p < .01$).

Hypothesis Testing

Since our hypotheses centered on CO₂ challenge reactivity, we will focus on the results of the second set of Level 2 equations (i.e., predictors of β_{1j}). Initial analyses indicated that neither gender nor the interaction of AS and PA for physical activity below the “threshold” were significant ($p = .59$ and $p = .65$, respectively), so they were dropped from the model and the analysis was recomputed. In this final model, age was marginally related to CO₂ challenge reactivity ($b = -0.38$, $SE_b = .21$, $t[125] = -1.77$, $p = .08$); we retained this term in the model in order to be conservative. As predicted, CO₂ challenge reactivity varied as a function of AS ($b = 0.35$, $SE_b = .17$, $t[125] = 2.05$, $p < .05$) but not as a function of PA ($b = -0.03$, $SE_b = .23$, $t[125] = -0.12$, $p = .90$) among persons whose PA was below the threshold (see Figure 1). Further, consistent with hypothesis, there was a significant interaction between AS and the PA slope difference ($b = -0.54$, $SE_b = .24$, $t[125] = 2.27$, $p < .05$), indicating that the relation between PA and CO₂ challenge reactivity changed at 1SD above the mean of PA, and that change depended on the level of AS. Following the guidelines put forth by Aiken and West (49), we examined the change in the relation between PA and CO₂ challenge reactivity for participants with high and normative levels of AS. We used a score of 1 SD above the mean AS score (25.32) to represent high levels of AS (51), and used the mean AS score in the sample (15.88) to represent normative levels (51). The results are presented in Figure 1. Consistent with hypothesis, among individuals with high levels of AS, there was a significant discontinuity in the relation between PA and CO₂ challenge reactivity when PA exceeded 1SD above the mean ($b_A = -0.87$, $SE_b = .35$, $t[125] = 2.47$, $p = .01$). Specifically, below the threshold, there was no relation between PA and CO₂ challenge reactivity ($b = -0.03$, $SE_b = .23$, $t[125] = -0.12$, $p = .90$), but above the 1 SD threshold, the relation was significant ($b = -0.90$, $SE_b = .21$, $t[125] = 4.25$, $p < .001$; see Figure 1). Also consistent with hypothesis, among individuals with normative levels of AS,

there was no discontinuity in the relation between PA and CO₂ challenge reactivity ($b_{\Delta} = -0.34$, $SE_b = .34$, $t[125] = 1.08$, $p = .28$). Specifically, the relation between PA and CO₂ challenge reactivity was not significant either below ($b = -0.03$, $SE_b = .23$, $t[125] = -0.12$, $p = .90$) or above the threshold ($b = -0.35$, $SE_b = .21$, $t[125] = 1.70$, $p = .09$; see Figure 1). The proportion of the total between-subjects variance of CO₂ challenge reactivity accounted for by this model was 9.3%.

In supplementary analyses, we investigated other lower potential “thresholds” (as low as the average level of PA). The results indicated that, as we lowered the threshold, the relation between PA and CO₂ challenge reactivity remained significant among individuals with high AS. However, the strength of this relationship generally decreased in magnitude as the threshold decreased. Thus, in this dataset, we could not identify a clear cut-off, over which there was a definite relation between PA and CO₂ challenge reactivity and under which such a relation did not exist. Therefore, we can only conclude that PA is related to reduced CO₂ challenge reactivity for high AS individuals when physical activity levels are high. Future research should examine whether this relation abruptly changes from non-significant to significant at a certain threshold.

Lastly, we examined the possibility that the moderating effects of AS were accounted for by one of the ASI subscales (ASI-physical, ASI-social, or ASI-mental) (43). Specifically, we reran the analysis three times, each time substituting the one of the ASI subscale scores for the ASI total score. The results of each of these three models mirrored those of the model with the ASI total score (i.e., significant and non-significant terms remained significant and non-significant, respectively). These findings suggest that the relation between AS and PA does not appear to be specific to, or accounted for, by any particular ASI subscale.

DISCUSSION

The present study sought to examine the hypothesis that AS would moderate the relation between physical activity and emotional reactivity to bodily perturbation. We found evidence consistent with this hypothesis. Specifically, we did not observe a significant effect of physical activity on CO₂ challenge reactivity for individuals with non-elevated levels of AS. However, consistent with hypothesis, for individuals with elevated levels of AS, higher levels of physical activity were related to significantly lower CO₂ challenge reactivity, but only among those who reported high levels of physical activity.

The finding that AS moderates the relation between regular physical activity and CO₂ challenge reactivity suggests that the apparent protective effects of regular physical activity with respect to anxiety vulnerability (1, 2) may be particularly applicable to persons who have elevated AS. The interplay between AS and physical activity observed in the present study also provides novel empirical insight into the potential effect of regular physical activity on modulating risk conferred by AS in terms of the development of anxiety disorders. Indeed, our results indicate that, for people with high levels of physical activity, those with high levels of AS show no greater CO₂ challenge reactivity than those with normal levels of AS. Accordingly, since CO₂ challenge reactivity is a predictor of future panic attacks (28, 29), these findings suggest that high levels of physical activity may reduce the risk of panic attacks and other anxiety related problems among those with high levels of AS. Future studies should examine whether regular physical activity indeed reduces the risk for panic attacks among persons high in AS using prospective designs and time sampling approaches (e.g., ecological momentary assessment protocols).

The observation that physical activity interacts with AS to predict CO₂ challenge reactivity also may help explain the relative predictive power of AS in any given study. That is,

because the effects of AS on fear reactivity to CO₂ challenge can vary from small to large (4, 52), it is possible that physical activity may serve as a qualifying, but often unrecognized, factor in understanding such variability. These data therefore highlight the potential importance of documenting physical activity and understanding its contribution to the expression of anxious and fearful responding to bodily sensations.

Although the present data provide evidence that high levels of physical activity were related to significantly lower CO₂ challenge reactivity among persons with elevated levels of AS, but not among individuals with normative levels of AS, the exact mechanisms underlying such effects remain unclear. There are a number of non-mutually exclusive possibilities that may warrant further scientific attention. One possibility is that higher levels of physical activity may facilitate corrective fear learning for those high in AS. It also may be possible that high levels of physical activity promotes more adaptive regulation of affect and thereby modulates fear responsivity. A final possibility is that high levels of physical activity for those high in AS may alter brain circuits that mediate fear responsivity. Clearly, elucidating the mechanisms linking risk and protective factors to clinical conditions will facilitate theoretical refinement of models of disorder development and aid in tailoring preventative work on specific conditions.

If replicated and extended, the present laboratory results, in conjunction with earlier field-based work (1, 2), provides guidance for anxiety disorder prevention program development. Initial work in this area has focused on the evaluation of cognitive-behavioral programs designed to target AS (53–55). Numerous scholars have suggested that such prevention programs may benefit from the inclusion of health-oriented tactics to modify AS and related anxiety risk processes (56, 57). Physical activity promotion may represent one such tactic. The present study findings indicate that adding a physical activity component to cognitive (e.g., cognitive restructuring) and behavioral (e.g., interoceptive exposure) strategies may offer a more powerful means to reduce risk for anxiety disorder development. Physical activity programs may also be useful as stand-alone interventions for reducing the deleterious effects of AS. Physical activity programs (either alone or in tandem with other interventions) may be especially efficacious since exercise has also been shown to reduce AS levels (58–60). Thus, incorporating physical activity into prevention programs targeting AS may be particularly potent because it buffers some of the negative consequences of AS (hyper-reactivity), as demonstrated in the present study, and it can reduce overall levels of AS. Lastly, because physical activity also has established physical health benefits, it would likely bolster global-based improvement in multiple domains of life functioning.

The present study has several limitations, some of which provide suggestions for future research. First, the sample was limited in that it was composed primarily of a relatively homogenous group of young adults. To increase the generalizability of these findings, it will be important for researchers to draw from populations other than those used in the present study. Second, although the present investigation examined the interplay between regular physical activity and AS, AS represents only one exemplar risk factor for anxiety psychopathology. Thus, exploration of the role of physical activity in mitigating the effects of other risk factors for anxiety disorders may inform the relative degree of specificity of the observed findings from a vulnerability-resilience perspective. Finally, the present study was focused on a laboratory model of fear responding. Laboratory findings may not fully generalize to naturally occurring fear behavior (61). Similarly, it is not possible to rule out spuriousness in these types of investigations. Physical activity and symptoms of anxiety and depression may be influenced by common factors (62). Accordingly, scientific attention should be given to the potential influence of other risk factors on the observed relationships, including genetic risk factors (63).

Overall, the present investigation adds uniquely to the extant empirical literature on the role of physical activity in modifying risk for anxious and fearful responding to bodily sensations. Results suggested that those with elevated levels of AS and high levels of physical activity showed significantly reduced CO₂ challenge reactivity relative to those with elevated levels of AS and low levels of physical activity. These laboratory findings highlight the potential promise of physical activity as a protective factor for the expression of fear reactivity to somatic perturbation.

Acknowledgments

Dr. Smits is supported by NIH grants R01MH075889 and R01DA027533 and has received royalties from Oxford University Press. Dr. Zvolensky is supported by NIH grants R01DA027533 and R01MH076629. All authors declare that they have no conflicts of interest.

Abbreviations

OR	Odds Ratio
AS	Anxiety Sensitivity
CO₂	Carbon Dioxide
SCID-NP	Structured Clinical Interview for DSM-IV-Non Patient Edition
EHS	Exercise Health Survey
ASI	Anxiety Sensitivity Index
SUDS	Subjective Units of Distress
MLM	Multi-Level Mixed Effects Regression Analysis
HLM	Hierarchical Linear and Nonlinear Modeling
PA	Physical Activity

References

1. Goodwin RD. Association between physical activity and mental disorders among adults in the United States. *Prev Med.* 2003; 36:698–703. [PubMed: 12744913]
2. Strohle A, Hofler M, Pfister H, Muller AG, Hoyer J, Wittchen HU, Lieb R. Physical activity and prevalence and incidence of mental disorders in adolescents and young adults. *Psychol Med.* 2007; 37:1657–66. [PubMed: 17579930]
3. Taylor, S., editor. *Anxiety Sensitivity: Theory, Research, and Treatment of the Fear of Anxiety.* Mahwah, NJ: Lawrence Erlbaum Associates; 1999.
4. McNally RJ. Anxiety sensitivity and panic disorder. *Biol Psychiatry.* 2002; 52:938–46. [PubMed: 12437935]
5. Reiss, S.; McNally, RJ. Expectancy model of fear. In: Reiss, S.; Bootzin, RR., editors. *Theoretical Issues in Behavior Therapy.* Orlando, FL: Academic Press, Inc; 1985.
6. McNally, RJ. Anxiety sensitivity is distinguishable from trait anxiety. In: Rapee, RM., editor. *Current controversies in the anxiety disorders.* New York, NY: Guilford Press; 1996. p. 214-27.
7. Zvolensky MJ, Kotov R, Antipova AV, Schmidt NB. Diathesis stress model for panic-related distress: a test in a Russian epidemiological sample. *Behav Res Ther.* 2005; 43:521–32. [PubMed: 15701361]
8. Brown M, Smits JA, Powers MB, Telch MJ. Differential sensitivity of the three ASI factors in predicting panic disorder patients' subjective and behavioral response to hyperventilation challenge. *J Anxiety Disord.* 2003; 17:583–91. [PubMed: 12941368]

9. Carter MM, Suchday S, Gore KL. The utility of the ASI factors in predicting response to voluntary hyperventilation among nonclinical participants. *J Anxiety Disord.* 2001; 15:217–30. [PubMed: 11442140]
10. Rapee RM, Medoro L. Fear of physical sensations and trait anxiety as mediators of the response to hyperventilation in nonclinical subjects. *J Abnorm Psychol.* 1994; 103:693–9. [PubMed: 7822570]
11. Zvolensky MJ, Feldner MT, Eifert GH, Stewart SH. Evaluating differential predictions of emotional reactivity during repeated 20% carbon dioxide-enriched air challenge. *Cogn Emot.* 2001; 15:767–86.
12. Li W, Zinbarg RE. Anxiety sensitivity and panic attacks: a 1-year longitudinal study. *Behav Modif.* 2007; 31:145–61. [PubMed: 17307932]
13. Mailer RG, Reiss S. Anxiety sensitivity in 1984 and panic attacks in 1987. *J Anxiety Disord.* 1992; 6:214–47.
14. Schmidt NB, Lerew DR, Jackson RJ. The role of anxiety sensitivity in the pathogenesis of panic: prospective evaluation of spontaneous panic attacks during acute stress. *J Abnorm Psychol.* 1997; 106:355–64. [PubMed: 9241937]
15. Schmidt NB, Cook JH. Effects of anxiety sensitivity on anxiety and pain during a cold pressor challenge in patients with panic disorder. *Behav Res Ther.* 1999; 37:313–23. [PubMed: 10204277]
16. Schmidt NB, Zvolensky MJ, Maner JK. Anxiety sensitivity: prospective prediction of panic attacks and Axis I pathology. *J Psychiatr Res.* 2006; 40:691–9. [PubMed: 16956622]
17. Salmon P. Effects of physical exercise on anxiety, depression, and sensitivity to stress: a unifying theory. *Clin Psychol Rev.* 2001; 21:33–61. [PubMed: 11148895]
18. Esquivel G, Schruers K, Kuipers H, Griez E. The effects of acute exercise and high lactate levels on 35% CO₂ challenge in healthy volunteers. *Acta Psychiatr Scand.* 2002; 106:394–7. [PubMed: 12366475]
19. Smits JA, Meuret AE, Zvolensky MJ, Rosenfield D, Seidel A. The effects of acute exercise on CO₂ challenge reactivity. *J Psychiatr Res.* 2009; 43:446–54. [PubMed: 18603261]
20. Strohle A, Feller C, Onken M, Godemann F, Heinz A, Dimeo F. The acute antipanic activity of aerobic exercise. *Am J Psychiatry.* 2005; 162:2376–8. [PubMed: 16330604]
21. Strohle A, Graetz B, Scheel M, Wittmann A, Feller C, Heinz A, Dimeo F. The acute antipanic and anxiolytic activity of aerobic exercise in patients with panic disorder and healthy control subjects. *J Psychiatr Res.* 2009; 43:1013–7. [PubMed: 19289240]
22. Binder E, Droste SK, Ohl F, Reul JM. Regular voluntary exercise reduces anxiety-related behaviour and impulsiveness in mice. *Behav Brain Res.* 2004; 155:197–206. [PubMed: 15364478]
23. Forcier K, Stroud LR, Papandonatos GD, Hitsman B, Reiches M, Krishnamoorthy J, Niaura R. Links between physical fitness and cardiovascular reactivity and recovery to psychological stressors: A meta-analysis. *Health Psychol.* 2006; 25:723–39. [PubMed: 17100501]
24. Rimmele U, Zellweger BC, Marti B, Seiler R, Mohiyeddini C, Ehlert U, Heinrichs M. Trained men show lower cortisol, heart rate and psychological responses to psychosocial stress compared with untrained men. *Psychoneuroendocrinology.* 2007; 32:627–35. [PubMed: 17560731]
25. Sinyor D, Schwartz SG, Peronnet F, Brisson G, Seraganian P. Aerobic fitness level and reactivity to psychosocial stress: physiological, biochemical, and subjective measures. *Psychosom Med.* 1983; 45:205–17. [PubMed: 6611800]
26. Throne LC, Bartholomew JB, Craig J, Farrar RP. Stress reactivity in fire fighters: An exercise intervention. *Int J Stress Manag.* 2000; 7:235–46.
27. Dishman, R.K.; Washburn, R.A.; Heath, G.W. *Physical Activity Epidemiology.* Champaign, IL: Human Kinetics; 2004.
28. Schmidt NB, Maner JK, Zvolensky MJ. Reactivity to challenge with carbon dioxide as a prospective predictor of panic attacks. *Psychiatry Res.* 2007; 151:173–6. [PubMed: 17395271]
29. Schmidt NB, Zvolensky MJ. Anxiety sensitivity and CO₂ challenge reactivity as unique and interactive prospective predictors of anxiety pathology. *Depress Anxiety.* 2007; 24:527–36. [PubMed: 17136755]
30. Forsyth JP, Zvolensky MJ. Anxiety sensitivity dimensions in the prediction of body vigilance and experiential avoidance. *Cog Ther Res.* 2002; 26:449–60.

31. State of Vermont Department of Health. Vermont population estimates: Overview of race and ethnicity data. 2007. Available from:
<http://healthvermont.gov/research/2007pop/documents/RACENOTE07.PDF>
32. First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. Structured Clinical Interview for DSM-IV Axis I Disorders, Non-patient Edition (SCID-I/NP, Version 2.0). New York, NY: Biometrics Research, New York State Psychiatric Institute; 1995.
33. Zvolensky MJ, Leen-Feldner EW, Feldner MT, Bonn-Miller WO, Lejuez CW, Kahler C, Stewart G. Emotional responding to biological challenge as a function of panic disorder and smoking. *J Anxiety Disord.* 2004; 18:19–32. [PubMed: 14725866]
34. Gelman, A.; Hill, J. *Data Analysis Using Regression and Multilevel/Hierarchical Models.* New York, NY: Cambridge University Press; 2007.
35. Yartz AR, Zvolensky MJ, Bernstein A, Bonn-Miller MO, Lejuez CW. Panic-relevant predictability preferences: a laboratory test. *J Abnorm Psychol.* 2008; 117:242–6. [PubMed: 18266502]
36. Lejuez CW, Forsyth JP, Eifert GH. Devices and methods for administering carbon dioxide-enriched air in experimental and clinical settings. *J Behav Ther Exp Psychiatry.* 1998; 29:239–48. [PubMed: 9847043]
37. Zvolensky, MJ. Anxiety and Health Research Laboratory Health Assessment Questionnaire. 2002. unpublished manuscript
38. Smits JA, Zvolensky MJ. Emotional vulnerability as a function of physical activity among individuals with panic disorder. *Depress Anxiety.* 2006; 23:102–6. [PubMed: 16400629]
39. Lee IM, Sesso HD, Paffenbarger RS Jr. Physical activity and coronary heart disease risk in men: does the duration of exercise episodes predict risk? *Circulation.* 2000; 102:981–6. [PubMed: 10961961]
40. Lee IM, Paffenbarger RS Jr. Associations of light, moderate, and vigorous intensity physical activity with longevity. The Harvard Alumni Health Study. *Am J Epidemiol.* 2000; 151:293–9. [PubMed: 10670554]
41. Leon AS, Connett J. Physical activity and 10. 5 year mortality in the Multiple Risk Factor Intervention Trial (MRFIT). *Int J Epidemiol.* 1991; 20:690–7. [PubMed: 1955253]
42. Reiss S, Peterson RA, Gursky DM, McNally RJ. Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. *Behav Res Ther.* 1986; 24:1–8. [PubMed: 3947307]
43. Peterson, RA.; Reiss, S. *Anxiety Sensitivity Index Manual (Revised Edition).* Worthington, OH: International Diagnostic Systems; 1992.
44. Zinbarg RE, Brown TA, Barlow DH, Rapee RM. Anxiety sensitivity, panic, and depressed mood: a reanalysis teasing apart the contributions of the two levels in the hierarchical structure of the Anxiety Sensitivity Index. *J Abnorm Psychol.* 2001; 110:372–7. [PubMed: 11502080]
45. Schmidt NB, Lerew DR, Santiago H, Trakowski JH, Staab JP. Effects of heart-rate feedback on estimated cardiovascular fitness in patients with panic disorder. *Depress Anxiety.* 2000; 12:59–66. [PubMed: 11091928]
46. Wolpe, J. *Psychotherapy by Reciprocal Inhibition.* Stanford, CA: Stanford University Press; 1958.
47. Raudenbush, SW.; Bryk, AS.; Cheong, YF.; Congdon, RT. *HLM 6: Hierarchical Linear and Nonlinear Modeling.* Lincolnwood, IL: Scientific Software International; 2004.
48. Singer, JD.; Willett, JB. *Applied longitudinal data analysis: Modeling change and event occurrence.* New York: Oxford University Press; 2003.
49. Aiken, LS.; West, SG. *Multiple Regression: Testing and Interpreting Interactions.* Newbury Park, CA: Sage; 1991.
50. Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System Survey Data. Atlanta, Georgia: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2005.
51. Peterson, RA.; Plehn, K. Measuring anxiety sensitivity. In: Taylor, S., editor. *Anxiety sensitivity: Theory research and treatment of the fear of anxiety.* Mahwah, NJ: Lawrence Erlbaum Associates Publishers; 1999. p. 61-81.
52. Bernstein A, Zvolensky MJ. Anxiety sensitivity: selective review of promising research and future directions. *Expert Rev Neurother.* 2007; 7:97–101. [PubMed: 17286543]

53. Feldner MT, Zvolensky MJ, Schmidt NB, Smith RC. A prospective test of anxiety sensitivity as a moderator of the relation between gender and posttraumatic symptom maintenance among high anxiety sensitive young adults. *Depress Anxiety*. 2008; 25:190–9. [PubMed: 17340601]
54. Gardenswartz C, Craske M. Prevention of panic disorder. *Behav Ther*. 2001; 32:725–37.
55. Schmidt NB, Eggleston AM, Woolaway-Bickel K, Fitzpatrick KK, Vasey MW, Richey JA. Anxiety Sensitivity Amelioration Training (ASAT): a longitudinal primary prevention program targeting cognitive vulnerability. *J Anxiety Disord*. 2007; 21:302–19. [PubMed: 16889931]
56. Watt, MC.; Stewart, SH.; Conrod, PJ.; Schmidt, NB. Personality-based approaches to treatment of co-morbid anxiety and substance use disorder. In: Stewart, SH.; Conrod, PH., editors. *Anxiety and substance use disorders: The vicious cycle of comorbidity*. New York, NY: Springer Publishing; 2008. p. 201-19.
57. Zvolensky, MJ.; Smits, JAJ., editors. *Anxiety in health behaviors and physical illness*. New York, NY: Springer; 2007.
58. Broman-Fulks JJ, Berman ME, Rabian BA, Webster MJ. Effects of aerobic exercise on anxiety sensitivity. *Behav Res Ther*. 2004; 42:125–36. [PubMed: 14975776]
59. Broman-Fulks JJ, Storey KM. Evaluation of a brief aerobic exercise intervention for high anxiety sensitivity. *Anxiety Stress Coping*. 2008; 21:117–28. [PubMed: 18350391]
60. Smits JA, Berry AC, Rosenfield D, Powers MB, Behar E, Otto MW. Reducing anxiety sensitivity with exercise. *Depress Anxiety*. 2008; 25:689–99. [PubMed: 18729145]
61. McNally RJ. Panic induction: A critical appraisal. *Behav Ther*. 1999; 30:333–41.
62. De Moor MH, Boomsma DI, Stubbe JH, Willemsen G, de Geus EJ. Testing causality in the association between regular exercise and symptoms of anxiety and depression. *Arch Gen Psychiatry*. 2008; 65:897–905. [PubMed: 18678794]
63. Mata J, Thompson RJ, Gotlib IH. BDNF genotype moderates the relation between physical activity and depressive symptoms. *Health Psychol*. 2010; 29:130–3. [PubMed: 20230085]

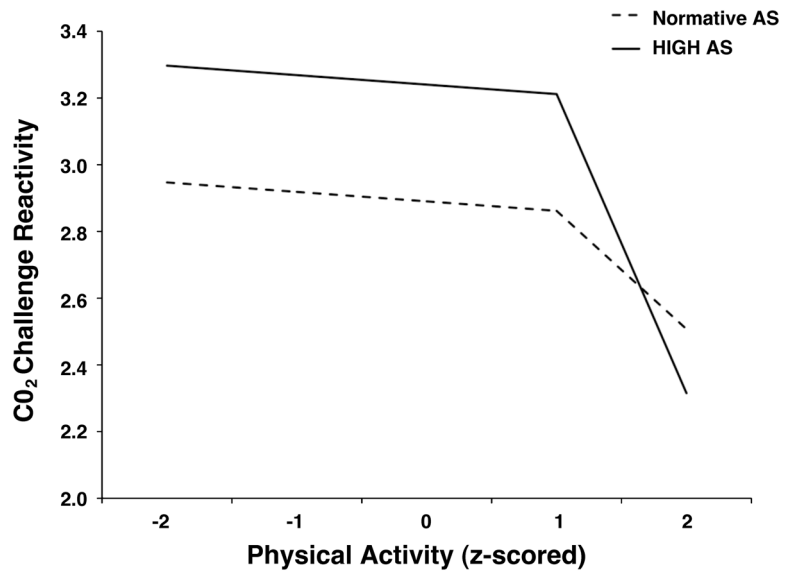


Figure 1. CO₂ challenge reactivity as a function of the interaction between physical activity and anxiety sensitivity.