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Links Between Anxiety and Allergies: Psychobiological Reality or Possible Methodological Bias?

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Abstract

The objective of the study was to examine the link between anxiety and allergies to establish whether it reflects a psychobiological reality or a possible methodological bias. A cohort of 1,037 children enrolled in the study. Anxiety disorders were assessed between 11 and 21 years. Anxious personality was assessed at 18 years. Allergies were examined at 21 years by (a) self reports, (b) skin pricks, and (c) serum total immunoglobulin E (IgE). Self-reported allergies were predicted by recurrent anxiety disorders (OR [95% CI]=1.56 [1.06–2.30], $p=.023$) and self-reports of anxious personality (OR [95% CI]=1.67 [1.17–2.37], $p=.004$): Objectively verified allergies were not. These results suggest that the link between anxiety and allergies may reflect a methodological artifact rather than a psychobiological reality.

It has long been assumed that anxiety has adverse effects on health. In particular, research with both children and adults has documented associations between allergies and anxiety, variously assessed by personality measures and as reflected in psychiatric disorders such as panic disorder, separation anxiety disorder, and generalized anxiety disorder (e.g., Bell, Jasnosi, Kagan, & King, 1990; Goodwin, Castro, & Kovacs, 2006; Hart, Lahey, Hynd, Loeber, & McBurnett, 1995; Kagan, Snidman, Juliasellers, & Johnson, 1991; Kennedy, Morris, & Schwab, 2002; Kovalenko et al., 2001; Slattery et al., 2002; Stauder & Kovacs, 2003). For example, an early study examined the links between self-reported allergies (including reports of having been professionally diagnosed with an allergy) and shyness in a sample of 375 university undergraduate students (Bell et al., 1990). There were reported links between shyness and hayfever but not other types of allergies. Other studies have revealed links between anxiety and more general measures of atopy, and one study found that children with symptoms of separation anxiety disorder were more likely to have been treated for asthma or allergies as compared to those not showing symptoms of separation anxiety disorder (Slattery et al., 2002).

There are numerous explanations for the associations between psychological and physical disorders, including biological, behavioral, cognitive, and social pathways (see Cohen & Rodriguez, 1995). Whereas the first two pathways are hypothesized to result in increased

occurrence of physical symptoms, the latter two may result in an increase in the reporting of physical symptoms. It is possible to provide psychobiological explanations for the link between anxiety and allergies by noting links between anxiety and both the immune and nervous systems. However, for two main reasons caution must be taken before accepting psychobiological theories exclusively. First, previous studies typically rely on allergy data collected via self-reports, and it is possible that the association between anxiety and allergies is due to anxious participants being more aware of or more likely to misinterpret and report physical symptoms of allergies (Feldman, Cohen, Doyle, Skoner, & Gwaltney, 1999), as opposed to actually having more allergies. Indeed, there is substantial literature documenting links between neuroticism and reports of medical symptoms, as compared to objectively measurable ones (e.g., Costa & McCrae, 1985). For example, numerous studies have replicated the finding that neuroticism is associated with self-reported chest pains but not objective signs of coronary heart disease (e.g., Costa, Fleg, McCrae, & Lakatta, 1982; Elias, Robbins, Blow, Rice, & Edgecomb, 1982). To examine the potential impact of this methodological factor, the current study examines allergies by self-report, skin-prick tests, and serum total immunoglobulin (IgE). Second, many previous studies have employed clinical or otherwise selected samples, limiting the generalizability of results. For example, anxiety has been studied in patients with various allergies, and one such study revealed that patients with allergic rhinitis and vasomotor rhinitis were more likely to report high levels of state and trait anxiety as compared to nonallergic controls (Addolorato et al., 1999). The current study assesses the association between anxiety and both self-reported and objectively verified allergies in a representative birth cohort, enabling us to examine the link between anxiety and allergies in the general population.

METHOD

Participants

Participants are members of the Dunedin Multidisciplinary Health and Development Study, a longitudinal investigation of the health and behavior of a complete birth cohort. The cohort of 1,037 children (52% male) was constituted at 3 years of age when the investigators enrolled 91% of consecutive births from April 1972 through March 1973 in Dunedin, New Zealand, who were still resident in the province of Otago. Cohort families are primarily White (91%) and represent the full range of socioeconomic status in the general population of New Zealand's South Island. At each assessment age, participants (including emigrants living overseas) are brought back to the research unit for a full day of individual data collection. Follow-ups have been performed at 5, 7, 9, 11, 13, 15, 18, 21, 26, and most recently 32 years of age ($n=972$, 96% of the living cohort members). In this article we present all available data on anxiety and stress reactivity (self-reports of anxious personality) obtained from ages 11 up until 21 years. We focus on allergy data collected at age 21, when allergies were examined by means of self-report, skin prick tests, and serum total IgE. Study members were asked if they had taken antihistamines in the past 7 days and 3 reported that they had. These 3 Study members were excluded from all analyses.

Measures

Anxiety: Psychiatric Diagnoses—Anxiety was assessed in private standardized interviews, using the Diagnostic Interview Schedule for Children (Costello, Edelbrock, Kalas, Kessler, & Klaric, 1982) at the younger ages (11–15 years) and the Diagnostic Interview Schedule (Robins, Cottler, Bucholz, & Compton, 1995; Robins, Helzer, Croughan, & Ratcliff, 1981) at the older ages (18 and 21 years), with a reporting period of 12 months at each age. Diagnoses followed the DSM-III criteria at ages 11, 13, and 15 and the DSM-III-R at ages 18 and 21.

Between 11 and 15 years, three anxiety disorders (overanxious disorder, separation anxiety, and phobias) were diagnosed. The six anxiety disorders diagnosed at 18 and 21 years were generalized anxiety disorder, obsessive compulsive disorder, panic disorder, agoraphobia, specific phobia, and social phobia. For analyses, anxiety was examined as a single group (anxiety disorders were not differentiated) reflecting their strong cross-sectional and longitudinal comorbidity (Gregory et al., 2007) and similarities between anxiety disorders in terms of genetic liability (Kendler, Prescott, Myers, & Neale, 2003), mental health histories (Gregory et al., 2007), and a common factor structure (Krueger, 1999). Because it is quite common for young people to have a single episode of anxiety lacking serious clinical consequences, we focused on recurrent disorder in relation to allergy. We divided participants into three groups: no anxiety diagnosis ($n=559$, 58%); single-episode anxiety disorder ($n=246$, 25%); or a recurrent history of anxiety disorder (anxiety was diagnosed at two or more time periods; $n=162$, 17%). Of note, prevalence rates of any anxiety disorder based on data from the Dunedin Study are virtually identical to the rates in the National Comorbidity Survey Replication (Kessler, Chiu, Demler, & Walters, 2005) for the young-adult age band.

Anxiety: Personality Assessment—Stress Reactivity was assessed at age 18 using the Multidimensional Personality Questionnaire (MPQ; Patrick, Curtin, & Tellegen, 2002). The MPQ is a self-report instrument designed to assess a broad range of individual differences in affective and behavioral style and has well-established psychometric properties (Krueger, Caspi, Moffitt, Silva, & McGee, 1996; Tellegen et al., 1988). The MPQ consists of 10 subscales, including a 14-item subscale measuring Stress Reactivity (the degree to which a person is nervous, vulnerable, sensitive, and prone to worry). This subscale shows good reliability in the Dunedin sample ($\alpha=.80$). The Stress Reactivity scores were split into terciles for certain analyses.

Allergies: Self-Report—At the 21 year assessment, study members were asked questions about possible allergies: “Have you ever had eczema or any kind of skin allergy?” “Are you allergic to insect stings?” “Have you ever had hayfever?” “Are you allergic to any medicines?” Study members could respond “yes” or “no” to each question and, if responding positively to the final question, were asked “Which medicine(s)?” In analyses, the proportion of participants self-reporting one or more allergies (62%) was examined in the three anxiety disorder groups. Of note, unreported analyses revealed no differences between those reporting a single allergy and those reporting multiple allergies in terms of association with anxiety.

Allergies: Objective Assessments—At age 21, study members were administered skin prick tests for 12 common allergens: house dust mite (*Dermatophagoides pteronyssinus*) (Bencard, UK), grass, cat, dog, horse, kapok, wool, *Aspergillus fumigatus*, alternaria, penicillium, cladosporium, and cockroach (Hollister Stier, US). Skin pricks are the most widely used allergy tests (Rusznak & Davies, 1998) and constitute an important diagnostic tool for allergies (for a review of the literature with regards to skin prick testing, see Oppenheimer & Nelson, 2006). As in previous reports (Sears et al., 1989), allergy was defined as one or more positive skin test with a maximum weal diameter of at least 2mm greater than that produced by the diluent control. Using this definition, we found that 65% of the sample had allergies (of note, 48% of the sample had two or more positive skin tests and 37% had three or more positive skin tests). The results were substantively identical when focusing upon those with a single allergy and those with multiple allergies (unreported). Furthermore, the associations with anxiety were largely unchanged employing a 3-mm cutoff. In analyses, the proportion of participants with one or more positive skin tests was examined in the three anxiety disorder groups.

Serum total IgE was also measured at age 21. IgE is a class of antibody that plays an important role in allergies, and serum total IgE is often raised in atopic individuals as compared to those without allergies (for a discussion of IgE and allergic disease, see Gould et al., 2003). At age 21 it was found that 48% of the study members had an elevated serum total IgE (defined here as 50 IU/ml or above). Fifty-four percent of the sample had serum total IgE of 35 IU/ml or above and 35% had a serum total IgE of 100 IU/ml or above. When these alternative cutoffs were used to define elevated serum total IgE, similar results were obtained. In analyses, the proportion of participants with serum total IgE > 50 IU/ml was examined in the three anxiety disorder groups.

Socioeconomic Status—Socioeconomic status (SES) was included as a covariate in analyses. The SES of the study members' families was measured on a 6-point scale that assessed parents' self-reported occupational status and allocates each occupation to 1 to 6 categories (1=*unskilled laborer*, 6=*professional*) on the basis of educational levels and income associated with that occupation from the New Zealand census (Elley & Irving, 1976).

Statistical Analyses

Two different sets of logistic regression analyses were run to establish whether anxiety-disorder status predicts allergies (dummy variables corresponded to single-episode anxiety and recurrent anxiety, with no anxiety disorder as a reference point). Model 1 examined the unadjusted odds ratio (OR) for anxiety disorder status predicting allergies. Model 2 examined the OR for anxiety disorder predicting allergies, after controlling for the effects of sex and SES. All analyses were then repeated using a personality measure of Stress Reactivity rather than anxiety-disorder status (dummy variables corresponded to moderate and high levels of stress reactivity, with low stress reactivity as a reference point).

RESULTS

Internal Associations for Different Measures of Anxiety and Allergies

There was a significant association between anxiety disorders and stress reactivity. Stress reactivity was lowest among participants never diagnosed with anxiety ($M=33.17$, $SD=23.98$), higher in those having experienced a single-episode of anxiety ($M=50.74$, $SD=27.72$), and highest in recurrent cases ($M=63.51$, $SD=26.03$; $F=102.44$, $df=2$, $p<.001$).

There were also strong links between self-reported and objectively verified allergies: A higher percentage of participants who reported allergies had one or more positive skin tests (75%) as compared to those who did not report allergies (49%; $\chi^2=62.19$, $df=1$, $p<.001$). Similarly, a higher percentage of participants who reported allergies had serum total IgE > 50 IU/ml (60%) as compared to those who did not report allergies (30%; $\chi^2=64.31$, $df=1$, $p<.001$). There was also an association between skin prick tests and serum total IgE, and 67% of those with positive skin tests had serum total IgE > 50 IU/ml. In contrast, only 14% of those without positive skin tests had serum total IgE > 50 IU/ml ($\chi^2=198.45$, $df=1$, $p<.001$).

Anxiety Disorders and Allergies

Anxiety disorders were significantly linked to self-reported allergies (Figure 1A). A higher proportion of study members with *recurrent* anxiety disorders self-reported allergies compared to those with no history of anxiety disorders (OR=1.56, 95% confidence interval=1.06–2.30, $p=.023$). Study members with single-episode anxiety were not more likely to self-report allergies compared to those with no history of anxiety (see Table 1). In contrast to the self-reported allergy data, anxiety-disorder status was not significantly

associated with objectively verified allergies (Figure 1B,C). A similar pattern of results was obtained after controlling for sex and SES (Table 1).

Anxious Personality and Allergies

Similar results were observed when we substituted our measure of anxiety disorders with our measure of anxious personality (Figure 2). Compared to low-anxious individuals, highly anxious (OR=1.67, 95% confidence interval=1.17–2.37, $p=.004$) study members were more likely to self-report allergies (Figure 2A). In contrast to the self-reported allergy data, anxious personality was not significantly associated with objectively verified allergies (Figure 2B,C). The results were largely unchanged when controlling for sex and SES (Table 2).

DISCUSSION

This study is the first to report that anxiety is associated with self-report but perhaps not objectively verified allergies. This was found when anxiety was assessed as a *disorder* and also as the *personality trait stress-reactivity*. Should our results be replicated, this would suggest that associations between anxiety and allergies reported by studies using self-report measures of allergies could be partially due to a methodological bias rather than a psychobiological reality. It is possible that specific individual anxiety disorders (Friedman & Morris, 2006) were associated with objective tested allergy. However, when subtypes of previously studied anxiety disorders were examined, we found that those suffering panic, generalized anxiety disorder, or specific phobia were significantly more likely to report allergies as compared to those without these disorders. In comparison, none of the anxiety subtypes were associated with objectively verified allergies.

The results should be considered in light of several limitations. First, different allergies were assessed by self-report and skin prick tests. It is therefore possible that different associations with anxiety could be due to different allergens being examined as opposed to a methods effect on the results. Indeed, one study reported associations between shyness and reports of professionally diagnosed hayfever although not asthma, eczema, or hives (Bell et al., 1990). It therefore remains possible that certain unmeasured allergens show similar associations with both self-reported and objectively verified allergies. However, physiological explanations for the associations between anxiety and allergies tend to be *general*, and we obtained similar patterns of results when defining allergies in different ways. For example, when we focused upon self-reported hayfever or skin allergy, which constitutes a more homogeneous group than including *any* of the four types of self-reported allergy, substantively identical associations with anxiety were obtained. Furthermore, when we examined serum total IgE, which constitutes a more general objective measure of allergies than skin prick tests, similar nonassociations with anxiety were found.

A second, related issue is that there is intrinsic difficulty in matching subjective reports of symptoms suggesting allergy with objective tests of allergy, even in those conditions that usually do have an allergic basis that is measurable by skin testing or IgE (such as hayfever). In the present study, self-reported allergies were reported in terms of hayfever and skin allergies or eczema. We also have questions relating to drug allergy and insect sting allergy, neither of which are appropriately identified by IgE levels or skin tests, and we have no objective testing for either of those allergies in the study. The panel of skin tests was assembled based on allergens commonly responsible for asthma and hayfever in New Zealand. It is, however, unlikely that somebody would be highly allergic to a substance for which we did not test without showing allergy to at least one of these environmental allergens, which included pollens, animal danders, molds, cockroach, and house dust mite. It would be most unusual to be atopic without showing a positive reaction to at least one of

these common allergens. A related issue is that it is possible to be atopic (i.e., have positive skin tests) without having any symptoms at all, and it is possible to have symptoms that are sometimes associated with allergy but for these symptoms in that individual to have a nonallergic basis. For example, nonallergic rhinitis due to vasomotor hyperactivity will give the same symptoms of sneezing and runny nose as allergic rhinitis, but skin tests will be negative. Although we are aware that the correspondence between subjective and objective assessments is not perfectly parallel and that such matching is intrinsically difficult in this area of research, this applies the same to anxious and nonanxious groups, and it is therefore difficult to see how it could contribute to the pattern of group differences that we have discovered.

A third limitation concerns the period of assessment of allergies. Whereas, by the nature of the assessment method, only *current* objectively verified allergies were examined, some of the self-reported allergies (eczema and hayfever) were assessed over the *life course*, which was necessary given the presentation of certain allergies (e.g., hayfever may occur seasonally and eczema sporadically). As allergies may not be stable across the life course it is possible that the stronger associations with anxiety for self-reported allergies as compared to objectively verified allergies could be partly due to time periods under investigation. This limitation is attenuated by the fact that certain psychobiological explanations for the links between anxiety and allergies, such as there being strong genetic influence on the association (Wamboldt, Schmitz, & Mrazek, 1998), are consistent with bidirectional associations and are compatible with the expectation of longitudinal links between anxiety and allergies.

Finally, our results were obtained from a single birth cohort from a single geographical location. Because rates of certain allergies have been increasing over time (Sears, 1997) and vary throughout the world (Beasley et al., 1998), it is important to replicate results in other cohorts and regions.

Despite these limitations, the results reported here have at least three potential implications. First, the results could have implications for the *assessment of allergies*. Although there was overlap between self-reported and objectively verified allergies, the former method of assessment may also reflect factors unrelated to allergies, such as levels of anxiety. Therefore, it is useful to additionally obtain objective measures of allergies in research settings and when making diagnoses of allergic illness in clinical settings.

Second, the results of this study could have implications for *explanations of the link between anxiety and allergies*. The finding that anxiety is linked to self-reports of allergies but not to objectively verified allergies suggests that psychobiological explanations alone may be inadequate. In contrast, the results of this study are perhaps more compatible with explanations that focus on the role of perceptual biases whereby anxious individuals misinterpret or misreport their physical symptoms or both. The results are also consistent with the possibility that anxious individuals are more sensitive to the physical symptoms of allergies (reporting allergies when present).

Third, the results of this study could have *clinical implications*. Anxious individuals may worry needlessly about physical problems. Although it would be ill founded to conclude that anxious individuals are not at risk for *any* health problem, mounting evidence suggests that links between negative affectivity and certain health problems are an artifact of using self-report methodologies in health research (Feldman et al., 1999; Watson & Pennebaker, 1989). Relaying this type of information back to anxiety disorder patients who do not show objectively assessed problems may help to reassure them (Andrews, 1994).

This study demonstrates an association between anxiety and self-reported but not objectively verified allergies, suggesting that it is possible that anxious individuals misinterpret, misreport, or are more sensitive to their physical symptoms, but do not actually experience more allergies. More generally, these findings suggest that psychosomatic research should seek to employ both subjective and objective measures of health status. Such multimethod research will go some way toward documenting and explaining the links between mental and physical health.

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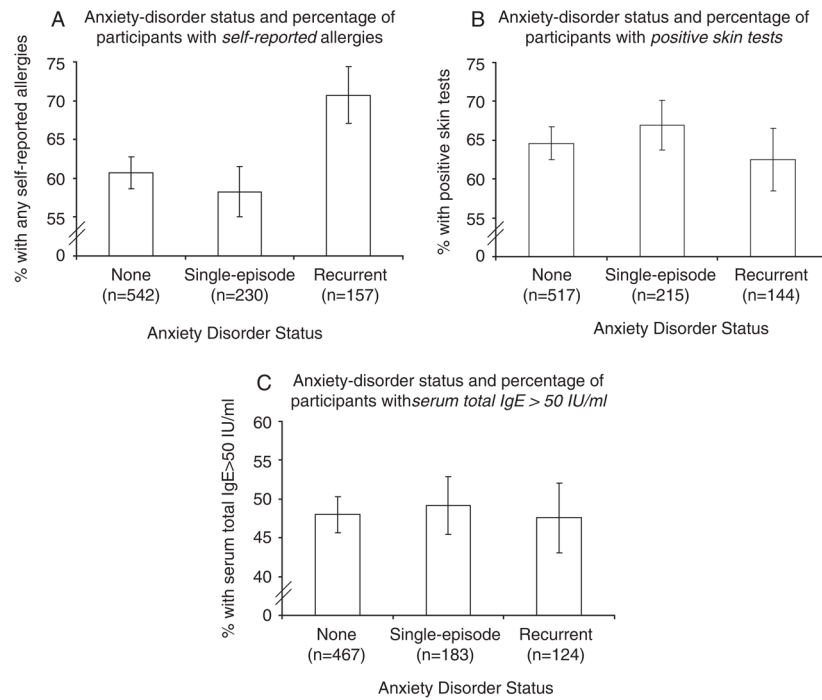


Figure 1. Anxiety disorder status and percentage of participants with allergies (standard error bars shown). Panel A: Anxiety-disorder status and percentage of participants with *self-reported* allergies. Panel B: Anxiety-disorder status and percentage of participants with *positive skin tests*. Panel C: Anxiety-disorder status and percentage of participants with *serum total IgE > 50 IU/ml*.

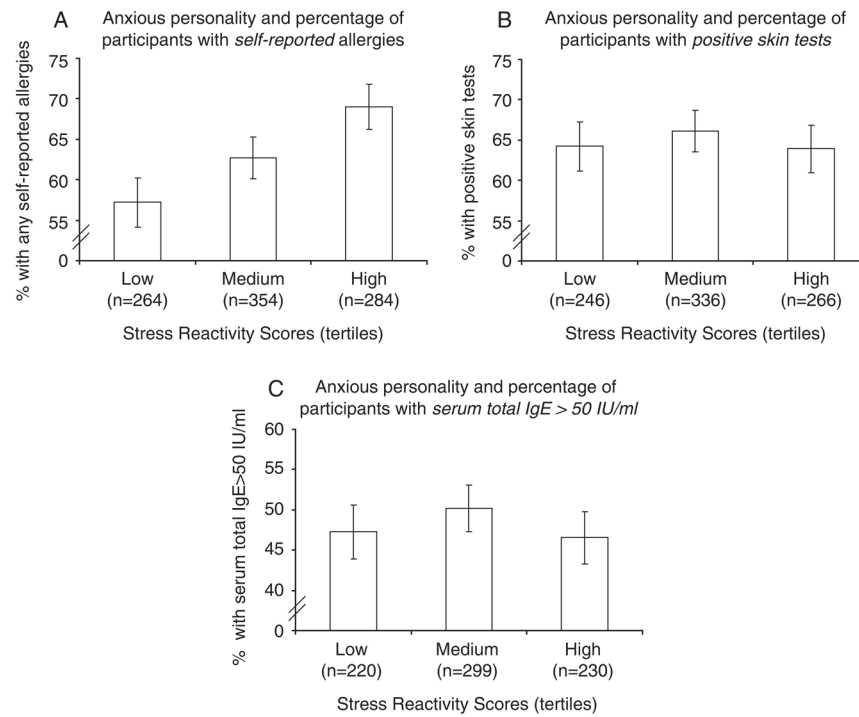


Figure 2. Anxious personality (assessed by the Stress Reactivity Scale) and percentage of participants with allergies (standard error bars shown). Panel A: Anxious personality and percentage of participants with *self-reported* allergies. Panel B: Anxious personality and percentage of participants with *positive skin tests*. Panel C: Anxious personality and percentage of participants with *serum total IgE > 50 IU/ml*.

Table 1
 Predicting Allergies (Assessed Using Self-Report, Skin Prick, and Total Serum IgE) From Anxiety Disorders

Model	Variable	β	SE	p	OR	95% OR
Predicting allergies (assessed by self-report) from anxiety disorders						
1	Anxiety (single episode)	-.10	.16	.527	0.90	0.66–1.24
	Anxiety (recurrent)	.45	.20	.023	1.56	1.06–2.30
2	Sex	-.25	.14	.073	0.78	0.59–1.02
	SES	.05	.06	.399	1.05	0.93–1.19
	Anxiety (single episode)	-.15	.16	.375	0.87	0.63–1.19
	Anxiety (recurrent)	.40	.20	.045	1.50	1.01–2.21
Predicting allergies (assessed by skin pricks) from anxiety disorders						
1	Anxiety (single episode)	.11	.17	.539	1.11	0.79–1.56
	Anxiety (recurrent)	-.09	.20	.642	0.91	0.62–1.34
2	Sex	.24	.15	.092	1.28	0.96–1.70
	SES	.11	.06	.086	1.12	0.99–1.26
	Anxiety (single episode)	.17	.18	.325	1.19	0.84–1.67
	Anxiety (recurrent)	.01	.20	.990	1.00	0.68–1.48
Predicting allergies (assessed by measuring serum IgE) from anxiety disorders						
1	Anxiety (single episode)	.05	.17	.780	1.05	0.75–1.48
	Anxiety (recurrent)	-.02	.20	.939	0.99	0.66–1.46
2	Sex	.28	.15	.055	1.33	0.99–1.78
	SES	.01	.06	.927	1.01	0.89–1.14
	Anxiety (single episode)	.11	.18	.538	1.12	0.79–1.58
	Anxiety (recurrent)	.05	.21	.801	1.05	0.70–1.58

Note: Dummy variables corresponding to single-episode anxiety and recurrent anxiety are compared to those with no anxiety disorder as a reference point. Models 1 provide the unadjusted odds ratio for anxiety predicting allergies. Models 2 provide the odds ratios after controlling for sex and socioeconomic status (SES). β =coefficient; SE=standard error of β ; p=significance level; OR=odds ratio. Sex is coded as 1=female; 2=male.

Table 2
 Predicting Allergies (Assessed Using Self-Report, Skin Prick, and Total Serum IgE) From Anxious Personality (Assessed by the Stress Reactivity Scale)

Model	Variable	β	SE	p	OR	95% OR
Predicting allergies (assessed by self-report) from anxious personality						
1	Anxiety (single episode)	.23	.17	.166	1.26	0.91–1.74
	Anxiety (recurrent)	.51	.18	.004	1.67	1.17–2.37
2	Sex	-.19	.14	.190	0.83	0.63–1.10
	SES	.03	.06	.628	1.03	0.91–1.17
	Anxiety (single episode)	.22	.17	.197	1.24	0.89–1.72
	Anxiety (recurrent)	.47	.18	.011	1.60	1.12–2.29
Predicting allergies (assessed by skin pricks) from anxious personality						
1	Anxiety (single episode)	.08	.18	.644	1.09	0.77–1.53
	Anxiety (recurrent)	-.01	.18	.940	0.99	0.69–1.42
2	Sex	.24	.15	.099	1.28	0.96–1.71
	SES	.11	.07	.100	1.11	0.98–1.27
	Anxiety (single episode)	.13	.18	.480	1.13	0.80–1.61
	Anxiety (recurrent)	.08	.19	.675	1.08	0.75–1.57
Predicting allergies (assessed by measuring serum IgE) from anxious personality						
1	Anxiety (single episode)	.12	.18	.515	1.12	0.79–1.59
	Anxiety (recurrent)	-.03	.19	.873	0.97	0.67–1.41
2	Sex	.29	.15	.059	1.33	0.99–1.79
	SES	.03	.06	.702	1.03	0.90–1.16
	Anxiety (single episode)	.15	.18	.403	1.16	0.82–1.65
	Anxiety (recurrent)	.08	.20	.691	1.08	0.74–1.58

Note: Dummy variables corresponding to moderate levels of stress reactivity and high levels of stress reactivity are compared to low stress reactivity as a reference point. Models 1 provide the unadjusted odds ratio for stress reactivity predicting allergies. Models 2 provide the odds ratios after controlling for sex and socio-economic status (SES). β =coefficient; SE=Standard error of β ; *p*=significance level; OR=odds ratio. Sex is coded as: 1=*female*; 2=*male*.