

# Major Depression and Allergy: Does Neuroticism Explain the Relationship?

RENEE D. GOODWIN, PhD, MPH, MARIO CASTRO, MD, MPH, AND MONIKA KOVACS, MD

**Objective:** To determine the association between major depression, neuroticism, and self-reported allergy among adults in the community. **Methods:** Data were drawn from the Midlife Development in the United States Survey, a nationally representative sample of 3,032 adults age 25 to 74. ANOVA and multiple logistic regression analyses were used to determine the association between depression and allergy and the role of neuroticism in these relationships. These links were also examined by gender. **Results:** Among adults in the community, major depression was associated with a significantly increased likelihood of allergy (odds ratio [OR], 1.5; 95% confidence interval [CI], 1.14–1.98). Higher levels of neuroticism were also significantly associated with increased likelihood of allergy (OR, 1.22; 95% CI, 1.04–1.43). Among women, major depression was associated with a significantly increased likelihood of allergy (OR, 1.67; 95% CI, 1.15–2.41), and this relationship persisted after adjusting for demographic characteristics and neuroticism. Among men, there was no significant relationship between allergy and depression, yet neuroticism was related to allergy (OR, 1.42; 95% CI, 1.42–1.82), which persisted after adjustment for depression. **Conclusion:** These data are consistent with results of previous studies showing an association between major depression and allergy among adults and extend these data by providing preliminary evidence suggesting that this association is specific to women and independent of the effects of neuroticism among women. In addition, the data provide preliminary evidence that neuroticism may be related to allergy among men, though no link between depression and allergy was found among men. Future research with prospective, longitudinal studies is needed next to understand the possible biological underpinnings of these associations. **Key words:** epidemiology, major depression, allergy, comorbidity, neuroticism, mental disorders, personality factors.

**MIDUS** = Midlife Development in the United States; **CIDI** = Composite International Diagnostic Interview; **CIDI-SF** = Composite International Diagnostic Interview Short Form.

## INTRODUCTION

Previous studies have shown an association between atopic disease and depression (1–6). These data come mainly from four sources. First, data from clinical studies have shown that allergy patients show higher levels of depressive symptoms (5) compared with control groups. For instance, Kovacs et al. (6) found higher levels of depressive symptoms among allergy patients compared with those without allergy. Second, data from psychiatric clinic patients have reported a higher-than-expected level of allergic disease among patients with depression. Third, data from twin studies suggest a genetic link between atopy and depression. Wamboldt et al. (2) reported a familial link between atopy and depression in Finnish adults twins. Finally, several epidemiologic studies have shown links between allergy and depression in nonclinical samples (1,3,4). Timonen et al. (3) recently provided strong evidence of an association between allergy and depression in a community sample, using methodology that included allergy tested with skin-prick test and clinically diagnosed depression in a birth cohort study. Moreover, a number of studies have found significant gender differences in the relationship between allergy and depression among females. The link between allergy and depression was not evident among males except in the presence of more severe symptoms of depression (3,7). This finding of a link between allergy and depression in females has been replicated (3,7). In addition, associations

have been found between allergy and increased rates of depression and anxiety among adults in clinical samples (6,11,12).

Similarly, other data have suggested a link between personality and temperament and the presence of allergic diseases. Several reports by Keogh (8), Bell et al. (9), Kagan et al. (10), and Gauze et al. (11) have found an association between self-reported allergies and increased likelihood of behavioral inhibition among youth. In one study, preschool children with a history of atopy had significantly higher levels of behavioral inhibition compared with those without atopy (9). A familial association between atopy and behavioral inhibition has also been documented (10). Associations between specific personality factors and risk of mental disorders have been noted in several population-based studies (13,14). For instance, neuroticism is associated with increased risk of psychotic disorders (13) and with anxiety and depressive disorders (14,15).

Personality factors are thought to develop early in life and to play a fundamental role in patterns of behavior and emotional functioning, which are relatively consistent throughout the lifespan. Some personality factors are thought to be linked with both physical and mental disorders (e.g., neuroticism). Therefore, it is conceivable that the co-occurrence of mental and physical disorders (e.g., allergy and depression) could be related to result from the presence of specific personality factors (i.e., neuroticism) that increase the risk for both. Previous studies, however, have not examined the influence of neuroticism on the co-occurrence of allergy and depression. Finally, although previous studies have shown links between depressive symptoms and participant report of physicians' diagnosis of major depression, previous studies have not included a standardized measure of depression using DSM criteria. Therefore, although previous studies have suggested a linear relationship between depression symptom severity and likelihood of allergy, the relationship between allergy and clinical depression (i.e., diagnosis based on DSM criteria) in a general population sample has not been thoroughly examined.

From the Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY (R.D.G.); Department of Pulmonology and Critical Care Medicine, Washington University, St. Louis, MO (M.C.); and Semmelweis Institute, Budapest, Hungary (M.K.).

Address correspondence and reprint requests to Renee D. Goodwin, PhD, MPH, Department of Epidemiology, Mailman School of Public Health, Columbia University, 1051 Riverside Dr., Unit 43, New York, NY 10032. E-mail: rdg66@columbia.edu

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Accordingly, the goal of the current study is to investigate the relationship between depression and allergy and the role of neuroticism in this association in a large representative sample in the United States. In addition, we investigated each of these relationships by gender. The rationale for examining gender differences was two-fold. One, previous studies have documented gender disparities in the link between allergy and depression among both adults (3,7) and youth (9). In addition to these previous findings, the strong role of gender in depression suggested that gender may also be involved in these links.

The goal of this study was to begin to fill this gap by addressing four main questions. First, is there an association between self-reported allergy and major depression among adults in the community? Second, is there an association between allergy and neuroticism among adults in the community? Third, does the relationship between allergy, major depression, and neuroticism differ by gender? Fourth, does neuroticism explain the relationship between allergy and major depression? We hypothesized that there would be a relationship between allergy and major depression. Based on previous findings, we expected that this association may be more prominent among females than males.

## METHODS

### Study Design

The Midlife Development in the United States (MIDUS) Survey is a nationally representative survey of 3,032 persons age 25 to 74 years in the noninstitutionalized civilian population of the 48 coterminous United States (16,17). The MIDUS Survey was carried out by the John D. and Catherine T. MacArthur Foundation Network on Successful Midlife Development between January 1995 and January 1996. All respondents completed a 30-minute telephone interview (70.0% response rate) and filled out two mailed questionnaires estimated to take a total of about 90 minutes to complete (86.8% conditional response rate in the subsample of telephone respondents). The overall response rate was 60.8%. The data reported in this paper were weighted to adjust for differential probabilities of selection and nonresponse. More details on the MIDUS Survey design, field procedures, and sampling weights are available elsewhere (16,17).

### Demographic Characteristics

Self-reported data were gathered on age, gender, race, marital status, and level of educational attainment. For the purposes of these analyses, age was the only continuous variable (ranging from 25 to 74). Race (Caucasian and minority racial status); Marital status (married and unmarried); and educational attainment (high school diploma and did not complete high school) were collapsed into dichotomous variables.

### Diagnostic Assessment

The MIDUS Survey diagnoses were based on the Composite International Diagnostic Interview Short Form (CIDI-SF), a series of diagnostic-specific scales that were developed from item-level analyses of the Composite International Diagnostic Interview (CIDI) questions in the National Comorbidity Survey (NCS) (18–20). The CIDI-SF was designed to reproduce the full CIDI diagnoses as well as possible with only a small subset of the original questions. Details of specificity and sensitivity of CIDI-SF classifications are available elsewhere (20). CIDI-SF was used to diagnose major depression (past 12-months). Participants were presented with a list of physical illnesses, which included hay fever (allergy), as well as asthma/chronic bronchitis, tuberculosis, other lung disease, hypertension, AIDS, diabetes, hernia, stomach problems, ulcer, autoimmune disorders, neurological disorders, persistent problems with teeth and gums, and migraine headaches and were asked to

endorse any or all of those which they had experienced or been diagnosed with in the past 12 months.

### Personality Factors

Assessment of personality traits in the MIDUS, based on the “big five” factor model, was developed using the results of a pilot study, which was conducted in 1994 with a probability sample of 1,000 men and women, age 30 to 70 (574 valid cases were usable for item analysis) (21–24). Items with the highest item to total correlations and factor loadings were selected for MIDUS. Forward regressions were also conducted to determine the smallest number of items needed to account for over 90% of the total scale variance. Scales included agreeableness (helpful, warm, caring, softhearted, sympathetic) ( $\alpha = 0.80$ ) (5-item scale); openness to experience (creative, imaginative, intelligent, intelligent, curious, sophisticated, adventurous) ( $\alpha = 0.77$ ; 7-item scale); conscientiousness (organized, responsible, hardworking, [not] careless) ( $\alpha = 0.57$ ; 4-item scale); extraversion (outgoing, friendly, lively, active, talkative) ( $\alpha = 0.78$ ; 5-item scale); and neuroticism (moody, worrying, nervous, [not] calm) ( $\alpha = 0.74$ ; 4-item scale). The  $\alpha$ s are based on the MIDUS national sample.

### Analytic Strategy

First, the association between allergy and major depression was examined using F-based tests of independence, with significance set at 0.05. We examined the differences in mean (SD) of neuroticism between those with and without allergy using ANOVA. Next, multiple logistic regression analyses were used to determine the association between allergy and depression. First, unadjusted analyses were run to calculate odds ratios (with 95% confidence intervals) of the link between allergy and depression. Next, these analyses were adjusted for demographic differences (i.e., gender, age, race, marital status, education); the analyses were then further adjusted for neuroticism. The same analyses were then rerun with the sample stratified by gender.

## RESULTS

### Prevalence and Sociodemographic Characteristics

Six hundred respondents (14%) reported having allergy and 617 (14.2%) reported depression. Those with allergy were younger (45.6 (12.2) versus 47.2 (13.2) years old,  $p = .03$ ) than those without allergy. There were no significant differences in gender, race, education, or marital status between adults with and without allergy.

### Association Between Major Depression, Neuroticism, and Allergy Among Adults

Major depression was associated with a significantly increased likelihood of allergy, compared with those without allergy (18.9% (79/418) versus 13.4% (296/2214);  $\chi^2 = 8.8$ ,  $df = 1$ ,  $p = .003$ ). Allergy was also associated with significantly higher levels of neuroticism (M (SD), 2.33 (0.67) versus 2.24 (0.66),  $F = 6.09$ ,  $p = .014$ ). After adjusting for demographics and neuroticism, the relationship between major depression and allergy persisted (OR, 1.36; (1.02, 1.81)) (see Table 1). Similarly, the link between neuroticism and allergy remained after adjusting for demographics and major depression (OR, 1.18; (1.0, 1.39)), suggesting that major depression and neuroticism are each independently related to allergy.

### Association Between Major Depression, Neuroticism, and Allergy Among Male Adults

Among males, depression was not associated with allergy (13.6% (27/196) versus 10.5% (113/1067),  $\chi^2 = 1.7$ ,  $df = 1$ ,

TABLE 1. Association Between Major Depression, Neuroticism, and Allergy Among Adults in the Community

	Allergy, Unadjusted OR (95% CI)	Allergy, AOR1 (95% CI)	Allergy, AOR2 (95% CI)
Major depression	1.5 (1.14–1.98)*	1.5 (1.13–1.98)*	1.36 (1.02–1.81)*
Neuroticism	1.22 (1.04–1.43)*	1.23 (1.05–1.45)*	1.18 (1.0–1.39)*

\*  $p < .05$ .

AOR1 = adjusted for differences in gender, age, race, marital status, and educational attainment. AOR2 = adjusted for demographic differences, depression, and neuroticism simultaneously.

$p = .19$ ); but higher neuroticism was associated with a significantly increased likelihood of allergy (M (SD) 2.27 (0.64) versus 2.13 (0.62),  $F = 8.7$ ,  $p = .003$ ). After adjusting for demographics, depression, and neuroticism, neuroticism remained significantly associated with increased likelihood of allergy. The link between depression and allergy was not significant among males (see Table 2). After adjusting for demographics, the link between neuroticism and allergy remained statistically significant and persisted after adjusting for depression (OR, 1.42 (1.1, 1.82)).

#### Association Between Major Depression, Neuroticism, and Allergy Among Female Adults

Major depression was associated with a significantly increased likelihood of allergy among females (23.6% (52/220) versus 16.1% (183/1129),  $\chi^2 = 7.3$ ,  $df = 1$ ,  $p = .007$ ). Neuroticism was not directly linked with allergy among females (M (SD) 2.38 (0.69) versus 2.35 (0.67),  $F = 0.4$ ,  $p = .5$ ). After adjusting for demographics, the link between depression and allergy persisted (OR, 1.67; (1.14, 2.37)) and continued to remain significant after adjusting for neuroticism (OR, 1.63; (1.15, 2.41)) (see Table 3). The link between neuroticism and allergy was not statistically significant.

#### DISCUSSION

Consistent with previous results, these data suggest that there is a significant relationship between allergy and depression among females but not males in the community. This relationship persists after further adjustment for differences in demographic characteristics and appears independent of the effects of neuroticism. Our results also provide preliminary evidence that there is a link between neuroticism and increased likelihood of allergy among adults and that this association appears specific to males and independent of the effects of major depression. These links have not previously

been demonstrated among a community-based population of adult in the United States.

The mechanism of association between allergy and depression in females cannot be determined due to the cross-sectional nature of these data. Although these findings are consistent with those of Timonen (3,7), they add to existing knowledge by replicating this gender difference in a sample of adults into older adulthood, whereas previous studies have been limited to relatively early adulthood. Therefore, the data suggest that age does not appear to play a role in this link and that it is consistent across age groups. These data also contribute to existing knowledge on the link between allergy and depression by providing data on depression collected using a well-validated epidemiologic instrument to assess depression using DSM criteria (20,25). Previous studies have relied on symptom measures and participant recall of having been given a diagnosis of depression by a physician during their lifetime, which are subject to treatment-seeking and recall biases. These results describe the relationship between allergy and past 12 months of depression, according to a standardized measure using DSM criteria (20,25). The results do not support the hypothesis that neuroticism explains the link between depression and allergy but instead suggest the link between depression and allergy is independent of neuroticism in females and that neuroticism is directly related to allergy among males independent of depression.

These data provide preliminary evidence that neuroticism may play a role in the vulnerability to allergy among males in the community. The mechanism of this link, however, is not known. It may be that individuals with high levels of neuroticism are more likely to develop both allergy and depression. Numerous studies have shown linkages between neuroticism and increased depression (13–15), though less is known about the linkage between neuroticism and allergy. Yet, this possible relation is consistent theoretically with results from clinical

TABLE 2. Association Between Major Depression, Neuroticism, and Allergy Among Male Adults in the Community

	Allergy, Unadjusted OR (95% CI)	Allergy, AOR1 (95% CI)	Allergy, AOR2 (95% CI)
Major depression	1.34 (0.85–2.1)	1.25 (0.79–1.98)	0.98 (0.6–1.6)
Neuroticism	1.43 (1.13–1.82)*	1.41 (1.11–1.8)*	1.42 (1.1–1.82)*

\*  $p < .05$ .

AOR1 = adjusted for differences in age, race, marital status, and educational attainment; AOR2 = adjusted for demographic differences, depression, and neuroticism simultaneously.

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**TABLE 3. Association Between Major Depression, Neuroticism, and Allergy Among Female Adults in the Community**

	Allergy, Unadjusted OR (95% CI)	Allergy, AOR1 (95% CI)	Allergy, AOR2 (95% CI)
Major depression	1.61 (1.14–2.28)*	1.67 (1.15–2.41)*	1.63 (1.14–2.32)*
Neuroticism	1.07 (0.87–1.33)	1.05 (0.84–1.31)	0.97 (0.77–1.22)

\*  $p < .05$ .

AOR1 = adjusted for differences in age, race, marital status, and educational attainment; AOR2 = adjusted for demographic differences, depression, and neuroticism simultaneously.

studies showing that behavioral inhibition is associated with increased allergy among male youth (9) and showing a familial association between behavioral inhibition and allergy (10). It may be that there is a common genetic vulnerability to both allergy and behavioral inhibition or neuroticism among males. Neuroticism and behavioral inhibition have been thought to be similar if not overlapping constructs. Alternatively, it may be that having high levels of neuroticism increases the likelihood of perceiving allergic responses to exposures that individuals with lower levels of neuroticism may not report. It is not known whether report bias or somatization occurs, (26), yet as high neuroticism is thought to be associated with perceiving the world and events in a negative light, those with high neuroticism may perceive symptoms more readily than those less sensitive with low neuroticism to such exposures or symptoms.

Another potential pathway that could explain this association is that allergy leads to functional impairment and distress in coping with uncomfortable and painful allergy symptoms daily, such that this leads to increased risk of depression onset. As allergy is chronic in the majority of cases (27), persisting for years, and has been shown to be associated with high levels of occupational disability and impairment in social relationships (28,29), it is conceivable that allergy may contribute to the risk of depression. Similarly, although neuroticism as a personality trait is thought to develop early in life, it may be that having allergy leads to an increase in negative thoughts and response patterns to external stimuli due to daily stress and discomfort associated with having allergy. Alternatively, it is possible that depression increases vulnerability to developing allergy through weakening the immune system or another biological pathway, as has been suggested in various clinically based studies (30,31). Still, none of these pathways fully address why these gender differences would emerge. The gender differences suggest that multiple pathways or a combination of pathways is more likely contributing or that there are other social, biological, or genetic factors at work.

Our findings are consistent with previous results showing consistent gender differences in the relationships between allergy and major depression in adults. As the data presented in this study are also cross-sectional and observational, rather than experimental, it is not possible to obtain evidence addressing the possibility of a causal relationship. Previous studies have shown strong differences in gender and depression and speculated extensively on the possible immune-related pathways of this association (see Timonen et al. (3)

and Kovacs et al. (6) for review). Although depression and allergy are strongly related in females, neuroticism does not appear to play a role in this link, nor is it directly related to allergy. In addition, the relationship between allergy and neuroticism among males persists, whereas there is no significant link between allergy and depression, and depression does not appear to affect the relationship between allergy and neuroticism. As such, these data may provide preliminary evidence suggesting that allergy is more strongly related to neuroticism in males and more strongly related to depression in females. These findings clearly require replication with more refined measures.

Limitations of this study are numerous and should be considered when interpreting these results. First, data on allergy was self-reported and therefore may be biased by tendencies toward overreporting among persons with depression, as previous studies suggest higher levels of somatic symptoms reported among persons with mental disorders compared with those without. It should be noted that depression was measured only for the past 12 months, rather than lifetime. Therefore, these limitations on the assessment of either or both depression and allergy could influence results. Second, information was available only on adults age 25 to 74; therefore these findings are not generalizable to other age groups. Future studies that can examine the linkages between personality traits, allergy, and depression using prospective, longitudinal epidemiologic data beginning in childhood with biological measures of allergy status and possibly on immune functioning, as well as longitudinal data on personality factors, major depression, and common behavioral risk factors for both, are needed next for replication of these findings and to further our understanding of the mechanism of these linkages, especially in uncovering the reason for gender differences in these relationships.

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