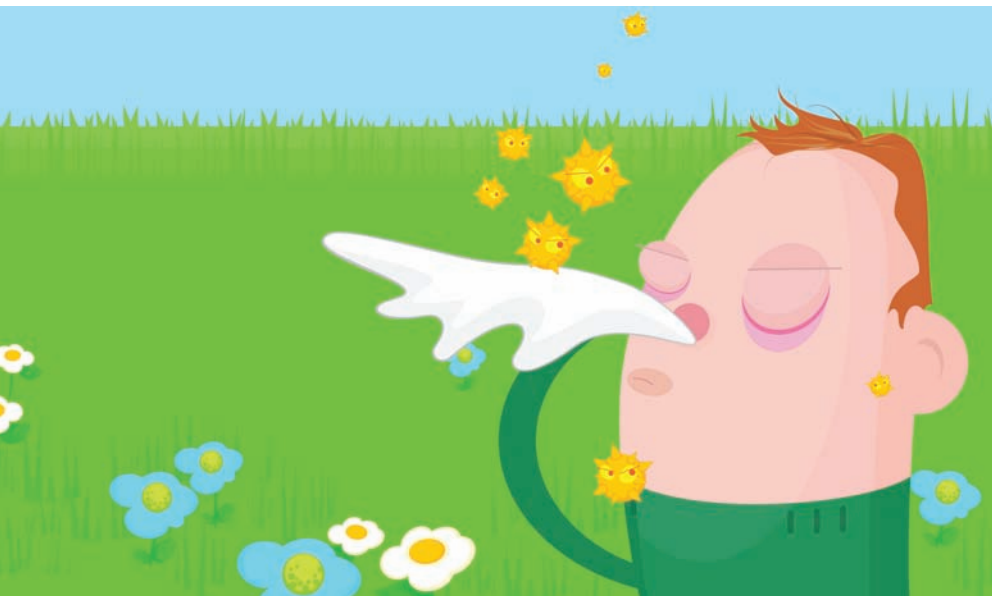


The Interface



ALLERGIC RHINITIS: Relationships with Anxiety and Mood Syndromes

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This ongoing column is dedicated to the challenging clinical interface between psychiatry and primary care—two fields that are inexorably linked.

ABSTRACT

In this article, the authors examine the preponderance of publications pertaining to relationships between allergies and anxiety and mood syndromes. Through a review of the relevant articles in the PubMed and PsycINFO databases, the authors found that the majority of studies (9 of 11 studies on anxiety syndromes, 10 of 12 studies on depressive syndromes) indicate associations

between allergies and anxiety/mood syndromes, despite a number of methodological variances. In addition, there appear to be a number of potential variables that mediate the relationship between allergies and these two psychiatric phenomena (e.g., allergies may heighten risk for these syndromes by triggering the immune system and cytokines; allergies may impair sleep through nasal obstruction and secondarily exacerbate psychiatric

symptoms; and allergies may negatively affect cognitive functioning and contribute to psychiatric disturbance) as well as a possible shared genetic risk. The authors review and discuss these variables.

KEY WORDS

Allergic rhinitis, anxiety, anxiety disorders, depression, mood disorders, panic disorder

INTRODUCTION

Runny itchy nose, sneezing, and nasal congestion—sound familiar? These are the commonplace symptoms of rhinitis, which we have all experienced at some point in our lives during a cold. These are also the identical symptoms for allergic rhinitis—the focus of this edition of *The Interface*.

Up to 30 percent of the adult population suffers from allergies.¹ Allergic rhinitis may be classified as seasonal (i.e., symptoms occur during a specific time of the year) or perennial (i.e., symptoms occur year round).¹ Seasonal rhinitis is typically caused by identifiable outdoor allergens, such as tree, grass, and weed pollens as well as molds. Perennial rhinitis may be precipitated by dust mites, cockroaches, animal proteins, and fungi.¹ In contrast to allergic rhinitis, some forms of reactive rhinitis, such as vasomotor rhinitis, manifest as a nonallergic reaction to environmental irritants, such as tobacco smoke, vehicle fumes, changes in temperature, strong fragrances, fibers, and alcoholic beverages.

Regardless of the nature of the allergen, the symptoms of allergic rhinitis are notably discomforting. In addition to acute discomfort, however, there appears to be empirical evidence for a relationship

between allergic rhinitis and specific psychiatric syndromes such as anxiety and mood disorders. In this edition of The Interface, we explore the possible relationships between allergic rhinitis and anxiety and mood disorders, which is relevant for contemplation in both psychiatric and primary care settings.

ALLERGIC RHINITIS AND ANXIETY SYNDROMES

Through a search of the PubMed and PsycINFO databases, we encountered 11 articles with empirical findings related to anxiety symptoms in individuals with allergies.²⁻¹² We eliminated articles that primarily focused on some adjunctive aspect of our query as well as those with very small sample sizes. The remaining articles are summarized in Table 1.

From a scientific perspective, it is very difficult if not impractical to directly compare these data sets because of varying population types, divergent assessment methods for the confirmation of allergies, and differing study measures for the determination of anxiety symptoms/disorders. For example, the 11 samples come from five different countries, participants either self-reported allergies or underwent formal confirmatory testing, and only two studies used the same measure to assess anxiety symptoms/disorders. So, at the outset, there are a number of potential methodological quagmires in meaningfully comparing these studies. However, as an overview, despite varying methodologies, 9 of the 11 studies reported a positive association between allergies and anxiety syndromes. For example, Cuffel et al⁵ examined the healthcare claims of more than 85,000 individuals and found that

anxiety symptoms were 1.41 times higher in individuals with allergies versus those without allergies. Likewise, in a sample of more than 12,000 individuals, Patten and Williams⁹ determined that allergic individuals evidenced a higher rate of panic disorder (odds ratio [OR]=1.7) as well as social phobia (OR=1.3).⁹

One fundamental approach to examining these data is to tally the number of participants in studies with positive results versus the number of participants in studies with negative results. In doing so, 102,068 individuals were in studies indicating a positive relationship between allergies and anxiety syndromes whereas 97 individuals were in studies indicating a negative relationship between allergies and anxiety syndromes. Thus, a very large majority of individuals (99.9%) were in studies that evidenced a decisive and positive relationship between allergy symptoms and anxiety syndromes.

We also examined studies with negative findings (i.e., those in the minority) for any potential or noteworthy confounds. In doing so, we found that researchers in the Marshall et al⁶ study used the Positive Affect Negative Affect Schedule (PANAS) for the assessment of anxiety symptoms. While negative affect may be associated with anxiety, Zevon and Tellegen found that the descriptors underlying the PANAS construct are, “being upset, distressed, hostile, irritable-angry, scared, afraid-fearful, ashamed, guilty, nervous,” and “jittery”—but there is no explicit descriptor for clinical anxiety.¹³ In other words, while the Marshall study did not confirm a relationship between allergies and anxiety, the study scale used to assess anxiety was inadequate,

thereby affecting the conclusions of the study. In the Kennedy study,⁷ in which researchers investigated the link between allergy and panic disorder patients, the sample was atypical (i.e., the sample consisted solely of panic disorder patients). Given that panic disorder is highly comorbid with other types of anxiety syndromes, it is likely that the unusual clinical composition of this sample washed out potential findings between panic-disorder participants with and without allergies.

ALLERGIC RHINITIS AND DEPRESSIVE SYNDROMES

In addition to studies on the association between allergies and anxiety syndromes, a number of studies have examined associations between allergies and depressive symptoms (Table 2).^{3,5,7-11,14-18} After eliminating articles according to the previous exclusion criteria, we encountered 12 relevant publications in the PubMed and PsycINFO databases.

Similar to the previous group of studies on anxiety syndromes, direct comparisons of these data are compromised for exactly the same cited reasons. Explicitly, the samples come from five different countries, participants either self-reported allergies or underwent formal confirmatory testing, and the assessments for depression markedly vary across studies. In addition, the assessments for depression in these studies vary in their ability to be translated into clinical or *Diagnostic and Statistical Manual for Mental Disorders (DSM)* diagnoses of depression. Despite these methodological variations, 10 of 12 studies report positive relationships between allergies and depression. For example, in their data analysis

TABLE 1. Studies in adults on the relationship between rhinitis and anxiety syndromes

FIRST AUTHOR/ YEAR OF PUBLICATION	SAMPLE SIZE/STUDY CHARACTERISTICS	RHINITIS CHARACTERISTICS	ANXIETY DISORDER ASSESSMENT	FINDINGS
Nal ² /1991	23 allergic patients/ Turkish sample	Allergies of organic origin	Symptom Checklist	Allergies correlated with anxiety scores
Gauci ³ /1993	22 females, controls/ Australian sample	Perennial allergic rhinitis; proven allergy status	Minnesota Multiphasic Personality Inventory (MMPI)	Number of allergies correlated with anxiety scale
Addolorato ⁴ /1999	24 allergic rhinitis and 21 vasomotor rhinitis patients/Italian sample; controls	Allergic vs. vasomotor rhinitis	State and Trait Anxiety Inventory (STAI)	Percentage of participants with high levels of state and trait anxiety significantly higher in both symptom groups vs. controls
Cuffel ⁵ /1999	85,298 patients/healthcare claims database	Diagnosis of allergic rhinitis	Anxiety diagnoses on claims forms	Odds of anxiety diagnosis 1.41 times higher in allergic rhinitis patients than controls
Marshall ⁶ /2002	69 patients allergic to ragweed vs. 65 controls	Self-reported allergy symptoms	Positive Affect Negative Affect Scales (PANAS)	No significant between-group differences regarding anxiety
Kennedy ⁷ /2002	28 panic-disorder patients with allergies; 11 panic-disorder patients without allergies/chart review	Seasonal allergies mixed in with drug, food, and contact allergies (“the allergic group”)	Structured Clinical Interview for DSM-III-R; Hamilton Anxiety Scale	No significant between-group differences regarding anxious mood, generalized anxiety disorder, social phobia, agoraphobia
Goodwin ⁸ /2002	418 nationally representative subjects with hay fever/interview, surveys	Self-reported hay fever	Composite International Diagnostic Interview, Short Form (CIDI short form)	Panic attacks greater in hay fever sufferers, but not generalized anxiety disorder
Patten ⁹ /2002	12,171 patients with self-reported allergies/ Canadian sample	Self-reported allergies	World Mental Health Composite International Diagnostic Interview	Allergy sufferers with greater panic disorder (OR=1.7) and social phobia (OR=1.3) diagnoses
Derebery ¹⁰ /2008	15,000 households	3831 participants with active rhinitis symptoms	Self-report symptom survey	Anxiety disorder, 9.3% in rhinitis sufferers vs. 3.9% in controls
Bhattacharyya ¹¹ /2008	230 patients with rhinosinusitis	Rhinosinusitis	Hospital Anxiety and Depression Scale	23.5% of those with rhinosinusitis with anxiety
Postolache ¹² /2009	51 patients with unipolar or bipolar depression	Tree-pollen positive = 12	Structured Clinical Interview for DSM-IV (SCID)	Allergies scores correlated with anxiety scores

NOTE: OR = odds ratio

of more than 85,000 individuals, Cuffel et al⁵ found that a depression diagnosis was 1.7 times higher in individuals with allergies compared to those individuals without allergies.⁵ Likewise, in their examination of more than 12,000 individuals, Patten and Williams⁹ determined that major depression was more frequent in individuals with allergies (OR=1.5) than in individuals without allergies.⁹

Using our previous tally strategy, 104,124 individuals were in studies indicating a positive relationship between allergies and depression, whereas 3,060 individuals were in studies indicating a negative relationship between allergies and depression. As before, a very large majority of individuals (97.1%) were in studies that evidenced a positive relationship between allergy symptoms and some type of depressive syndrome.

In examining the two studies with negative statistical associations between allergies and depression,^{7,8} we encountered some interesting methodological issues. In the study by Kennedy et al,⁷ which again investigated whether there was an association between allergies and panic disorder, the assessment of depression was undertaken with the Hamilton Anxiety Scale, which is a 14-item clinician-rated scale.¹⁹ Only one item in this scale addresses depression, with the rater prompts being, “decreased interest in activities,” “anhedonia,” and “insomnia.” Given the nine *DSM* (4th edition, text revision)²⁰ criteria for major depression, this inquiry for mood disorder is likely to be inadequate. In the second study with purportedly negative findings (the Goodwin study),⁸ there was a significantly higher prevalence of major depression among hay-fever sufferers (18.9%) compared with

non-sufferers (13.4%). However, these initial differences apparently dissipated after controlling for sociodemographic differences and other mental disorders.

VARIABLES THAT MIGHT MEDIATE ALLERGIES AND ANXIETY/MOOD SYNDROMES

Given the strong evidence for relationships, albeit indistinct, between allergies and anxiety/mood syndromes, are there any potential mediating variables? Possible mediators might include but are not limited to 1) the effects of either syndrome on immunity and immune-related illnesses, with each possibly contributing to the presence of the other,²¹ perhaps via the presence of cytokines;²² 2) the physiological role of nasal obstruction and its impairing effects on sleep, with subsequently negative effects on psychiatric symptoms;^{23,24} 3) allergy-related disturbances in cognitive functioning and their subsequent effect on psychological well-being;^{25,26} and 4) a possible shared genetic risk between both allergies and depression.²⁷

CONCLUSION

Despite stark differences in methodologies, the majority of published studies indicate some type of indistinct relationship between allergies and anxiety and mood syndromes. The strength of these associations is difficult to discern, given the present data. There may be a number of allergy-related mediating variables, such as alterations in immunity/cytokines, the effects of nasal obstruction on sleep, disturbed cognitive functioning, and genetic overlap. Regardless, current evidence indicates that individuals with allergies appear to be at a higher risk, of an unknown degree, for

developing various types of anxiety and/or mood syndromes.

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TABLE 2. Studies in adults on the relationship between rhinitis and depressive syndromes

FIRST AUTHOR/YEAR OF PUBLICATION	SAMPLE SIZE/STUDY CHARACTERISTICS	RHINITIS CHARACTERISTICS	DEPRESSIVE DISORDER ASSESSMENT	FINDINGS
Gauci ³ /1993	22 females, controls/ Australian sample	Perennial allergic rhinitis; proven allergy status	Minnesota Multiphasic Personality Inventory	Number of allergies correlated with the depression scale
Cuffel ⁵ /1999	85,298 patients/healthcare claims database	Diagnosis of allergic rhinitis	Depressive diagnoses on claim forms	Odds of depression diagnosis 1.7 times higher in allergic rhinitis patients than controls
Hurwitz ¹⁴ /1999	599 patients with hay fever	Hay fever	Diagnostic Interview Schedule	Major depression in 8.9% of hay fever sufferers vs. 5.4% of controls
Kennedy ⁷ /2002	28 panic-disorder patients with allergies; 11 panic- disorder patients without allergies/chart review	Seasonal allergies mixed in with drug, food, and contact allergies (“the allergic group”)	Structured Clinical Interview for DSM-III-R; Hamilton Anxiety Scale	No association with depressed mood
Goodwin ⁹ /2002	418 nationally representative subjects with hay fever/interviews, surveys	Self-reported hay fever	Composite International Diagnostic Interview, Short Form	No association with depression
Patten ⁹ /2002	12,171 patients with self- reported allergies/Canadian sample	Self-reported allergies	World Mental Health Composite International Diagnostic Interview	Major depression greater in allergy sufferers (OR=1.5)
Timonen ¹⁵ /2002	1,654 participants/Finnish sample	Skin-test positive allergic rhinitis	Diagnosis based upon hospital discharge data	Women, depression OR=1.8; men, depression OR=0.9
Huurre ¹⁶ /2002	249 participants/Finnish sample	Self-reported allergies	Beck Depression Inventory	Allergy participants with greater depression
Bavbek ¹⁷ /2002	41 participants/Turkish sample	Seasonal and perennial allergic rhinitis	Symptom Checklist-90	Depression greater in allergy sufferers
Muluk ¹⁸ /2003	29 participants/Turkish sample	Self-reported allergic rhinitis	Minnesota Multiphasic Personality Inventory	Male subjects with higher depression scores
Derebery ¹⁰ /2008	3,831 participants	Active rhinitis symptoms	Self-report symptom survey	Depressive disorder in 17.2% of rhinitis sufferers vs. 8.3% of controls
Bhattacharyya ¹¹ /2008	230 participants	Rhinosinusitis	Hospital Anxiety and Depression Scale	13.0% with depression

NOTE: OR=odds ratio; DSM-III-R=*Diagnostic and Statistical Manual for Mental Disorders, Third Edition, Revised*

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