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Impact of allergy treatment on the association between allergies and mood and anxiety in a population sample

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Abstract

Background—Previous studies have suggested an association between allergy and mood and anxiety disorders. Yet, extant work suffers from methodologic limitations.

Objective—To investigate the association between physician diagnosed allergy and DSM-IV mood and anxiety disorders in the general population, and to examine the role of allergy treatment in this relationship.

Methods—Data were drawn from the German National Health Interview and Examination Survey, a population-based, representative sample of 4,181 adults aged 18-65 in Germany. Allergy was diagnosed by physicians during medical examination and mental disorders were diagnosed using the CIDI.

Results—Allergy was associated with an increased prevalence of any anxiety disorder (OR=1.3 (1.1, 1.6)), panic attacks (OR=1.6 (1.1, 2.1)), panic disorder (OR=1.6 (1.01, 2.3)), GAD (OR=1.8 (1.1, 3.0)), any mood disorder (OR= 1.4 (1.1, 1.7)), depression (OR=1.4 (1.1, 1.7)), and bipolar disorder (OR=2.0, (1.0, 3.8)). After adjusting for desensitization treatment status, these relationships were no longer significant. Those treated for allergy were significantly less likely to have any mood or anxiety disorder (OR=0.65 (0.4, 0.96)), compared to those untreated. All relationships were adjusted for age, sex and socioeconomic status (SES).

Conclusions & Clinical Relevance—These findings provide the first evidence of a link between physician diagnosed allergy and DSM-IV mood and anxiety disorders in a representative sample. Treatment for allergy may mitigate much of this relationship.

Keywords

allergy; asthma; epidemiology; anxiety; depression; mood

INTRODUCTION

Several epidemiologic studies have shown an association between allergy and depression [1-7], and, to a lesser extent, between allergy and anxiety disorders [7, 8]. Timonen et al 2002 [9] found a significant association between positive skin prick test (SPT) for a range of allergens and self-report of doctor diagnosis of depression among 31 year old females, and similarly that atopy (positive SPT and allergy symptoms) is associated with elevated depression among both males and females. In a subsequent study, Timonen et al 2003 [1] found an association between both any depressive symptoms and self-report of physician diagnosis of depression and increased risk of allergy (assessed with both positive SPT and self-report allergy symptoms) among females; among males in this study the risk of allergy was only evident among males with severe depression. Similarly, Wamboldt et al [10] found an association between parent-reported doctor diagnosis of allergy and internalizing symptoms among children. Possible mechanisms include specific immune indicators that appear common to both allergy and depression [11]. Other evidence has suggested a possible genetic link; a familial link between atopy and depression was also reported in one study [10, 12]. In terms of anxiety, Gregory et al [13] found that recurrent diagnoses of Diagnostic and Statistical Manual of Mental Disorders (DSM) anxiety disorders over the course of several years were associated with elevated self-report of specific allergies (medicine, hay fever, skin allergy, eczema, insect bites), but no association was found between anxiety disorders and positive skin-prick test or immunoglobulin E among 21 year olds in a New Zealand birth cohort.

Mixed findings and methodological limitations of research to date have resulted in uncertainty about the nature of the relationship between allergy and mood and anxiety disorders. First, few population-based, representative samples have assessed both clinical diagnosis of allergy and mood and anxiety disorders using well-validated diagnostic measures. Accordingly, results are uncertain, as there is concern over whether there is actually a relationship between allergy and mood and anxiety problems, or whether the link is due to report bias among those who have mental disorders misreporting allergy symptoms/diagnosis. Second, studies that have used detailed assessment of allergy have been limited by scale scores of depressive symptoms and/or self-reports of physician diagnosis depression rather than diagnoses of depression using validated, diagnostic measures [1]. Specifically, to our knowledge, no previous population based studies on allergy and depression have included DSM disorders assessed with comprehensive validated interviews. Therefore, it is unclear whether allergy may be related to depressive symptoms or to diagnostic level major depressive disorder. The distinction is important in terms of evaluating whether and to what degree this group may experience impaired functioning and/or potentially benefit from mental health treatment. Third, despite observed links between treatment for allergy and mood and anxiety, this relationship has not been examined in a representative population-based sample.

Using a population-based, representative sample of adults with physician diagnosed allergy, information on allergy treatment, and structured diagnostic evaluations of mental disorders, the current study examines the relationship between allergy and mood and anxiety disorders, and investigates the relationship between treatment for allergy and mood and anxiety disorders.

METHODS

Sample

The sample of the German National Health Interview and Examination Survey (GHS) survey was drawn from the population registries of subjects aged 18-79 living in Germany

in the year 1997. It represents a stratified random sample from 113 communities throughout Germany with 130 sampling units. The first sampling step was the selection of communities; the second step was the selection of sampling units. The third step was the selection of inhabitants. Reasons for non-participation, analyses of non-respondents, and further information on samples and weighting are provided elsewhere [14, 15]. The current analyses include only the subsample that also underwent comprehensive mental health assessment (participants of the Mental Health Supplement; GHS-MHS). The GHS-MHS included only persons aged 18 to 65 years of age. The conditional response rate of the GHS-MHS was 87.6%, resulting in a total of 4,181 respondents who completed both core survey (physical assessment) and mental health assessment. After providing a complete description of the study to the subjects, written informed consent was obtained.

Assessment of allergies

The core survey assessment included a standardized computer assisted medical interview conducted by study physicians. Allergy was diagnosed within the medical interview. Allergies were assessed with the following questions, and diagnoses were made by a medical doctor: 1. "Have you ever been diagnosed by a physician with the following allergies? [hay fever/allergic conjunctivitis, allergic contact eczema, neurodermatitis, food allergies, allergic wheals, other allergies]; 2. If yes to one of these: "Have you ever been (laboratory) tested positive to one of the following allergies?" [pollen, epithelium/proteins/ etc. from animals (e.g., cat, dog), mold fungus, dust mite, food, other substances]; Study physicians considered the answers to these questions, and any other clinically relevant information obtained during the interview, in making an allergy diagnosis; 3. If respondents answered yes to any allergy of question 1, they were asked: "Have you been treated with desensitization?" Those who responded in the affirmative were considered treated, versus those who said no. Respondents who received treatment were then asked whether they completed desensitization treatment.

Assessment of mental disorders

Most interviews of the GHS-MHS took place within two to four weeks of the core survey medical examination in order to ensure that data gathered in both examinations was contemporaneous. Psychopathological and diagnostic assessments were based on the computer-assisted version of the Munich Composite International Diagnostic Interview [16-18]. The computer-assisted version of the Munich Composite International Diagnostic Interview is a modified version of the World Health Organization CIDI, version 1.2, supplemented with questions to cover DSM-IV and the International Classification of Diseases version 10 criteria. The computer-assisted version of the Munich Composite International Diagnostic Interview is a fully structured interview that allows for the assessment of symptoms, syndromes, and current and lifetime diagnoses of DSM-IV mental disorders [19]. The following diagnoses (time frame: past 12 months) were included in this analysis: mood disorders (unipolar major depression and bipolar disorder), anxiety disorders (panic disorder with or without agoraphobia), social phobia, specific phobias and generalized anxiety disorder.

Analytic strategy

First, bivariate analyses were used to investigate the relationships between allergy and demographic characteristics, and between allergy and mood and anxiety disorders. Multiple logistic regression analyses were then used to examine the association between allergy and the odds of each mood and anxiety disorder by comparing the likelihood of each mental disorder among those with, compared to those without, allergy in each analysis. These analyses were adjusted for differences in sex, age, and SES, and then for treatment status. The same procedure was then used to examine the prevalence of mental disorders among

those with untreated versus treated allergy, and to examine the prevalence of mental disorders among those who did and did not complete desensitization treatment (among the group who reported receiving this treatment). Odds ratios with 95% confidence intervals were calculated with Stata software package, release 7.0 [20].

RESULTS

Demographic characteristics associated with allergy

Participants with allergy were more likely to be female and younger, compared with those without allergy (See Table 1). There was no statistically significant difference in socioeconomic status (see composite measure derived from educational level, job status and income; see Jacobi et al 2002) [14] between adults with and without allergy, or between adults with allergy who were and were not treated for allergy, or between those who did and did not complete treatment.

Allergy and mental disorders

Having allergies was associated with a statistically significant increased likelihood of having any past 12-month for aggregated diagnostic groups (any mood/anxiety disorder, any anxiety disorder, any mood disorder), as well as for most specific diagnoses (panic attacks, panic disorder, generalized anxiety disorder, specific phobia, major depression and bipolar disorder), compared with those without allergies (Table 2). These associations were slightly attenuated but remained statistically significant after adjusting for age, sex and SES. When these analyses were adjusted for allergy treatment status, relationships were no longer statistically significant, and those who were treated were significantly less likely to have any mood/anxiety disorder (OR=0.65 (0.4, 0.96)) and any anxiety disorder (OR=0.58 (0.4, 0.9)) than those who were not treated. After adjusting for age, sex and SES, the relationships between any mood/anxiety disorder (AOR=2.2 (1.1, 4.5)) and any anxiety disorder (AOR=2.3 (1.0, 5.5)) remained statistically significant while major depression was attenuated (AOR=2.1 (0.9, 5.0) (p=.08)) though small cell size was not adequate for adjustment.

Desensitization treatment for allergy and mental disorders

Adults who had allergies and did not receive treatment had significantly higher odds of any mood/anxiety disorder and major depression, compared to those with allergies who were treated with desensitization (see Table 3); the association with major depression slightly lost statistical significance after adjusting for age sex and SES (AOR=1.6 (1.0-2.6). Among those who received treatment, those who did not complete treatment were significantly more likely to have any anxiety/mood disorder, any anxiety disorder compared with those who completed treatment (Table 4).

DISCUSSION

These findings provide the first evidence of a link between physician diagnosed allergy and DSM-IV mood and anxiety disorders in a representative sample of adults, and provide preliminary data suggesting that treatment for allergy may affect this link. Specifically, adults with allergy have more mood and anxiety disorders, compared with those without allergy. Among those with allergy, those who did not receive desensitization treatment had higher levels of mood and anxiety disorders, compared with those who were treated.

Our results in the context of previous findings

Our findings are consistent with and extend those of Timonen et al [9] and Timonen et al [1] by documenting a link between allergy and major depression—and bipolar disorder—using

structured diagnostic interviewer-based measures. Our results are also consistent with findings of a link between self-report allergy and recurrent DSM anxiety disorders among 21 year olds. The mechanistic pathways underlying the observed relationship between allergy and mood and anxiety disorders cannot be investigated in the present study. There could be a causal relationship between the two, or their co-occurrence could be driven by exposure to common social, genetic or environmental risk factors for both allergy and mental health problems. It is not possible to evaluate the potential role of immunologic changes which could be affected in both allergy and depression/anxiety. Little work has been done toward this end, with the exception of Wamboldt et al 1998 who found evidence of a common genetic vulnerability to depression and allergy among children [10]. Future studies that look into possible genetic factors, as well as social and environmental pathways among adults would facilitate a better understanding of this link.

Possible mechanisms

The underlying mechanism of the potential mediating effect of allergy treatment on the relationship between allergy and mood and anxiety disorders cannot be determined from these data. We speculate on several possibilities that should be examined in future mechanistic studies. First, while the exact mechanism of immunotherapy is not fully understood, there is evidence of a substantial role of T-regulatory cells and associated cytokines during the initial phases, followed by a down-regulation of the T helper-cell type 2 immune response that is associated with allergic disease [21]. The central nervous and immune systems are tightly connected and thus there could be an association either between cytokines produced during the initial phases of immunotherapy or with a decrease in T helper-cell type 2 cytokines after tolerance has been established, and neurotransmitters/hormones involved in mental disease [22]. Second, it could be that people with fewer mental health problems are more likely to pursue and follow-through with allergy treatment, especially because immunotherapy often involves weekly shots for months to years, thereby creating a selection bias leading to a finding of a lower rate of mental disorders among those who are treated. We performed additional analyses comparing those who did and did not complete treatment and similarly found that those who completed treatment appeared to have lower levels of any anxiety and mood disorders overall. When specific disorders were considered individually, however, differences were not statistically significant. This could reflect an effect of allergy treatment on improving mental health, or an equally plausible scenario, that those with better mental health are more likely to complete treatment. These relationships remained largely unchanged after adjusting for SES. Our results are also fairly consistent with data from a clinical sample suggesting that allergy treatment moderated an association between increased healthcare expenditures and comorbid allergic rhinitis, depression and anxiety [7]. As health care (including specialist allergy treatment) is universally available in Germany, it is possible that the potential role of SES impact may be less prominent than might be found in a study in the US.

Study limitations

Limitations of the study include the examination of only one type of treatment for allergy (desensitization). Although this is one standard treatment for allergies, it is conceivable that other participants used other forms of treatment (e.g., pharmaceuticals) and as such we could not examine the potential impact of other treatments. In addition, the present study did not have detailed or objective measures of treatment outcomes. Future studies that can objectively examine a wider range of treatments—for both allergy and mental disorders—are needed. Earlier studies have used self-report, positive SPT alone and clinically defined allergy (which also requires biological verification and the presence of allergy symptoms) to examine the link between allergy and anxiety, depressive symptoms and self-reported doctor diagnosed depression. The definition of atopy, which is a clinical diagnosis, requires both

demonstrated sensitization (SPT or immunoglobulin E) and symptoms [10]. In relation to previous work: the Gregory study examined the relation between positive SPT and immunoglobulin E and anxiety but did not consider the presence of allergy symptoms in these participants (and did not find an association between allergy and any anxiety disorder); Timonen looked both at positive SPT alone (and found no link with depression) and used clinical definition of allergy (positive SPT and symptoms) and found a link with depression. The present study relied on physician diagnosis; a physician can diagnose symptoms that probably have allergic origins, which a patient may or may not report as such, but this approach also has a limitation – without testing it cannot definitively be determined that allergy caused the symptoms. This was a prominent limitation of the present study. It is also the case that previous studies examined allergy and mental disorders measured at specific ages (e.g., 21 year olds and 31 year olds) while our study included adults of all ages up to 65. It is not immediately clear how this age difference would influence results, although it is possible that there are differences both in immune function/allergy status and depression/anxiety between those in early adulthood and older individuals, which could contribute to differences in findings. As we did not have data on SPT, we could not objectively verify the sensitization component of the diagnosis. However, allergy is a clinical diagnosis, and the present study is the first to examine the relationship between allergy and anxiety and depression using physician assessed allergy. Further, the present study was not able to confirm the sequence of allergy, treatment and mental disorders (because timing of allergy treatment was not assessed). As with any form of treatment, immunotherapy has a psychological component. It is not possible to say from these data whether the results (of decreased mood/anxiety disorders) are related to specific changes in the immune system, or a result of psychological consequences of engaging in a therapy [23] and/or whether these psychological changes would then have an impact on the immune system. Prospective studies that can illuminate the sequence of events would begin to provide more insight into potential mechanisms. Finally, although SES does not appear to affect these relationships, the degree to which allergy severity, health literacy or other psychological factors may play a role in who seeks and/or completes treatment is not known. Future studies that take help seeking factors into account in further examining relationships are needed.

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Table 1

Demographic Characteristics and Mental Disorders Among Adults Living in Germany in 1997 With and Without Physician Diagnosed Allergy

	No allergy (3324) % (n)	Allergy (857) % (n)	$\chi^2, p\text{-value}^a$
Gender			
Male	49.1% (1632)	32.8% (281)	$\chi^2 = 73.0$ $p < 0.001^b$
Female	50.9% (1692)	67.2% (576)	
Age			
18-34	30.2% (1003)	41.3% (354)	$\chi^2 = 62.2$ $p < 0.001^b$
35-54	34.7% (1153)	36.4% (312)	
Over 55	35.1% (1168)	22.3% (191)	
SES			
Lower	20.2% (659)	19.0% (158)	$\chi^2 = 0.8$ $p < 0.7$
Middle	57.5% (1875)	59.1% (492)	
High	22.3% (729)	22.0% (183)	

n = sample size; SES = Socioeconomic status

^a = 2-sided

^b = statistically significant

Table 2

Association between Physician Diagnosed Allergy and Mental Disorders Among Adults Living in Germany in 1997

	No allergy (n=3324)	Allergy (n=857)	OR (95% CI)	p value	AOR ^a (95% CI)	p value	AOR ^b (95% CI)	p value
Any anxiety disorder or mood disorders	21.8% (700)	29.0% (248)	1.52 (1.3, 1.8)	p<.0001	1.3 (1.1, 1.6)	.001	0.65 (0.4, 0.96)	.031
Any anxiety disorder	14.1% (467)	19.7% (168)	1.5 (1.2, 1.8)	p<.0001	1.3 (1.1, 1.6)	.009	0.58 (0.4, 0.9)	.026
Panic attacks	5.1% (171)	8.2% (70)	1.6 (1.2, 2.2)	.001	1.6 (1.1, 2.1)	.004	0.6 (0.3, 1.2)	.17
Panic disorder	2.6% (85)	4.2% (36)	1.7 (1.1, 2.5)	.011	1.6 (1.01, 2.3)	.046	.6 (.2, 1.6)	.3
GAD	1.5% (51)	2.6% (22)	1.7 (1.0, 2.8)	.042	1.8 (1.1, 3.0)	.03	0.8 (0.3, 2.3)	.6
Social phobia	2.1% (68)	3.0% (26)	1.5 (0.9, 2.4)	.085	1.3 (0.8, 2.0)	0.3	0.6 (0.4, 1.1)	0.1
Specific phobia	8.7% (289)	11.6% (99)	1.3 (1.1, 1.7)	.042	1.1 (0.9, 1.4)	.4	0.8 (0.3, 2.3)	.6
Any mood disorder	12.2% (407)	17.6% (151)	1.5 (1.3, 1.9)	<.0001	1.4 (1.1, 1.7)	.002	0.7 (0.4, 1.1)	.06
Major Depression	11.3% (374)	15.6% (134)	1.5 (1.2, 1.8)	<.0001	1.4 (1.1, 1.7)	.0001	0.6 (0.4, 1.0)	.07
Bipolar disorder	0.8% (25)	1.8% (15)	2.4 (1.2, 4.5)	.009	2.0 (1.0, 3.8)	.04	1.2 (0.4, 4.0)	.5

AOR = adjusted odds ratio; CI = confidence interval; GAD = generalized anxiety disorder; n = sample size; OR = odds ratio

^a = adjusted for age, sex and SES

^b =adjusted for age, sex, SES and treatment status

Table 3

Association between Self-reported Desensitization Treatment for Allergy and Mental Disorders among Adults Living in Germany in 1997 with Allergy

	Received desensitization treatment (n=196)	Did not receive desensitization treatment (n=661)	OR (95% CI)	p value	AOR ^a (95% CI)	p value
Any anxiety disorder or mood disorders	22.1% (43)	31.0% (205)	1.6 (1.1, 2.3)	.016	1.5 (1.02, 2.2)	.04
Any anxiety disorder	13.9% (27)	21.3% (141)	1.7 (1.1, 2.6)	.02	1.6 (1.01, 2.5)	.04
Panic attacks	5.1% (10)	9.1% (60)	1.9 (0.9, 3.7)	.078	n/a	
Panic disorder	2.6% (5)	4.7% (31)	n/a	n/a	n/a	
GAD	2.0% (4)	2.7% (18)	n/a	n/a	n/a	
Social phobia	1.5% (3)	3.5% (23)	n/a	n/a	n/a	
Specific phobia	8.2% (16)	12.6% (83)	1.6 (0.9, 2.8)	.6	1.6 (0.9, 2.8)	.1
Any mood disorder	13.3% (26)	18.9% (125)	1.5 (1.0, 2.4)	.07	1.4 (0.9, 2.3)	.1
Major depression	10.7% (21)	17.1% (113)	1.7 (1.05, 2.8)	.03	1.6 (1.0, 2.6)	.07
Bipolar disorder	2.0% (4)	1.7% (11)	n/a	n/a	n/a	

AOR = adjusted odds ratio; CI = confidence interval; GAD = generalized anxiety disorder; n = sample size; OR = odds ratio

^a = adjusted for age, sex and SES; n/a: not calculated due to small cell sizes (n<10)

Table 4

Association between Self-reported Completed Desensitization Treatment for Allergy and Mental Disorders

	Completed desensitization treatment (n=131)	Did not complete desensitization treatment (n=65)	OR (95% CI)	p value
Any anxiety disorder or mood disorders	17.6% (23)	31.3% (20)	2.1 (1.1, 4.3)	.032
Any anxiety disorder	10.7% (14)	20.6% (13)	2.2 (1.0, 5.0)	.065
Panic attacks	3.8% (5)	7.7% (5)	n/a	n/a
Panic disorder	2.3% (3)	3.1% (2)	n/a	n/a
GAD	1.5% (2)	3.1% (2)	n/a	n/a
Social phobia	1.5% (2)	1.6% (1)	n/a	n/a
Specific phobia	1.5% (2)	3.1% (2)	n/a	n/a
Any mood disorder	9.9% (13)	20.0% (13)	2.3 (1.0, 5.2)	.05
Major depression	8.4% (11)	15.4% (10)	2.0 (0.8, 4.9)	.1
Bipolar disorder	0	6.2% (4)	n/a	n/a

CI = confidence interval; GAD = generalized anxiety disorder; n = sample size; OR = odds ratio; n/a: not calculated due to small cell sizes (n<10)