Neuropsychiatric and Somatic Characteristics of Young Adults With and Without Self-Reported Chemical Odor Intolerance and Chemical Sensitivity

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ABSTRACT. The psychological, neuropsychiatric, and somatic characteristics of young adults who have different degrees of cacosmia (i.e., feeling “ill” from the odor of xenobiotic chemicals) and who have self-described “chemical sensitivity” were examined. A total of 800 college students completed the following: a self-rating scale for frequency of odor intolerance for 10 common substances, Simon Environmental Illness Symptom Survey, the SCL-90-R, Barsky Amplification Scale, Pearl-Schoenker Mastery Scale, Cheek-Buss and Kagan Shyness scales, Marlowe-Crowne Social Desirability Scale, and a health-symptom and physician-diagnosed checklist. Two pairs of groups were compared: (1) subjects in the top 16% (i.e., cacosmics) and bottom 15% (non-cacosmics) of the sample with respect to odor intolerance scale scores; and (2) subjects from the entire sample who did (28%) or did not (72%) consider themselves to be “especially sensitive to certain chemicals.” Cacosmics and the chemically sensitive subjects scored significantly higher on measures of psychological distress and amplification of somatic symptoms, but there was little evidence of lifestyle change, as assessed by the Simon Survey. Compared with their respective comparison groups, cacosmic and chemically sensitive groups had significantly higher incidences of illnesses associated with chemicals, alcohol intake, opiate drug use, and caffeine use, even after controlling for the psychological measures and histories of atopic allergy. Subjects with and without neuropsychiatric symptoms were differentiated with respect to chemical odor intolerance, but subjects with and without atopic allergies and possible autoimmune diseases were differentiated with respect to chemical sensitivity. Females were more cacosmic than males. Cacosmia is defined by a population subset, with or without occupational xenobiotic exposures or disability, that has distress and symptom amplification and neuropsychiatric and somatic symptoms, none of which are explained fully by psychological measures. Prospective clinical studies are possible with such individuals. The data are also consistent with a time-dependent sensitization model for illness from low-level chemical exposures.

CHEMICAL ODOR INTOLERANCE ("cacosmia") is a symptom that involves a negative hedonic response to, and illness (e.g., headache, dizziness, nausea) from, the odor of common environmental chemicals (e.g., perfume, gasoline) that have no adverse effect(s) on "normal" individuals. Limited epidemiological data suggest that a substantial proportion of various populations report cacosmia, (i.e., approximately 60% of solvent-exposed workers [mainly male blue-collar workers] presenting to an occupational medicine setting; 30% of a sample of almost 4,000 office workers [mainly female, professional, white-collar workers]; and
15–30% of college students [mainly female6-10] and active retired elderly individuals [both sexes with a trend toward more females, community dwelling]).11,12
In occupational12-5,13 and geropsychiatric14 samples, cacosmia has predicted objective deficits in learning and memory task performance, independent of comitant psychopathology. Given that the symptoms claimed by most cacosmics include cognitive and affective dysfunctions,3,6,7,15 the current debate over the existence, nature, and possible etiologies of environmental chemical odor intolerance and chemical sensitivity is an emerging concern for neuropsychiatry and human behavioral toxicology.

The most controversial environmental health problems for which cacosmia has been reported include multiple chemical sensitivity (MCS)6-15 and sick building syndrome (SBS).21 Multiple chemical sensitivity is a polysymptomatic syndrome (including central nervous system symptoms) of unestablished etiology, often noted in well-educated females between the ages of 30–50 y. Patients report chemical odor intolerance (cacosmia) and perceived chemical sensitivity to a disabling degree from many chemically unrelated substances.13 Some, but not all such patients identify a specific high-level chemical-exposure event at work (e.g., chemical spill) or at home (e.g., remodeling or pesticide treatment), after which their clinical illness from subsequent low-level exposures begins.15-21 Sickness building syndrome is a site-specific, building-related illness in primarily white-collar workers between the ages of 20 and 65 y, with an estimated prevalence of 20–30% of U.S. buildings—usually those with recirculated, air-conditioned ventilation.22-27 Sick building syndrome includes upper-airway and mucous-membrane irritation and central nervous system complaints (e.g., difficulty concentrating).24,25 The diverse hypotheses previously proposed to account for illness in patients with cacosmia13 ranged from (a) mistaken belief (e.g., misattribution or suggestion [mass hysterical]);22 to (b) symptom amplification on a presumptively psychogenic basis (e.g., somatization disorder, depression, anxiety and/or panic, posttraumatic stress disorder (PTSD), and/or classical conditioning);5,6,16-18; to (c) symptom amplification on a presumptively organic or neurobiological basis (e.g., organic mood disorder or toxic encephalopathy).8,28-35

The development of tools to identify chemical-odor-intolerant and/or chemically sensitive persons who function in society would facilitate cross-sectional and prospective studies of individual differences in later susceptibility to occupational solvent- and pesticide-related neuropsychiatric syndromes, MCS, and SBS. Skeptics have postulated a major role for self-perception, attribution, and belief in clinical MCS.16-18,36 Prior research indicates that a subset of patients who developed MCS may have had increased levels of premorbid symptomatology.13,17,18,37 If this is true, it may be possible to examine the characteristics of populations who currently have some degree of chemically related problems and who are likely to be in white-collar settings, but who generally have not yet entered the full-time workforce or have not declared themselves to be clinically ill or disabled (e.g., college students).9,10

The purpose of the present study was to assess the descriptive characteristics of individuals, identified by self-report as being ill from or sensitive to environmental chemicals, on the basis of questions that employed different phraseology. The current lack of generally accepted objective physiological measures to diagnose MCS or SBS has made it necessary to develop and refine subjective measures to characterize and differentiate preclinical and clinical populations from normal populations. However, differences in the phrasing of questionnaire items may identify different individuals and populations; a given item may be sensitive or specific, but not both. Cases and controls in previous studies have been identified on the basis of questions regarding (a) "feeling ill" from specific chemical odors;12-18; (b) considering oneself to be especially "sensitive" to certain chemicals; (c) having certain symptom patterns (e.g., fatigue, difficulty concentrating, and arthralgias) attributable to chemicals;17,38; (d) making lifestyle changes in diet, clothing, or home furnishings, all of which are motivated by perceived chemical sensitivity;17,39; and/or (e) receiving a physician's diagnosis of MCS.16,18,40-43 Two different wordings of questions were used in this study: self-perceived illness from, versus sensitivity to, chemicals in young adult college students to examine concomitant, self-reported health patterns.

Materials and Method

Subjects. The subjects were male and female college students who were enrolled in an introductory psychology course at the University of Arizona (i.e., independent cohort from all previously reported student allergy/cacosmia samples studied by Bell et al.5,10,44). Subjects received course credit for their participation.

Questionnaires. The questionnaires for this study were part of a packet of scales administered by faculty at the beginning of the course as part of the students' research experience. Thus, on a specific day, subjects received the packet and had the option to complete it, without any specific recruitment procedure targeting their involvement in the present or any other given project. For this study, in addition to demographics (i.e., age, gender, handedness, history of current smoking, but not ethnic background), we asked the subjects to rate frequency of illness on a 5-point Likert scale (i.e., 1 = almost never; 5 = almost always). Items rated included drinking a small amount of alcohol; taking opiate analgesics (e.g., codeine, morphine, meperidine); ingesting caffeine; odors of 10 environmental chemicals (i.e., chemical odor intolerance), including tobacco smoke, pesticide, drying paint, fresh tar, household disinfectants, fresh newspaper, perfume, new carpet, car exhaust, and natural gas. Students were also asked to answer a single question about whether or not they considered themselves "to be especially sensitive to certain chemicals" (i.e., chemical sensitivity) and to complete a 28-item checklist of physician-diagnosed psychiatric, allergic, and medical disorders. In addition,
they were asked to rate frequency, on a 5-point Likert scale (1 = almost never; 5 = almost always), of experiencing each of 13 symptoms associated with cacosmia,2,9,12,13,25,45 and/or PTSD,46,47 from previous research (without reference or attribution of these symptoms to chemicals, stress, or any other factor). Students were also asked to circle any other drugs on a 7-item list to which they had ever had an adverse reaction.

Additional scales included the 4-item Simon Environmental Illness Symptom Survey17 (i.e., a list of possible lifestyle changes in diet, home furnishings, choice of clothing, shopping in stores, or eating in restaurants—all initiated "because of chemical sensitivity"); the SCL-90-R,48—a standardized, multidimensional measure of psychological symptoms found in both solvent-exposed workers3 and in MCS patients17,18; Barsky Amplification Scale,17,49—a measure of tendency to amplify subjective somatic sensations; Pearlin-Schooler Mastery Scale50—a measure of degree of feeling in control of one's fate (higher scores indicate greater perceived mastery); Cheek-Buss Shyness Scale51—a measure of current shyness, a trait previously found to be elevated in certain cacosmics10; a 5-item version of the Kagan Lifetime Shyness Index,6,26,52 obtained from previous studies (includes items on childhood shyness and school phobia) as a putative measure of possible inborn, or at least long-term, vulnerability to behavioral and physiological overreactivity to environmental novelty3,41; and the Marlowe-Crowne Social Desirability Scale,45—a measure of repressive defensiveness, a trait previously associated with denial of psychiatric illness56 and of negative information about oneself, as well as with increased intolerance for opiate drugs.37

A cacosmia score with a possible range of 10–50 (10 = lowest, 50 = highest) was created by summing the ratings of frequency of illness from the 10 chemicals listed above. High cacosmic and noncacosmic groups were derived, respectively, from the subjects with cacosmia scores at least 1 standard deviation above the sample mean and from the subjects with the minimum possible score. Cacotypically sensitive and not-sensitive groups resulted from dividing the entire sample into subjects who indicated, respectively, that they did or did not consider themselves especially sensitive to certain chemicals. Data analysis with SPSS-PC used one-way analyses of variance, analyses of covariance, and multivariate analyses of covariance. Also used were linked univariate tests for significant factors, as well as chi-square tests and Fisher's exact tests for dichotomous variables. Dichotomous data are reported with and without the Bonferroni correction for multiple comparisons, in view of the debate in statistical texts58 about the risks of making Type II errors while trying to limit Type I errors. Missing values for specific items within any given questionnaire were excluded from individual analyses.

Results

Of approximately 1000 course enrollees, 800 students (mean age = 18.8 ± 2.7 y; 59.6% females) completed the cacosmia section of the questionnaire, and 809 students completed the item on considering oneself to be especially sensitive to certain chemicals. Mean total score for frequency of illness from the 10 chemical odors was 17.2 ± 6.6 (possible range 10–50). Tobacco smoke was the most common odor and new carpet the least common odor that induced self-rated illness (Fig. 1). In the overall sample, 14.6% (n = 117) of the students rated themselves with no illness ever from any of the chemical odors.

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**Fig. 1.** Percentage of sample that reported cacosmia "sometimes or more often."
the 10 chemicals (noncacosmic), and 16.4% (n = 131) had cacosmia scores of 24+ above the sample mean (mean ± 1 standard deviation) (high cacosmic). A surprisingly high 9.7% of the sample reported illness, sometimes or more often, from 6–10 chemicals, although only 1 subject rated herself with maximal illness from all 10 chemicals. Only two subjects (0.2%) indicated a physician diagnosis of multiple chemical sensitivity.

Approximately one-third of the subjects (28.3%) considered themselves to be especially sensitive to certain chemicals. The overlap between extremes of cacosmia ratings and self-description as a chemically sensitive individual was significant but limited in degree (i.e., only 46.9% of those in the high cacosmic group also rated themselves as being especially sensitive to chemicals, whereas 16.2% of the noncacosmics [i.e., those who rated none of the 10 chemical odors as ever causing illness] nevertheless ranked themselves as being especially sensitive to chemicals [Table 1]). With respect to the Simon chemically related lifestyle change questionnaire, the mean score was 0.16 ± 0.5 (possible range = 0–4); 8 subjects (1%) rated themselves with a 3 or 4 (i.e., disabled range)12 on the Simon scale. Females scored significantly higher on the cacosmia scale (18.1 ± 6.8) than males (15.7 ± 5.7) (F(1, 735) = 24.1; p < .001). However, females and males did not differ with respect to Simon scores (after covarying for age); SCL-90R Global Severity Index; and Barsky, Cheek-Buss, and Kagan indexes (variables on which the genders also differed).

High Cacosmics Versus Noncacosmics

Descriptive characteristics. High cacosmics included significantly more females than did noncacosmics (Table 1). Less than half as many high cacosmics reported current smoking, compared with the noncacosmics. The group differences with respect to cacosmia score, illness from a small amount of alcohol, illness from opiate drugs, and illness from caffeine remained highly significant, even after controlling for the following: gender; all of the psychological measures (Table 2) on which the groups differed, including SCL-90-R, which was represented by the Global Severity Index and Barsky Amplification; and the four atopic allergy diagnoses (i.e., nasal allergy, asthma, eczema, and hives). As noted above, more high cacosmics than noncacosmics indicated their belief that they were especially sensitive to chemicals. The high cacosmics rated themselves with significantly higher psychological distress on all subscales and summary scales of the SCL-90-R, with greater Barsky Amplification scores, with lower Mastery scores, and with greater Kagan Lifetime Shyness (Table 2). Groups did not differ with respect to defensiveness (Marlowe-Crowne Scale) or current shyness (Cheek-Buss Scale).

Physician-diagnosed disorders and symptom patterns. In terms of diagnoses (Table 3), the high cacosmics had significantly more nasal allergies, hives, and family histories of allergies (but not asthma or eczema). The male high cacosmics had more childhood hyperactivity, and the female high cacosmics had more premenstrual syndrome and breast cysts than did their respective peers. In addition, high cacosmics reported more sinusitis, peptic ulcer, and chronic pain diagnoses, with trends toward more anxiety disorders, migraine headache, multiple-food sensitivities, and chronic fatigue syndrome. In terms of neuropsychiatric and somatic symptoms (Table 4), the high cacosmics were significantly higher in ratings of frequency of fearfulness, startle, difficulty concentrating, sleep disturbance, daytime grogginess, headaches, tinnitus, constipation, and indigestion, with a trend for irritability; this remained the case even after controlling for gender, psychological scale variables described above, and the atopic allergy diagnoses. Although groups differed with respect to nightmares, memory trouble, and joint/muscle pain, these differences were not significant after controlling for the covariates indicated in Table 4.

Self-Reported Chemically Sensitive Versus Not Chemically Sensitive Groups

Descriptive characteristics. With respect to the true/false item (i.e., considering oneself to be especially sensitive to certain chemicals), the chemically sensitive were significantly older and included more left-handers than did the not-chemically sensitive group (Table 1). These groups did not differ with respect to gender distribution or status as current smokers. In addition to a higher cacosmia score (but lower than that of the high cacosmics), the chemically sensitive were also higher on the Simon Lifestyle Change Scale. The 2 patients with MCS diagnoses (both male) were divided between these groups, and both MCS patients also reported having “allergy” diagnoses. The 1 male who reported an MCS diagnosis, but denied considering himself to be chemically sensitive, also identified himself as a physician-diagnosed asthmatic, with maximal frequency of illness from only tobacco smoke and some illness from all 9 other chemicals. The chemically sensitive rated themselves with significantly more frequent illness from a small amount of alcohol, opiate drugs, and caffeine—after controlling for age, psychological scale differences, and atopic allergy diagnoses. More individuals in the chemically sensitive group also reported adverse reactions to aspirin, novocaine, and penicillin, compared with the not-sensitive group. The sensitive group was significantly higher on all SCL-90-R subscales and summary scales, the Barsky Amplification, and Kagan Lifetime Shyness Index scales, compared with the not-sensitive group (Table 2). Also, sensitive and not-sensitive groups were not different on the defensiveness, mastery, or current shyness (Cheek-Buss Scale) dimensions.

Physician-diagnosed disorders and symptom patterns. The sensitive/not-sensitive groups showed a somewhat different pattern of diagnoses (Table 3) than the high cacosmic-noncacosmic comparison. For example, the chemically sensitive subjects reported significantly higher rates of all types of atopic allergies
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>High cacomics ($n = 131$)</th>
<th>Noncacomics ($n = 117$)</th>
<th>$\chi^2$</th>
<th>$F$</th>
<th>$df$</th>
<th>$p$</th>
<th>Chem. sensitive ($n = 229$)</th>
<th>Not chem. sensitive ($n = 580$)</th>
<th>$\chi^2$</th>
<th>$F$</th>
<th>$df$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>19.2 ± 3.7</td>
<td>19.3 ± 3.7</td>
<td>—</td>
<td>1</td>
<td>—</td>
<td>.00002</td>
<td>19.1 ± 3.4</td>
<td>18.7 ± 2.3</td>
<td>—</td>
<td>4.0</td>
<td>1,795</td>
<td>.047</td>
</tr>
<tr>
<td>Gender distribution (% female)</td>
<td>70.5</td>
<td>43.6</td>
<td>18.3</td>
<td>—</td>
<td>1</td>
<td>.00002</td>
<td>58.8</td>
<td>59.8</td>
<td>—</td>
<td>1</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>12.4</td>
<td>26.5</td>
<td>7.9</td>
<td>—</td>
<td>1</td>
<td>.005</td>
<td>18.8</td>
<td>17.3</td>
<td>—</td>
<td>1</td>
<td>.013</td>
<td></td>
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<tr>
<td>Write with left hand (%)</td>
<td>11.1</td>
<td>8.8</td>
<td>—</td>
<td>—</td>
<td>1</td>
<td>.00001</td>
<td>13.0</td>
<td>6.9</td>
<td>6.2</td>
<td>1</td>
<td>&lt;.00001</td>
<td></td>
</tr>
<tr>
<td>Ten-item cacomics score (10-50)</td>
<td>28.9 ± 4.9</td>
<td>10.0 ± 0.0</td>
<td>—</td>
<td>1354</td>
<td>1,211</td>
<td>&lt;.001</td>
<td>19.4 ± 7.4</td>
<td>16.3 ± 6.0</td>
<td>—</td>
<td>19.3</td>
<td>1,718</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Simon Lifestyle Change Scale (0-4)</td>
<td>0.39 ± 0.8</td>
<td>0.13 ± 0.4</td>
<td>—</td>
<td>—</td>
<td>1</td>
<td>&lt;.00001</td>
<td>0.39 ± 0.8</td>
<td>0.06 ± 0.03</td>
<td>—</td>
<td>44.2</td>
<td>1,728</td>
<td>&lt;.001</td>
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<tr>
<td>Consider self &quot;especially sensitive&quot; to chemicals (%)</td>
<td>46.9</td>
<td>16.2</td>
<td>—</td>
<td>—</td>
<td>1</td>
<td>.00001</td>
<td>100</td>
<td>0</td>
<td>—</td>
<td>19.8</td>
<td>1,730</td>
<td>.00001</td>
</tr>
<tr>
<td>Doctor-diagnosed multiple chemical sensitivity (%)</td>
<td>0</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>1</td>
<td>.00001</td>
<td>0.4</td>
<td>0.2</td>
<td>—</td>
<td>19.8</td>
<td>1,730</td>
<td>.00001</td>
</tr>
<tr>
<td>Illness rating from a small amount of alcohol (1-5)</td>
<td>2.0 ± 1.3</td>
<td>1.2 ± 0.7</td>
<td>—</td>
<td>11.9</td>
<td>1,211</td>
<td>.001</td>
<td>1.8 ± 1.2</td>
<td>1.4 ± 0.9</td>
<td>—</td>
<td>14.5</td>
<td>1,718</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Illness rating from opiate painkillers (1-5)</td>
<td>2.1 ± 1.4</td>
<td>1.3 ± 0.9</td>
<td>—</td>
<td>8.2</td>
<td>1,213</td>
<td>.005</td>
<td>1.9 ± 1.4</td>
<td>1.2 ± 0.9</td>
<td>—</td>
<td>16.3</td>
<td>1,730</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Illness rating from caffeine (%)</td>
<td>1.6 ± 0.9</td>
<td>1.1 ± 0.5</td>
<td>—</td>
<td>6.8</td>
<td>1,210</td>
<td>.01</td>
<td>1.4 ± 0.8</td>
<td>1.2 ± 0.5</td>
<td>—</td>
<td>10.2</td>
<td>1,730</td>
<td>.001</td>
</tr>
<tr>
<td>Adverse reactions to medications (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Aspirin</td>
<td>9.2</td>
<td>0.9</td>
<td>8.6</td>
<td>—</td>
<td>1</td>
<td>.003</td>
<td>7.4</td>
<td>3.8</td>
<td>4.7</td>
<td>1</td>
<td>.03</td>
<td></td>
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<tr>
<td>Ibuprofen</td>
<td>3.8</td>
<td>0.0</td>
<td>2.6</td>
<td>1.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>3.1</td>
<td>0.1</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Novocaine</td>
<td>3.1</td>
<td>0.9</td>
<td>2.2</td>
<td>1.7</td>
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<td></td>
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<tr>
<td>Penicillin</td>
<td>13.0</td>
<td>8.5</td>
<td>15.7</td>
<td>6.4</td>
<td>17.3</td>
<td>1</td>
<td>.00003</td>
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</tbody>
</table>

Notes: High cacomics scored 1 \(SD\) above sample mean for frequency of self-rated illness ratings for odors of 10 different xenobiotic chemicals; noncacomics rated no illness from any of the 10 odors. The "chem. sensitive" group included subjects who endorsed a separate item, i.e., they considered themselves to be especially sensitive to certain chemicals; the not-chem. sensitive group included individuals who denied considering themselves to be especially sensitive to certain chemicals.

Analyses of covariance results show main effect for group after controlling for demographics, psychological measures, and atopic allergy diagnoses on which each pair of groups may differ. Covariates in comparing high cacomics and noncacomics were gender, SCL-90-R Global Severity Index, Barsky Amplification Scale score, Mastery scores, Chem-Buss Shyness and Kagan Lifetime Shyness scores, and atopic allergy diagnoses (i.e., nasal allergies, asthma, eczema, hives). Covariates in comparing chemically sensitive and not chemically sensitive were age, SCL-90-R Global Severity Index, Barsky Amplification Scale score, Mastery scores, Chem-Buss Shyness and Kagan Lifetime Shyness scores, and atopic allergy diagnoses (i.e., nasal allergies, asthma, eczema, hives).

Use of a conservative Bonferroni correction for 7 total medications would set the acceptable level of significance at \(p < .007\). This would make all, except the following, nonsignificant: for high cacomic-noncacomic groups, aspirin; for chemically sensitive-not sensitive groups, novocaine and penicillin.

* Fisher's exact test (1-tailed) = .04.
† Fisher's exact test (1-tailed) = .06.
Table 2.—Results of Psychological Measures of Young Adults With and Without Marked Cacosmia and With and Without Self-Reported Sensitivity to Chemicals

<table>
<thead>
<tr>
<th></th>
<th>High cacomics (n = 131)</th>
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<th>Chem., sensitive (n = 229)</th>
<th>Not chem. sensitive (n = 580)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCL-90-R subscales</td>
<td></td>
<td></td>
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<tr>
<td>Somatization</td>
<td>11.6 ± 8.6</td>
<td>5.4 ± 6.0*</td>
<td>9.5 ± 7.9</td>
<td>7.3 ± 6.5*</td>
</tr>
<tr>
<td>Obsessive-compulsiveness</td>
<td>10.7 ± 7.2</td>
<td>6.8 ± 6.1*</td>
<td>10.0 ± 7.4</td>
<td>8.1 ± 6.8†</td>
</tr>
<tr>
<td>Interpersonal sensitivity</td>
<td>10.0 ± 7.4</td>
<td>6.6 ± 6.4*</td>
<td>10.0 ± 7.7</td>
<td>8.2 ± 6.6†</td>
</tr>
<tr>
<td>Depression</td>
<td>13.1 ± 9.9</td>
<td>7.5 ± 7.7*</td>
<td>12.4 ± 10.1</td>
<td>9.3 ± 8.3</td>
</tr>
<tr>
<td>Anxiety</td>
<td>8.3 ± 6.6</td>
<td>4.2 ± 4.1*</td>
<td>7.4 ± 6.8</td>
<td>5.7 ± 5.4†</td>
</tr>
<tr>
<td>Hostility</td>
<td>4.9 ± 4.6</td>
<td>3.3 ± 3.0*</td>
<td>4.6 ± 4.4</td>
<td>3.7 ± 4.1‡</td>
</tr>
<tr>
<td>Phobic anxiety</td>
<td>3.5 ± 4.7</td>
<td>1.3 ± 2.6*</td>
<td>2.9 ± 4.4</td>
<td>1.9 ± 3.2†</td>
</tr>
<tr>
<td>Paranoid ideation</td>
<td>5.7 ± 4.7</td>
<td>3.6 ± 4.0*</td>
<td>5.4 ± 5.0</td>
<td>4.3 ± 4.2†</td>
</tr>
<tr>
<td>Psychoticism</td>
<td>6.4 ± 6.6</td>
<td>3.2 ± 4.6*</td>
<td>6.2 ± 7.0</td>
<td>4.1 ± 5.2*</td>
</tr>
<tr>
<td>General Severity Index</td>
<td>0.89 ± 0.6</td>
<td>0.51 ± 0.5§</td>
<td>0.81 ± 0.6</td>
<td>0.63 ± 0.5‡</td>
</tr>
<tr>
<td>Positive Symptom Total</td>
<td>42.6 ± 23.1</td>
<td>26.8 ± 19.3∥</td>
<td>39.9 ± 21.2</td>
<td>33.0 ± 19.7**</td>
</tr>
<tr>
<td>Positive Symptom Distress Index</td>
<td>1.8 ± 0.5</td>
<td>1.5 ± 0.5§§</td>
<td>1.7 ± 0.5</td>
<td>1.6 ± 0.5††</td>
</tr>
<tr>
<td>Barsky Amplification Scale</td>
<td>10.1 ± 3.6</td>
<td>8.3 ± 3.6*</td>
<td>10.5 ± 3.4</td>
<td>9.1 ± 3.6*</td>
</tr>
<tr>
<td>Mastery Scale</td>
<td>21.0 ± 3.8</td>
<td>23.1 ± 4.2*</td>
<td>21.5 ± 4.6</td>
<td>22.1 ± 4.1‡</td>
</tr>
<tr>
<td>Cheek-Buss Shyness Scale</td>
<td>15.7 ± 7.2</td>
<td>14.7 ± 8.0∥</td>
<td>15.7 ± 6.8</td>
<td>14.6 ± 7.1∥</td>
</tr>
<tr>
<td>Kagan Lifetime Shyness Index</td>
<td>7.9 ± 4.0</td>
<td>7.0 ± 4.0∥</td>
<td>8.0 ± 3.8</td>
<td>7.1 ± 3.8∥</td>
</tr>
<tr>
<td>Marlowe-Crowne Scale</td>
<td>16.4 ± 4.7</td>
<td>15.9 ± 5.4∥∥</td>
<td>15.9 ± 5.0</td>
<td>16.1 ± 5.2∥∥</td>
</tr>
</tbody>
</table>

Notes: Main effects for the high cacosmia-non cacosmia pair of groups reflect multivariate analyses of variance, using nine SCL-90-R subscales: Barsky, Mastery, Cheek-Buss, Kagan, and Marlowe-Crowne scales as dependent measures, with univariate tests; all controlled for gender as a covariate. Hotellings = 0.22, F(14, 202) = 3.1, p < .001. Univariate df = 1, 215.

Main effects for the chemically sensitive-chemically non-sensitive pair of groups reflect multivariate analyses of variance, using nine SCL-90-R subscales: Barsky, Mastery, Cheek-Buss, Kagan, and Marlowe-Crowne scales as dependent measures, with univariate tests; all controlled for gender as a covariate. Hotellings = 0.05, F(14, 711) = 2.6, p = .001. Univariate df = 1, 724.

*p < .001.
tp < .01.
*tp < .05.
§F = 15.6, df = 1, 235, p < .001.
∥F = 30.0, df = 1, 235, p < .001.
$F = 16.8, df = 1, 771, p < .001.
**F = 16.6, df = 1, 771, p < .001.
††F = 7.4, df = 1, 771, p = .007.
‡‡Not significant, univariate tests.
§§F = 9.6, df = 1, 232, p = .002.
∥∥∥p < .05 < p < .10.

(e.g., nasal, asthma, eczema, hives)—not just nasal—in addition to family histories of allergies. The comparisons for hyperactivity and premenstrual syndrome were not significant. However, sensitive subjects noted more depression diagnoses than the not-sensitive subjects. The sensitive group exhibited more sinusitis, multiple-food sensitivities, irritable bowel, hypertension, and arthritis, with trends for more diabetes, yeast infections in females, and hypothyroidism, compared with the not-sensitive group. The overall multivariate analysis of covariance between the sensitive/not-sensitive groups for the 13 symptoms in Table 4 was not significant.

Combined Analyses

In an effort to examine directly some characteristics of persons who report chemical odor intolerances, but who may or may not consider themselves especially sensitive to certain chemicals, we subdivided the high cacosmic and noncacosmic groups, based on their answer to the chemical-sensitivity question. As implied by the analyses above, the high cacosmic/sensitive subjects (n = 61 [1 additional high cacosmic subject was excluded from these analyses because of missing data on the sensitive item]) included the largest proportion of females (78%; χ²(3) = 25.0, p = .00002). These subjects rated themselves with significantly higher Simon lifestyle change scores (0.6 ± 1.0) than did the high cacosmic/not-sensitive (n = 69 [0.1 ± 0.5]) and noncacosmic/not-sensitive (n = 98 [0.1 ± 0.3]) subgroups (F(3,234) = 7.9, p < .001), even after controlling for SCL-90-R grand-total score, Barsky Amplification Scale, Mastery Scale, Cheek-Buss Shyness, Kagan Shyness, and gender. Similarly, the high cacosmic/sensitive subgroup rated itself with the highest frequency of illness after ingestion of a small amount of alcohol (2.4 ± 1.5 versus 1.4 ± 0.8 for the non cacosmic/sensitive [n = 19], versus 1.5 ± 1.0 for the high cacosmic/not sensitive, and
Table 3.—Percentages of Groups With Histories of Physician-Diagnosed Disorders of Young Adults With and Without Marked Cacosmia and With and Without Self-Reported Sensitivity to Chemicals

<table>
<thead>
<tr>
<th>Disorder</th>
<th>High cacosmins (n = 131)</th>
<th>Noncacosmins (n = 117)</th>
<th>$\chi^2$</th>
<th>p</th>
<th>Fisher's exact test</th>
<th>Chem. sensitive (n = 229)</th>
<th>Not chem. sensitive (n = 580)</th>
<th>$\chi^2$</th>
<th>p</th>
<th>Fisher's exact test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal allergies</td>
<td>34.4</td>
<td>20.5</td>
<td>5.9</td>
<td>.015</td>
<td>—</td>
<td>40.2</td>
<td>19.0</td>
<td>&lt;.000001</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Asthma</td>
<td>19.1</td>
<td>12.8</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>21.8</td>
<td>9.5</td>
<td>22.2</td>
<td>.001</td>
<td>—</td>
</tr>
<tr>
<td>Eczema</td>
<td>5.3</td>
<td>3.4</td>
<td>6.6</td>
<td>.28</td>
<td>—</td>
<td>6.6</td>
<td>2.8</td>
<td>6.4</td>
<td>.01</td>
<td>—</td>
</tr>
<tr>
<td>Hives</td>
<td>11.5</td>
<td>4.3</td>
<td>4.3</td>
<td>.038</td>
<td>—</td>
<td>11.4</td>
<td>3.4</td>
<td>19.1</td>
<td>&lt;.00001</td>
<td>—</td>
</tr>
<tr>
<td>Family history of allergies</td>
<td>78.0</td>
<td>58.6</td>
<td>10.5</td>
<td>.001</td>
<td>—</td>
<td>81.5</td>
<td>60.6</td>
<td>31.8</td>
<td>&lt;.00001</td>
<td>—</td>
</tr>
<tr>
<td>Childhood hyperactivity</td>
<td>13.2</td>
<td>0</td>
<td>9.1</td>
<td>.003</td>
<td>—</td>
<td>9.0</td>
<td>6.6</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Premenstrual tension syndrome (females only)</td>
<td>14.3</td>
<td>3.9</td>
<td>3.7</td>
<td>.05</td>
<td>—</td>
<td>7.4</td>
<td>3.1</td>
<td>7.4</td>
<td>.007</td>
<td>—</td>
</tr>
<tr>
<td>Depression</td>
<td>7.6</td>
<td>4.3</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3.1</td>
<td>2.1</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Anxiety</td>
<td>6.1</td>
<td>1.7</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.7</td>
<td>0.5</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>3.8</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.04</td>
<td>0.5</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>8.4</td>
<td>1.7</td>
<td>5.6</td>
<td>.018</td>
<td>—</td>
<td>8.7</td>
<td>3.4</td>
<td>9.8</td>
<td>.002</td>
<td>—</td>
</tr>
<tr>
<td>Migraine headache</td>
<td>12.2</td>
<td>6.0</td>
<td>2.9</td>
<td>.09</td>
<td>—</td>
<td>11.8</td>
<td>8.8</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Breast cysts (women only)</td>
<td>7.7</td>
<td>0</td>
<td>4.1</td>
<td>.04</td>
<td>—</td>
<td>3.7</td>
<td>1.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Multiple food sensitivities</td>
<td>2.3</td>
<td>0</td>
<td>2.7</td>
<td>.10</td>
<td>—</td>
<td>2.6</td>
<td>0.7</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Irritable bowel</td>
<td>6.1</td>
<td>2.6</td>
<td>4.7</td>
<td>.03</td>
<td>—</td>
<td>3.5</td>
<td>1.4</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Peptic ulcers</td>
<td>7.6</td>
<td>0.9</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3.1</td>
<td>0.7</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.3</td>
<td>0.9</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.3</td>
<td>0.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.8</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>6.1</td>
<td>2.2</td>
<td>7.6</td>
<td>.006</td>
<td>—</td>
</tr>
<tr>
<td>Arthritis</td>
<td>3.8</td>
<td>3.4</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.7</td>
<td>0.3</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>0.8</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.8</td>
<td>0.3</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Chronic fatigue syndrome</td>
<td>3.1</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>2.2</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Yeast infections (females only)</td>
<td>26.4</td>
<td>23.5</td>
<td>—</td>
<td>—</td>
<td>0.08</td>
<td>23.9</td>
<td>16.5</td>
<td>3.5</td>
<td>.06</td>
<td>—</td>
</tr>
</tbody>
</table>

Notes: Neither set of groups differed significantly in proportions having the following diagnoses: panic disorder, ovarian cysts, nasal polyps, heart problems, cancer, and endometritis. All $\chi^2$ tests had df = 1. Fisher exact tests were performed 1-tailed because of a priori hypotheses that cacosmins and chemically sensitive would have higher prevalence of these disorders. Use of a conservative Bonferroni correction for multiple tests would set the acceptable level of significance at $p < .002$. This would make all, except the following, nonsignificant: for high cacosmin-noncacosmin groups, family history of allergies; for chemically sensitive-not sensitive groups, nasal allergies, asthma, hives, and family history of allergies. However, some epidemiologists have argued that the Bonferroni correction can lead to excessive Type II error and, therefore, recommend direct reporting of all findings, but in the context of noting the total number of comparisons made (see Methods for no. of items).
Table 4.—Self-Rated Frequency of Specific Symptoms, by Groups of Young Adults With and Without Marked Cacosmia and With and Without Self-Reported Sensitivity to Chemicals

<table>
<thead>
<tr>
<th>Symptom</th>
<th>High cacosmics (n = 131)</th>
<th>Noncacosmics (n = 117)</th>
<th>Chem. sensitive (n = 229)</th>
<th>Not chem. sensitive (n = 580)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>2.7 ± 1.2</td>
<td>1.9 ± 1.1*</td>
<td>2.7 ± 1.2</td>
<td>2.3 ± 1.2†</td>
</tr>
<tr>
<td>Ringing in the ears</td>
<td>2.3 ± 1.1</td>
<td>1.6 ± 1.0*</td>
<td>2.0 ± 1.1</td>
<td>1.8 ± 0.9†</td>
</tr>
<tr>
<td>Constipation</td>
<td>2.0 ± 1.0</td>
<td>1.3 ± 0.7†</td>
<td>1.8 ± 1.0</td>
<td>1.6 ± 0.9†</td>
</tr>
<tr>
<td>Indigestion</td>
<td>2.2 ± 1.1</td>
<td>1.5 ± 0.8‡</td>
<td>2.0 ± 1.1</td>
<td>1.7 ± 0.9‡</td>
</tr>
<tr>
<td>Joint and/or muscle pain</td>
<td>2.3 ± 1.2</td>
<td>1.7 ± 1.0†</td>
<td>2.2 ± 1.2</td>
<td>1.8 ± 1.0†</td>
</tr>
<tr>
<td>Fearfulness</td>
<td>2.0 ± 1.0</td>
<td>1.4 ± 0.8§</td>
<td>1.9 ± 1.0</td>
<td>1.7 ± 0.9†</td>
</tr>
<tr>
<td>Irritability</td>
<td>2.4 ± 1.1</td>
<td>2.0 ± 1.0/</td>
<td>2.3 ± 1.1</td>
<td>2.1 ± 1.0†</td>
</tr>
<tr>
<td>Easily startled</td>
<td>2.3 ± 1.2</td>
<td>1.6 ± 0.9§</td>
<td>2.1 ± 1.2</td>
<td>1.9 ± 1.1†</td>
</tr>
<tr>
<td>Trouble sleeping at night</td>
<td>2.2 ± 1.2</td>
<td>1.7 ± 0.9*</td>
<td>2.3 ± 1.2</td>
<td>2.0 ± 1.1*</td>
</tr>
<tr>
<td>Nightmares</td>
<td>2.1 ± 1.1</td>
<td>1.6 ± 0.9†</td>
<td>2.0 ± 1.1</td>
<td>1.8 ± 0.9†</td>
</tr>
<tr>
<td>Daytime grogginess</td>
<td>2.8 ± 1.0</td>
<td>2.2 ± 1.1*</td>
<td>2.8 ± 1.1</td>
<td>2.5 ± 1.1‡</td>
</tr>
<tr>
<td>Memory trouble</td>
<td>2.2 ± 1.0</td>
<td>1.6 ± 1.0†</td>
<td>2.1 ± 1.1</td>
<td>1.9 ± 1.0†</td>
</tr>
<tr>
<td>Difficultly concentrating</td>
<td>2.6 ± 1.1</td>
<td>1.9 ± 1.0*</td>
<td>2.4 ± 1.1</td>
<td>2.2 ± 1.1‡</td>
</tr>
</tbody>
</table>

Notes: Multivariate analyses of covariance results below show main effect for group after controlling for demographics, psychological measures, and atopic allergy diagnoses on which each pair of groups may differ.

Covariates in comparing high cacosmics and noncacosmics were gender, SCL-90-R Global Severity Index, Barksy Amplification Scale score, Mastery scores, Cheek-Buss Shyness and Kagan Lifetime Shyness scores, and atopic allergy diagnoses (i.e., nasal allergies, asthma, eczema, and hives). Hotelling's = 0.22, F(13, 198) = 3.3, p < .001. Univariate df = 1, 210.

Covariates in comparing chemically sensitive and not chemically sensitive were age, SCL-90-R Global Severity Index, Barksy Amplification Scale score, Mastery scores, Cheek-Buss Shyness and Kagan Lifetime Shyness scores, and atopic allergy diagnoses (i.e., nasal allergies, asthma, eczema, and hives). Hotelling's = 0.02, F(13, 707) = 1.2, p > .2 (not significant). Univariate df = 1, 719.

*p < .05
†Not significant.
‡p < .001
§p < .01
∥.05 < p < .10

versus 1.2 ± 0.7 for the noncacosmic/not sensitive; F[3,234] = 10.4, p < .001), even after controlling for the same covariates listed for the Simon Scale analysis. The high cacosmic/sensitive subjects reported the highest prevalence of adverse reactions to foods overall (14.5% versus 5.3%, 2.5%, and 3.1%, respectively; $\chi^2[3] = 12.1, p = .007$).

The noncacosmic/sensitive subgroup included the highest proportion of males (68%), and subjects reporting the highest rate of current smoking (37% versus 13% for the high cacosmic/sensitive group, versus 13% for the high cacosmic/not sensitive group, and versus 25% for the noncacosmic/not-sensitive group; $\chi^2[3] = 9.7, p = .02$). Such a finding might suggest that these subjects were not really ill but, rather, had misunderstood the questions. However, this same subgroup of noncacosmic/sensitive individuals, like the high cacosmic/sensitive subgroup (i.e., most were female), reported comparably higher rates of atopic allergy-like diagnoses, compared with the high cacosmic/not-sensitive and noncacosmic/not-sensitive subgroups (i.e., asthma [respectively, 32%, 25%, 12%, and 9%; $\chi^2[3] = 11.6, p = .009$]); hives [respectively, 16%, 22%, 4%, and 2%; $\chi^2[3] = 24.2, p = .0002$]); and nasal allergy (respectively, 42%, 54%, 19%, and 16%; $\chi^2[3] = 34.2, p < .00001$).

Discussion

The data in this study extend earlier findings that nondisabling cacosmia and chemical sensitivity, without marked lifestyle changes or physician diagnoses of MCS, are widespread in the college-student and elderly populations. Combined with previous research, the findings raise questions about differences in self-perceived health, symptoms, and causal attribution among community cacosmics, compared with MCS patients. The combination of multiple-chemical odor intolerances and self-perceived chemical sensitivity may assist in the design of prospective cohort investigations and in the finding of subject samples with MCS-like medical histories, without lifestyle changes. Finally, in addition to the odor intolerances and self-perceived chemical sensitivity, high scores on the Simon Lifestyle Change Survey may detect impaired individuals, equivalent to “MCS” patients, with or without physician diagnoses. Specifically, illness from new carpet and newprint odors may help discriminate between the most and least affected subsets of young adults for future population-based studies.

Erroneous assignment to chemically intolerant or to normal groups is a risk from self-report alone. Some members could be assigned incorrectly to “chemical-
odor-intolerant," "sensitive," and/or "normal" populations. Also, "physician-diagnosed" medical conditions could, absent examinations, laboratory tests, and other confirmation, be in error. Objective confirmatory tests will assist in the recognition and categorization of individuals and should correct "erroneous" self-report.

It is untested whether findings in college students will apply to cacosmics overall or to MCS patients. Typically, college students neither work full-time nor express their potential for ill health. In light of its warm and dry climate, southern Arizona has attracted migrants who may have more self-perceived and/or diagnosed atopy, asthma, and rheumatic diseases; consequently, these individuals are overrepresented in the present generation. Students may enroll in psychology courses to understand increased rates of personal or familial psychopathology. Similarly, willingness to participate for receipt of course credit may have biased these subjects; however, a presumption that the cacosmics or chemically sensitive were motivated differentially to exaggerate their symptoms for secondary gain, compared with the noncacosmics or chemically not sensitive, is unreasonable. Presenting oneself for one class session and handing in the packet of questionnaires fulfilled our expectations. Given that the investigators did not teach the introductory psychology course, there was no reason for students to provide answers to please us. In contrast to clinical studies of MCS patients with disability claims or lawsuits, monetary gain, validation of patient status, or attribution of symptoms to chemicals could not motivate students' responses. Population-based studies are needed in other regions of the country, using similar instruments.

**Cacosmia versus chemical sensitivity: phrasing the question.** How one asks about cacosmia or chemical sensitivity may identify subsets of the population (i.e., in cacosmics identified by illness scores from 10 chemical odors, less than one-half felt "especially sensitive to certain chemicals"). Similarly, in older adults with more personal medical issues, only 67% of cacosmics considered themselves to be chemically sensitive. The wording of questions may lead to different self-identification (e.g., acknowledgment of frequent rates of chemical intolerance with "feel ill from the odor of..." implies transient, reversible states of poor health observed repeatedly—but intermittently—over time, under exposure conditions). On the other hand, labeling oneself "especially sensitive to..." connotes a chronic, stable individual trait, a persistent self-perception that could result from a single memorable, albeit nontoxic, chemically related event. In addition, the "feel-ill" items limited the chemical exposure route to odors, whereas the "sensitive-to" item could have identified more persons with prior skin irritation or other non-odor-related chemical responses.

The psychological implications of wording may elicit acceptance or denial of a descriptor. Healthy individuals in the community may view the word "sensitive" (with both its negative and positive connotations for the general public) more positively than the expression "feel ill" (an expression that is wholly negative), thus leading to greater endorsement for the former phrasing (28% from the chemical-sensitivity item versus 16% from the chemical odor intolerance/cacosmia items). Thus, males and females endorsed the "sensitive" wording equally; females, however, who acknowledged more symptoms and usually see doctors more readily,59 chose "feel ill from" more often in this study, as well as in prior studies. Some persons may be more comfortable reporting physician diagnoses than acknowledging self-perceived "flaws." For example, the "1 MCS"-diagnosed man (from tobacco smoke) admitted a physician diagnosis of asthma, but did not consider himself to be "especially sensitive to certain chemicals." This individual, who was atypical for the anecdotal MCS patient (i.e., female, nonasthmatic, and often ill from numerous chemicals), also questioned the reliability and validity of a diagnosis of chemical sensitivity attributed to his physician.

Despite such limitations in the methodology, the chemically sensitive group nevertheless differed from the cacosmics. First, the cacosmia items elicited group differences in gender distribution similar to those reported in MCS and SBS (i.e., more females), whereas the chemical-sensitivity question did not. Second, the self-described chemically sensitive group had more classical atopic allergic disorders and more potential autoimmune disorders (e.g., juvenile arthritis, hypothyroidism, juvenile diabetes mellitus). Having more left-handed individuals in the chemically sensitive group is consistent with some, but not all, prior research.60-62 More allergies and autoimmune in left-handed subjects are still disputed.63

Whether the eventual definition of MCS should include or exclude traditional immunological diagnoses continues to be debated.49-53 The cacosmia questions focus on neuropsychiatric and neurogenic inflammatory (i.e., sensory peptide-mediated) presentation, whereas the chemical-sensitivity question chooses the atopic, immunological, and/or immune inflammatory type. The word "odors" in the cacosmia items invokes the sense of smell; the olfactory system directly accesses the limbic brain, which regulates emotions, startle, memory, social and appetitive behaviors, and the automatic nervous system.53,54,65-68 Third, neuropsychiatric and somatic symptoms were significantly more common in cacosmics than in their noncacosmic peers, but not for the chemically sensitive, compared with their peers. The symptoms (Table 4) were reported by solvent-exposed workers, as well as MCS and SBS patients; therefore, these cacosmia items may be particularly useful in the location of persons with neuropsychiatric dysfunctions for future clinical studies.55,69,70

Moreover, the individuals in the present study who reported higher rates of illness from xenobiotic odors showed more global distress on the SCL-90-R subscales, more illness from alcohol and other drugs, and more neuropsychiatric and somatic symptoms, compared with those who denied chemical illness. Nonetheless, scores on the SCL-90-R scales were not elevated to pathological levels. In view of the lack of significant group differences for the Marlowe-Crowne...
Scale, such psychological findings were not the result of differing levels of repressive defensiveness. Thus, as hypothesized, these cacosmic young adults exhibited subclinical parallels to persons with occupational solvent exposure, MCS, or clinical SBS, thus demonstrating the feasibility of prospective studies of cacosmias, without disability, entering the workforce.

**Cacosmia and psychopathology.** Increased psychological distress was associated with an increase in the reporting of symptoms and accords with findings of prior studies. The symptom differences for fearfulness, startle, difficulty concentrating, insomnia, and gogginess persisted in the cacosmias, after controlling for this heightened distress via the covared contributions of gender, SCL-90-R and Barsky Amplification, Mastery and Shyness scale differences, and presence of atopic allergies. Therefore, even though cacosmics amplified somatic symptoms on the Barsky scale with overall distress, their cacosmia, illness from alcohol, illness from opiates, illness from caffeine, and symptom scores remained higher than scores of their non-cacosmic peers. This finding reinforces the fifth demonstration by Bell et al. that psychological factors are a concomitant of, but not a full explanation for, subjective chemical odor intolerance. In other words, psychogenic amplification accounts for only the increased symptom and substance intolerance ratings.

Blinded chemical exposure test studies are essential to determine if organic, neurobiological amplification factors, related to chemicals per se, account for the remaining variance or if there are other factors involved. Amplification of symptoms might cause excess reporting of certain diagnoses shown in Table 3. Further research with direct clinical examinations (e.g., breast ultrasound, thyroid studies) and medical-record audits should assist in determining whether rates of diagnoses reported are inflated subjectively. Earlier research has confirmed objective evidence of increased nasal resistance and of abnormal rhinolaryngoscopic findings in MCS patients.

Some investigators consider chemical odor intolerance and/or chemical sensitivity to be manifestations of traditional psychiatric disorders. Alternatively, subsets of psychiatric disorders may require modification to include cacosmia as a clinical feature (e.g., "major depression with cacosmia"). This approach would acknowledge the comorbidity of depression and cacosmia, without attributing causality. For example, in American psychiatry, descriptive modifiers for major depression have included "with seasonal pattern"; for dementia, descriptive modifiers of Alzheimer's dementia include "with delirium," "with depression," "with delusions," or "uncomplicated." The reason for considering cacosmia or chemical sensitivity as a possible modifier of diagnoses (e.g., major depression or panic disorder) is that the clinical picture of such persons may differ significantly from classical psychiatric presentations.

Unlike psychiatric patients with major depression, MCS patients report that their moods worsen primarily during chemical exposures and improve during chemical avoidance. Unlike the general psychiatric population, MCS patients also report decreased—rather than increased—rates of alcohol and substance use and abuse. Unlike typical patients with somatization disorder, many MCS patients have a later age of onset (i.e., after 30 y of age), a good premorbid occupational history, and no premorbid medical-disability history. Furthermore, the multiple-drug intolerances reported by some cacosmics appear to suggest that those who blossom into clinically depressed or anxious patients might also have poorer tolerance of psychotropic medications, thus making standard treatments more difficult. Finally, associations between cacosmia and objective learning and memory deficits suggest the testable hypothesis that a history of cacosmia may select the subset of depressed patients at risk for concomitant and subsequent cognitive difficulties. A growing body of literature would suggest that older patients, with late-onset depression associated with reversible cognitive symptoms, have more similar biological markers and long-term outcomes to patients with Alzheimer's dementia than to those with depression alone.

**Cacosmia and the time-dependent sensitization model.** The present data are consistent with the previous hypothesis of Bell et al.: that cacosmia may be a manifestation of time-dependent sensitization (TDS). Time-dependent sensitization is the progressive amplification of responsivity to a given stimulus or cross-sensitizing stimulus, by the passage of time between the first and later exposures. Animal studies parallel some aspects of cacosmia, MCS, and/or SBS. Female animals are more vulnerable than are males to TDS, related in part to gonadal hormones. Multiple, intermittent low doses or a single high dose of a pharmacological agent—including pesticides, ethanol, and opioids—can initiate the process, possibly by similar and/or convergent effects of different environmental stressors on the same dopaminergic mesolimbic pathways in the brain. Multiple, structurally unrelated agents can subsequently elicit amplified reactions at the same or lower levels, independent of dopaminergic mediation. Both conditioned and unconditioned TDS can occur, depending on the physical setting(s) in which sensitization and elicitation exposures occur. One initially high dose will increase reactivity to subsequent low doses. Finally, sensitized and nonsensitized individuals may not differ on first test exposure, but will diverge on later reexposures over time.

Time-dependent sensitization is postulated as a model for certain time-related and amplification features of several different disorders that are related to environmental chemical-related illnesses, including posttraumatic stress disorder, chronic neuropsychiatric sequelae of acute toxic exposures, panic disorder, recurrent major depression, and some "somato-
form" disorders, such as irritable bowel. Rather than focus debate on whether some cacomasics fall under a discrete diagnosis called MCS or SBS, it might be more productive to investigate chemical odor intolerance as a symptom of a nonspecific, noninflammatory, time-dependent sensitization, amplification process relevant to a spectrum of psychiatric, neuropathological, and psychophysiological conditions. The prevalence of reported illness from low-level chemical exposures in industrial and nonindustrial populations merits further research on chemical odor intolerance and on chemical sensitivity, with measurement of doses of chemicals and blinded chemical challenges, using objective measurements of outcome.

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References


89. Kalivas PW, Alesdatter JE. Involvement of N-methyl-D-aspartate receptor stimulation in the ventral tegmental area and amygdala in behavioral sensitization to cocaine. J Pharmacol Exp Ther 1993; 267:486–95.
112. Bell IR, Schwartz GE, Peterson JM, Kline JP. Quantitative EEG patterns during nose versus mouth inhalation of filtered room air in young adults with and without self-reported chemical odor intolerances. (In preparation.)
114. Bell IR, Schwartz GE, Bootzin RR, Wyatt JK. Time-dependent sensitization of heart rate and blood pressure over multiple laboratory sessions in elderly individuals with and without chemical odor intolerance (under review).