

INVESTIGATIVE REPORT

Patient–Doctor Interaction, Psychobehavioural Characteristics and Mental Disorders in Patients with Suspected Allergies: Do They Predict “Medically Unexplained Symptoms”?

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In approximately 20% of patients with suspected allergies, no organic symptom explanation can be found. Limited knowledge about patients with “medically unexplained symptoms (MUS)” contributes to them being perceived as “difficult” and being treated inadequately. This study examined the psychobehavioural characteristics of patients presenting for a diagnostic allergy work-up. Patients were interviewed and completed various self-rating questionnaires. Patient–Doctor interaction was evaluated, and the organic explicability of the patients’ symptoms was rated by allergists. Patients with vs. those without MUS differed in several respects. Mental comorbidity, female sex, dissatisfaction with care, and a problematic countertransference (the interviewer’s feelings towards the patient) independently predicted MUS. Patients whose symptoms could be explained organically reported more psychobehavioural problems than a control group of immunotherapy patients. There were no differences in patient–doctor interaction. In patients with suspected allergies, recognition of psychological burden and concurrent mental disorders is important. Mental comorbidity and a difficult patient–doctor interaction may predict MUS. Key words: allergy; medically unexplained symptoms; patient–doctor interaction; psychobehavioural characteristics; somatization.

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When Pirquet coined the term “allergy” in 1906, little was known about the biological basis of hypersensitivities towards common external triggers (1). Nowadays, “allergy” is defined as immunologically mediated hypersensitivity reactions. However, the term is still

a very common lay descriptor of various symptoms attributed to subjective intolerance reactions towards, for instance, foods or chemicals (2, 3). Approximately 20% of the adult population in western industrialized countries report adverse reactions to foods, but only 1–4% have true food allergies (4). For up to 90% of food intolerances in adult clinical samples, no immunological explanation can be found (3). In blinded provocation tests of self-reported adverse reactions to foods, drugs, or chemicals, the rates of negative reactions to verum, or positive reactions to placebo are high (40–85%) (5–9). When other organic explanations are also ruled out, the symptoms are considered as “medically unexplained”. Medically unexplained symptoms (MUS) are a neglected health problem, and evidence is needed on risk factors and pathophysiology, but also on how to provide better healthcare for these patients (10).

Most of the few existing studies about psychobehavioural features associated with MUS attributed to allergies indicate a higher physical symptom burden as well as a higher rate of mental disorders and psychological distress (3, 4, 11–13).

On the other hand, allergic diseases *per se* carry a considerable psychological burden: raised levels of anxiety, depression, and somatization, as well as reduced quality of life due to bothering and sometimes life-threatening symptoms, have been shown to be associated with various types of allergic diseases (3, 5, 14–19). There is growing evidence for a higher susceptibility *for* as well as an increased intensity *of* allergic reactivity in times of psychological distress (5, 18, 19). In many types of allergies (such as food, additive or drug reactions), symptoms tend to be diffuse, testing is complex, and only placebo-controlled testing in highly specialized institutions can establish, or rule out, a diagnosis. Many patients may therefore feel additionally distressed by prolonged diagnostic uncertainty (5).

Early consideration of psychosocial factors is the cornerstone of appropriate management of MUS (20). It is possible that specific psychobehavioural characteristics

can also facilitate their clinical recognition, even if psychobehavioural factors associated with MUS have to be differentiated from psychobehavioural factors associated with phenomenologically similar organic diseases.

In order to explore possible predictors for MUS among patients with suspected allergies, we describe here psychopathological, psychobehavioural and interactional characteristics of patients undergoing intensive allergy diagnostic procedures, as well as a comparison group of patients with proven hymenoptera allergies.

MATERIALS AND METHODS

Patients

Over a period of 11 months, we invited 245 consecutive patients who were admitted as inpatients to the Technische Universität München (TUM) allergy department for an allergy work-up because of symptoms that could not be diagnosed with sufficient certainty in an outpatient setting ("work-up group") (21). The only inclusion criterion for this cross-sectional study was presentation with physical symptoms due to suspected allergies. Exclusion criteria were: (i) age < 18 or > 65 years, and (ii) insufficient command of the German language. The same exclusion criteria were applied to 55 consecutive patients hospitalized for specific immunotherapy due to an established diagnosis of hymenoptera venom allergy (venom immunotherapy (VIT)), who served as controls.

Study procedure and study instruments

Interview. Patients who gave informed consent underwent an interview with a psychiatrist (CHW or SB) of approximately 45 min duration. The interview covered subjective symptoms, healthcare utilization, past medical history, a structured diagnostic interview for somatoform disorders (for details see (19)), and instructions for a set of self-rating questionnaires (see below). Afterwards, the interviewing psychiatrists classified their impression of the patient's interactional behaviour into one of five categories (5 = "Warm, authentic, active participation/commitment and 'we' feeling"; 4 = "Warm, but patient makes an effort to control the dialogue; quite good participation/commitment and 'we' feeling"; 3 = "Warm contact, though patient shows limited capacity for emotional interaction"; 2 = "Patient shows difficulty in maintaining interactional contact; hostile and/or aggressive emotions towards interviewer"; 1 = "Patient shows no self-disclosure; no emotions; totally impossible to establish contact with the subject") according to Brand et al. (22). Additionally, the interviewer's countertransference (i.e. feelings towards the patient after the contact) was scored in 10 dimensions ("overwhelmed/disorganized", "helpless/inadequate", "positive" (reversed coded), "special/overinvolved", "sexualized", "disengaged", "parental/protective", "criticized/mistreated", "controlled/patronized", and "angry/enraged") on 5-point Likert-scales resulting in a sum score (range 10–50), a higher score reflecting a more problematic countertransference (23).

Self-rating questionnaires. Self-rating questionnaires covered relevant mental morbidity and various psychobehavioural features (21). The modules for somatoform, depressive, panic, and bulimia nervosa/binge-eating syndromes of the Patient Health Questionnaire (PHQ) were used for categorical assessment of the presence of probable mental diagnoses (24). Three PHQ modules were additionally used for the dimensional assessment

of somatization (PHQ-15), depression (PHQ-9), and anxiety (GAD-7) (25–27). Moreover, the patients completed the Illness Perception Questionnaire, Revised (IPQ-R (28)) for the assessment of seven aspects of illness perception (timeline; consequences; personal control; treatment control; coherence; cyclical course; emotional representations); the 7-item short form of the Whiteley-Index (WI-7 (29)); the Reassurance Questionnaire (RQ (30)); and four subscales of the Health Attitude Survey (HAS (31)) (dissatisfaction with care; frustration with ill health; excessive health worry; psychological distress).

Rating of symptom explanation. Subject to their agreement, all work-up patients underwent examinations commensurate with their clinical problem, including blood and skin testing, double-blind, placebo-controlled provocation tests, and consultations with other departments for differential diagnostic procedures. In order to avoid biasing placebo testing, patients were told about their test results and final diagnoses in a closing discussion with their responsible allergist on the very last day of their stay. Afterwards, the same physician rated the degree of organic symptom explanation by means of a systematic stepped review of all findings (from history to blinded provocation testing). The final decision was summarized by means of a 5-step rating scale (0 = not at all explained; 1 = almost not explained; 2 = approximately 50% explained; 3 = almost fully explained; 4 = fully explained). For subgroup analyses of work-up patients, the rating was dichotomized into "not or almost not explained" (0 or 1; in the following referred to as "EXPL⁻") and "at least partly explained" (2, 3, or 4; "EXPL⁺").

Ethics

All procedures were performed as approved by the ethics committee of the Medical Faculty, TUM, in accordance with the principles expressed in the Declaration of Helsinki.

Statistical analyses

Statistical analyses were conducted with the Statistical Package for the Social Sciences (SPSS), version 17.0. Data were analysed descriptively reporting absolute numbers (percentages) for categorical variables and means (standard deviations) for continuous variables. Pair-wise comparisons were conducted with χ^2 tests and Mann-Whitney *U* tests. All statistical comparisons were performed using a 0.05 level of significance. Due to uneven gender distribution in both work-up groups, pair-wise comparisons were corrected for sex by applying binary logistic regression analysis for categorical variables and univariate analysis of covariance (ANCOVAs) for continuous variables. To reduce the likelihood of statistically significant results by chance, pair-wise comparisons were conducted between EXPL⁺ and EXPL⁻ and between EXPL⁺ and VIT only, and the levels of significance were adjusted accordingly (*p* multiplied by 2).

To establish a prediction model for EXPL⁻, variables with notable differences between EXPL⁻ and EXPL⁺ groups (entry criterion *p* ≤ 0.05) were considered simultaneously in multiple logistic regression analyses (forward conditional selection procedure). The dependent variable of the logistic regression model was the allergologic rating of organic symptom explicability (EXPL⁺/EXPL⁻), the classification cut-off was 0.25. Goodness of fit was assessed with the Hosmer-Lemeshow test. Odds ratios (OR) were calculated with 95% confidence intervals (CI); for continuous variables they were reported for 1-point increases on the according test scales. To assess predictive performance of the predictive model, receiver operating characteristics (ROC) were conducted and the areas under the curve (AUCs) were described as illustrative measures for predictive sensitivity and specificity.

RESULTS

Participation

A total of 218 of the 245 (89%) included work-up patients participated in the interview. The allergists rated the organic explicability of the presenting symptoms of 216 patients (99%); two patients decided to leave the hospital before a sufficient work-up could be performed. Of the 216 patients who were interviewed and who received a rating of organic explicability, 204 returned their questionnaires. Thus, full participation and datasets with only single items missing were obtained from 204 patients (83%). In the VIT group, 50 of 55 patients participated in the interview, and 49 patients returned their questionnaires (participation rate 89%).

Organic symptom explanation in the work-up group

In the work-up group, the symptoms of 20 patients (9.8%) were rated as "0 = not explained", of 36 patients (17.6%) as "1 = almost not explained", of 39 patients (19.1%) as "partly explained", of 63 patients (30.9%) as "3 = almost fully explained", and of 46 patients (22.5%) as "4 = fully explained". Thus, 56 work-up patients with "not or almost not explained" symptoms (EXPL⁻) were contrasted with 148 work-up patients with at least "partly explained" symptoms (EXPL⁺).

Sociodemographic data, organic comorbidity and suspected allergens

Apart from a significant predominance of women in the EXPL⁻ group, sociodemographic profile and organic comorbidity were similar in both subgroups of work-up patients (Table I). EXPL⁺ and VIT patients were similar in terms of their sociodemographic profile and organic comorbidity (Table I).

The spectrum of suspected allergens differed between EXPL⁻ and EXPL⁺ patients, and of course also between EXPL⁺ and VIT patients (Table I).

Interviewer assessment of patient–doctor interaction

In the work-up group, interactional behaviour of, and countertransference towards, EXPL⁻ patients were rated clearly more problematic compared with EXPL⁺ patients (Table II). In detail, countertransference towards EXPL⁻ patients was described as more overwhelmed/disorganized ($p < 0.001$), more helpless/inadequate ($p = 0.008$), less positive ($p < 0.001$), and more criticized/mistreated ($p = 0.006$). The patients' interactional behaviour was rated as "warm, authentic, active participation/commitment and 'we'-feeling" in only 31% of EXPL⁻ patients (Table II).

Table I. Sociodemographic variables, duration of presenting symptoms, organic comorbidity and suspected allergens in 204 work-up patients and 49 venom immunotherapy (VIT) patients

	Work-up: EXPL ⁺ n = 148	Work-up: EXPL ⁻ n = 56	VIT patients n = 49	p-values of χ^2 -test	
				p ^a	p ^b
Age ^c , years, mean \pm SD	43.8 \pm 13.1	42.5 \pm 12.1	43.8 \pm 10.9	0.48	0.70
Sex, n (%)				0.02	0.88
Female	101 (68.2)	47 (83.9)	34 (69.4)		
Male	47 (31.8)	9 (16.1)	15 (30.6)		
Current partnership, n (%)				0.86	0.93
Yes	111 (75.0)	41 (73.2)	36 (73.5)		
No	32 (21.6)	11 (19.6)	10 (20.4)		
No answer/Not applicable	5 (3.4)	4 (7.2)	3 (6.1)		
Number of school years ^c , mean \pm SD	13.6 \pm 3.8	12.8 \pm 3.7	12.7 \pm 3.6	0.13	0.11
Current occupation (including training), n (%)				0.98	0.21
Yes	126 (85.1)	47 (83.9)	44 (89.8)		
No	19 (12.8)	7 (12.5)	3 (6.1)		
No answer/Not applicable	3 (2.0)	2 (3.6)	2 (4.1)		
Duration of presenting symptoms ^c , years, mean \pm SD	6.3 \pm 9.4	6.5 \pm 7.1	6.2 \pm 8.2	0.17	0.18
History of other allergy, n (%)				0.15	0.38
Yes	68 (45.9)	32 (57.1)	19 (38.8)		
No	80 (54.1)	24 (42.9)	30 (61.2)		
Number of concurrent somatic diagnoses (other than allergy), n (%)				0.48	0.13
0	66 (44.6)	32 (57.1)	33 (67.3)		
1–2	67 (45.3)	22 (39.3)	14 (28.6)		
\geq 3	15 (10.1)	2 (3.6)	2 (4.1)		
Suspected allergens, n (%)				0.001	<0.001
Drugs	58 (39.2)	24 (42.9)	0		
Foods	45 (30.4)	25 (44.6)	0		
Chemicals	1 (0.7)	4 (7.1)	0		
Hymenoptera venom	0	0	49 (100)		
Other/mixed/unclear	44 (29.7)	3 (5.4)	0		

^aEXPL⁺ vs. EXPL⁻ patients; ^bEXPL⁺ vs. VIT patients; ^cp-values of Mann–Whitney U test.

EXPL⁺: work-up patients with medically explained symptoms; EXPL⁻: work-up patients with medically unexplained symptoms; SD: standard deviation.

Table II. Interviewer perspective: rating of interactional behaviour and countertransference in 204 work-up patients and 49 venom immunotherapy (VIT) patients

	EXPL ⁺	EXPL ⁻	VIT	Bonferroni-adjusted <i>p</i> -values	
	<i>n</i> = 148 <i>n</i> (%)	<i>n</i> = 56 <i>n</i> (%)	<i>n</i> = 49 <i>n</i> (%)	<i>p</i> ^a	<i>p</i> ^b
Interactional behaviour				<0.001	>0.99
5 = Warm, authentic, active participation/commitment; "we" feeling	87 (58.8)	17 (30.6)	31 (63.3)		
4 = Warm, but patient makes an effort to control the dialogue; quite good participation/commitment and "we" feeling	48 (32.4)	23 (41.2)	12 (24.5)		
3 = Warm contact, though patient shows limited capacity for emotional interaction	12 (8.8)	15 (26.8)	6 (12.2)		
2 = Patient shows difficulty in maintaining interactional contact; hostile and/or aggressive emotions towards interviewer	1 (0.7)	1 (1.8)	0		
1 = Patient shows no self-disclosure; no emotions; totally impossible to establish contact with the subject	0	0	0		
Countertransference sum score, mean ± SD ^c	11.2 ± 1.5	12.6 ± 1.9	11.1 ± 1.4	<0.001	>0.99

^aEXPL⁺ vs. EXPL⁻ patients; ^bEXPL⁺ vs. VIT patients; ^c*p*-values of analysis of covariance (ANCOVA) with subgroup and sex as fixed factors.

EXPL⁺: work-up patients with medically explained symptoms; EXPL⁻: work-up patients with medically unexplained symptoms; SD: standard deviation.

With respect to both these measures of patient–doctor interaction, there were no significant differences between EXPL⁺ and VIT patients (Table II).

Self-reported psychobehavioural characteristics

A higher dissatisfaction with care was the only self-descriptor that differentiated EXPL⁻ from EXPL⁺ patients (Table III). Psychobehavioural differences between EXPL⁺ and VIT patients, however, were more frequent and more pronounced, indicating health-related and general psychosocial distress in EXPL⁺ as well as EXPL⁻ patients (Table III).

Mental comorbidity

Among work-up patients, mental comorbidity according to PHQ was significantly higher in the EXPL⁻ than in the EXPL⁺ group, especially regarding the prevalence of depressive syndromes (Table IV). Dimensional assessment showed higher depression and a trend towards higher somatization in EXPL⁻ patients.

Between EXPL⁺ patients and VIT patients, mental comorbidity was comparable (Table IV). Dimensional assessment revealed more psychological distress (somatization and depression) in the EXPL⁺ group (Table IV).

Table III. Self-reported psychobehavioural characteristics in 204 work-up patients and 49 venom immunotherapy (VIT) patients. *P*-values of analysis of covariance (ANCOVA) with subgroup and sex as fixed factors

	Work-up: EXPL ⁺ <i>n</i> = 148 Mean ± SD	Work-up: EXPL ⁻ <i>n</i> = 56 Mean ± SD	VIT patients <i>n</i> = 49 Mean ± SD	<i>p</i> ^a	<i>p</i> ^b
<i>Interview</i>					
Number of consulted physicians (last 12 months)	4 ± 2	6 ± 6	4 ± 2	0.06	0.06
Number of outpatient visits (last 12 months)	14 ± 15	19 ± 25	8 ± 6	0.48	0.008
<i>Self-rating questionnaires with test ranges^c</i>					
IPQ-R timeline (acute/chronic) (5–25)	14.8 ± 4.6	16.4 ± 5.1	14.6 ± 4.0	0.08	>0.99
IPQ-R consequences (5–25)	12.2 ± 4.4	13.8 ± 5.1	9.3 ± 3.3	0.06	<0.001
IPQ-R personal control (4–20)	11.5 ± 4.2	10.3 ± 3.7	10.8 ± 4.1	0.22	0.57
IPQ-R treatment control (4–20)	13.7 ± 2.9	12.7 ± 3.6	16.7 ± 2.3	0.06	<0.001
IPQ-R illness coherence (5–25)	15.2 ± 5.8	14.6 ± 5.7	19.2 ± 6.1	0.98	<0.001
IPQ-R timeline cyclical (4–20)	10.6 ± 3.8	11.0 ± 3.8	7.6 ± 3.2	0.80	<0.001
IPQ-R emotional representations (5–25)	12.3 ± 5.4	12.3 ± 5.3	10.6 ± 3.9	>0.99	0.08
WI-7 disease conviction (3–15)	6.8 ± 2.8	7.6 ± 3.2	5.6 ± 2.2	0.10	0.02
WI-7 illness worrying (3–15)	6.1 ± 2.4	6.6 ± 3.0	5.6 ± 2.2	0.12	0.46
Reassurance Questionnaire sum score (0–40)	13.9 ± 5.4	15.0 ± 5.8	13.1 ± 4.9	0.30	0.72
HAS dissatisfaction with care (0–36)	10.7 ± 5.5	13.8 ± 6.2	7.9 ± 5.0	0.002	0.006
HAS frustration with ill health (0–16)	9.0 ± 3.6	10.0 ± 4.3	5.4 ± 3.7	0.14	<0.001
HAS excessive health worry (0–12)	3.1 ± 2.5	3.0 ± 2.5	2.6 ± 2.4	>0.99	0.42
HAS psychological distress (0–16)	6.5 ± 3.0	6.4 ± 3.2	5.6 ± 2.9	>0.99	0.18

^aEXPL⁺ vs. EXPL⁻ patients; ^bEXPL⁺ vs. VIT patients. ^cPossible subscale scores (minimum–maximum), with direction indicating psychobehavioural distress in bold.

PHQ: Patient Health Questionnaire; IPQ-R: Illness Perception Questionnaire-Revised; HAS: Health Attitude Survey; EXPL⁺: work-up patients with medically explained symptoms; EXPL⁻: work-up patients with medically unexplained symptoms; SD: standard deviation.

Table IV. Concomitant mental disorders according to Patient Health Questionnaire (PHQ) in 202 work-up patients and 48 venom immunotherapy (VIT) patients. One patient in each group did not complete the PHQ

		EXPL ⁺ n = 147	EXPL ⁻ n = 55	VIT n = 48	p ^a	p ^b
PHQ Categorical assessment*, n (%)	Somatoform syndrome	19 (12.9)	13 (23.6)	2 (4.2)	0.08	0.22
	Major or other depressive syndrome	8 (5.4)	14 (25.5)	2 (4.2)	<0.001	>0.99
	Panic or other anxiety syndrome	8 (5.4)	5 (9.1)	1 (2.1)	0.36	0.72
	Bulimia nervosa or binge eating syndrome	0	2 (3.6)	0	n/a	n/a
	Any PHQ mental disorder	29 (19.7)	25 (45.5)	5 (10.4)	<0.001	0.30
PHQ Dimensional assessment**, mean ± SD	Somatization (PHQ-15)	7.1 ± 4.1	8.7 ± 5.5	5.4 ± 3.5	0.06	0.02
	Depression (PHQ-9)	4.7 ± 3.3	6.6 ± 5.0	3.2 ± 2.8	0.006	0.01
	Anxiety (GAD-7)	4.0 ± 2.	4.2 ± 3.4	3.1 ± 2.5	>0.99	0.10

^aEXPL⁺ vs. EXPL⁻ patients; ^bEXPL⁺ vs. VIT patients.

*Numbers (%) and Bonferroni-adjusted *p*-values of binary logistic regression including subgroup and sex as covariates; **Means (standard deviation (SD)) and Bonferroni-adjusted *p*-values of analysis of covariance (ANCOVA) with subgroup and sex as fixed factors.

EXPL⁺: work-up patients with medically explained symptoms; EXPL⁻: work-up patients with medically unexplained symptoms; n/a: not analysed due to small sample sizes.

Independent predictors

Among work-up patients, a multiple logistic regression model including sex, presence of a mental disorder according to PHQ, and the HAS score “dissatisfaction with care” identified all three variables as independent predictors of EXPL⁻ status, with an OR of 1.08 (CI 1.01–1.14; *p* = 0.02) for every 1-point increase on the HAS “dissatisfaction with care” scale, an OR of 3.02 (CI 1.26–7.24; *p* = 0.01) for female sex, and an OR of 3.72 (CI 1.77–7.79; *p* = 0.001) for the presence of a mental disorder. This model showed good fit (Hosmer-Lemeshow test: $\chi^2 = 2.06$; *df* = 8; *p* = 0.98), and moderate predictive sensitivity and specificity (AUC 0.73; CI 0.66–0.81; *p* < 0.001; correct classification: 69% of EXPL⁻ and 64% of EXPL⁺ patients). When the interviewer-assessed interactional parameters were added to this logistic regression, the final model had still good fit ($\chi^2 = 4.52$; *df* = 6; *p* = 0.61). It correctly classified 69% of EXPL⁻ and 72% of EXPL⁺ patients, and again contained three independent predictors of EXPL⁻ status: presence of a mental disorder with an OR of 2.65 (CI 1.21–5.80; *p* = 0.02); female sex with an OR of 3.70 (CI 1.49–9.17; *p* = 0.005); and countertransference sum score with an OR of 1.50 (CI 1.22–1.85; *p* < 0.001), for every 1-point increase on the test scale. This model had slightly better predictive sensitivity and specificity (AUC 0.77; CI 0.70–0.85; *p* < 0.001).

DISCUSSION

To our knowledge, this is the first study that has attempted to predict MUS in patients with suspected allergies on the basis of psychobehavioural characteristics. The results reveal interesting new aspects. Of all investigated self-reported features only one interactional feature differentiated patients with MUS. To a small extent, but consistently, physicians’ interactional ratings were also indicative of more interactional problems with MUS patients. Furthermore, assessment of the

patient–doctor interaction bore considerable diagnostic value: A lack of organic symptom explanation, which was independently assessed by experienced allergists based on highly specialized medical procedures, could be predicted by both patient-sided (dissatisfaction with care) and doctor-sided (a problematic countertransference) evaluations.

It is already known that physicians perceive patients with MUS as especially “difficult” (10, 22, 31). Possible reasons are manifold. First, unexplained symptoms are known to be associated with mental disorders, which are often perceived as difficult to handle, especially by doctors in the somatic setting (32). Secondly, even in absence of mental disorders, physicians are frustrated by the “vagueness” of MUS and their own inability to make a diagnosis (32). Thirdly, when physicians evaluate symptoms, they usually focus on pathophysiological processes, whereas patients are often more concerned with subjective experiences and the illness’ impact on quality of life (32, 33). And finally, physical (especially somatoform) symptoms may be generated and sustained because they establish the sick role and alter a patient’s social relationships in a way that transcends traditional diagnostic paradigms altogether (32, 34). However, empirical evidence of such assumptions based on valid psychometric instruments is sparse.

Even less is known about the patient’s notice of patient–doctor relationships. In one study, somatizing patients were less satisfied with their medical care than subjects with severe organic illness (31). In another, patients with somatoform, eating, and personality disorders were less satisfied than patients with affective, anxiety, and adjustment disorders (35). Our healthcare system is not well prepared to care for patients with MUS, and patients may be rightly dissatisfied. However, it has been shown that patients with MUS genuinely tend to have a more insecure attachment style, arguing for more profound disturbances in personality development and not just *reactive* interactional difficulties (36). Thus, professional reflection of patient–doctor interactions

should become not only a matter of course in daily routine, but also an object of research further to investigate its diagnostic and therapeutic value. Frostholm et al. (37) have demonstrated that patients are more content when they are treated by physicians who have been specially trained in communication skills. Above all, we need training in how to think about symptoms in a non-dualistic way and how to respond appropriately to patients' emotional needs (10).

Even if other authors found, for example, more negative illness perceptions in patients with MUS than in patients with organically defined illness (38), the majority of all evaluated psychobehavioural characteristics in this study did *not* sufficiently identify patients with MUS. It is probable that this is due to the heterogeneity of this group of patients (20). When MUS are persistent and lead to functional impairment, a so-called somatoform disorder (SFD) is usually present (20, 39). In other patients, MUS are bodily manifestations of depression or anxiety (20, 39). However, patients can also have a psychosocially uncomplicated course of MUS without qualifying for any mental diagnosis (20). In our study, only approximately 25% of patients with MUS screened positive for a somatoform syndrome, and approximately 46% for any mental illness. In the majority of patients, the PHQ did not detect any mental diagnosis. It has been shown that subgroups can quite reliably be identified based on distinct psychobehavioural features, since patients with specific mental disorders appear to have distinct illness perceptions and health attitudes (21, 31, 40, 41). Thus, the usefulness of self-reported psychobehavioural characteristics and psychosocial distress as adequate descriptors of the very heterogeneous group of MUS patients as a whole is clearly limited, at least without knowledge about coexisting mental illness. In accordance with the literature, mental comorbidity and female gender could be confirmed as independent predictors for MUS (42, 43).

On the other hand, by describing several psychobehavioural (but to a lesser extent interactional) differences between EXPL⁺ and VIT patients, we confirmed that yet unproven but "true" allergy is associated with higher psychological burden than an established allergy diagnosis (4, 5). Furthermore, other authors have shown that negative illness perceptions predict self-reported health in patients with MUS *as well as* patients with organically defined illness of up to 2 years' duration (38). Clinicians should therefore detach themselves from an all-too dualistic thinking and rather be attentive for psychosocial distress in *every* patient presenting with suspected allergies, regardless of causality, especially in the diagnostic phase.

Our study has several limitations. To our knowledge, there is no "gold standard" for the evaluation of relational (dis-)abilities and notions of the patient–doctor interaction. Empirical literature on patient–doctor

interaction and countertransference is limited, their quantification is quite uncommon, and the few available measures are relatively new and insufficiently validated compared with measurements of general interpersonal problems (22, 23, 31, 32, 34). Therefore, even with its intended focus on subjective statements, our study has much of a pilot approach. Furthermore, it is cross-sectional and does not allow any conclusions about temporal relations between variables; for example, whether patients with MUS may have become dissatisfied with care *over time*.

By focusing on illness-related and interactional characteristics, many other contextual aspects (such as gender, ethnicity, or quality of life) have not been adequately considered in this study, even if they do influence health perception, health utilization, satisfaction with care etc., in allergic disease.

Furthermore, our work-up sample represents typical inpatients of a university allergy department. It is possible that patients from a different setting would have been less complex, because of less mental comorbidity or less dangerous suspected allergies and allergens. The comparison of undiagnosed mixed allergies in the EXPL⁺ group and diagnosed specific allergies in the VIT group may also be flawed. A control group of non-allergic healthy subjects would also have been useful. Therefore, these preliminaries prevented us from conducting further statistical analyses of our data (such as an internal validation of the predictive model). The validity and generalizability of our findings has yet to be proven.

We used the PHQ as a screening instrument for mental disorders and mental distress, to roughly estimate these moderators by applying an economic self-rating tool. The validity of the PHQ's categorical assessment of various mental diagnoses is not comparable with that of more sophisticated diagnostic tools. Therefore, we cannot draw any conclusions about the relevance of *specific* mental diagnoses from our data.

And, finally, multiple testing is a statistical limitation of our work that we tried to account for by a limited number of pair-wise comparisons and Bonferroni-adjustments of levels of significance.

Conclusion

- The quality of the patient–doctor interaction may provide clues about the likelihood of "MUS": When confronted with unclear physical symptoms, clinicians should be aware of the patient's interactional behaviour and their own feelings towards him or her.
- The presence of mental disorders (especially somatoform, depressive and anxiety disorders, because they tend to present with physical symptoms) also indicates a lack of organic findings. Screening questions or self-report questionnaires allow screening in daily routine.

- Psychosocial distress and negative illness perceptions should not automatically be taken as evidential of non-organic illness. Regardless of whether they are causal, reactive, or coincident, they contribute significantly to the patients' suffering and have an impact on the prognosis. Thus, they merit appropriate recognition and management.

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