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Personality Characteristics and Their Association with Biological Stress Responses in Patients with Atopic Dermatitis

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Key Words
Personality · Atopic dermatitis (AD) · Stress · Psychobiology

Summary
Background: The potential relevance of personality factors on atopic dermatitis (AD) has long been a focus of psychodermatological research. A central premise underlying this line of research is that AD sufferers show a distinct personality profile that may increase the vulnerability to develop or to exacerbate AD especially under stress. **Objective:** The specific goal of the present study was to assess specific personality traits in AD sufferers and their possible relationship to biological stress responses. **Material and Methods:** 36 AD patients, 23 patients suffering from psoriasis (PSO) and 37 non-atopic controls were investigated. To determine different personality domains, Spielberger's State-Trait Anxiety Inventory (STAI), the Questionnaire for Competence and Control (FKK) and the Questionnaire for Stress Vulnerability (MESA) were administered. In order to investigate whether these personality dimensions are related to biological stress responses, AD subjects and healthy controls were confronted with a standardized laboratory stressor (Trier Social Stress Test; TSST). Blood and saliva samples were obtained before and after the stress test to measure endocrine (cortisol, ACTH, catecholamines) and immunological (immunoglobulin-E, cytokines, leukocyte subsets) stress responses. Furthermore, heart rate responses to the stressor and morning cortisol after awakening were recorded. **Results:** When compared to healthy controls, AD and PSO patients showed significantly higher scores in trait anxiety (STAI) and stress vulnerability (MESA) in situations characterized by failure, job overload, social conflicts and uncertainness. In addition, they scored significantly lower in positive self-concept (FKK). No difference in these personality traits could be detected between AD and PSO subjects. When confronted with the laboratory stressor (TSST), significantly altered endocrine and immune responses in AD patients could be determined which are described elsewhere [J Clin Endocrinol Metab 2002;87:4245–4251; J Neuroimmunol 2002;129:161–167]. However, Pearson correlational analysis indicated no significant correlation between the different personality domains and any of the endocrine, immunological or physiological stress responses. The cortisol response to awakening in the morning, however, was significantly correlated with the stress vulnerability in situations characterized by job overload and criticism. **Conclusions:** AD patients show a distinct personality pattern, which does not differ from that found in PSO patients suggesting that there may be no specific 'atopic' personality type but rather a personality pattern linked to chronic inflammatory skin disorders.

Schlüsselwörter
Persönlichkeit · Atopische Dermatitis (AD) · Stress · Psychobiologie

Zusammenfassung
Aspekte der Persönlichkeit und ihre Beziehung zu biologischen Stressreaktionen bei Patienten mit atopischer Dermatitis
Hintergrund: Persönlichkeitsfaktoren und ihre Rolle bei der Entstehung und dem Verlauf der atopischen Dermatitis (AD) sind schon lange ein Forschungsgebiet der Psychodermatologie. Eine Hypothese hierbei ist, dass AD-Patienten ein spezifisches Persönlichkeitsprofil aufweisen, das eine Exazerbation der Erkrankung insbesondere in akuten Belastungssituationen induziert. **Ziel:** Mit der vorliegenden Untersuchung sollten Atopie-spezifische Persönlichkeitsmerkmale und ihre Beziehung zu biologischen Stressreaktionen bei AD-Patienten überprüft werden. **Methoden:** 36 AD-Patienten, 23 Patienten mit Psoriasis (PSO) und 37 nicht-atopische Kontrollpersonen wurden mittels verschiedener Fragebögen (State-Trait-Angstinventar [STAI]; Fragebogen zur Kompetenz- und Kontrollüberzeugung [FKK]; Messinstrument zur Erfassung der Stressanfälligkeit [MESA]) untersucht. Um einen möglichen Zusammenhang zwischen spezifischen Persönlichkeitsmerkmalen und der biologischen Stressreaktivität bei AD-Patienten zu überprüfen, wurden AD-Patienten und nicht-atopische Kontrollpersonen mit einem standardisierten Stress-Test («Trierer Sozial-Stress-Test», TSST) konfrontiert. Zur Bestimmung von endokrinen (Kortisol, ACTH, Katecholamine) und immunologischen (Immunglobulin-E, Zytokine, Leukozytensubpopulationen) Parametern wurden Blut- und Speichelproben vor und nach dem TSST entnommen. Weiterhin wurden die stressinduzierte Veränderung der Herzrate sowie die Kortisolspiegel morgens nach dem Erwachen erfasst. **Ergebnisse:** Im Vergleich zu den gesunden Kontrollpersonen zeigten AD- und PSO-Patienten signifikant erhöhte Werte in den Merkmalen Ängstlichkeit (STAI) und Stressvulnerabilität (MESA) in Situationen, die durch Misserfolgserlebnisse, Arbeitsüberlastung, soziale Konflikte und Unsicherheit gekennzeichnet sind. Weiterhin zeigten AD- und PSO-Patienten signifikant niedrigere Werte in der Skala «Vertrauen in die eigenen Fähigkeiten» (FKK). AD- und PSO-Patienten unterschieden sich bezüglich der genannten Persönlichkeitsmerkmale nicht voneinander. Bei Konfrontation der Versuchspersonen mit dem TSST zeigten AD Patienten deutlich veränderte endokrine und immunologische Stressreaktionen, die an anderer Stelle beschrieben werden [J Clin Endocrinol Metab 2002;87:4245–4251; J Neuroimmunol 2002;129:161–167]. Allerdings ließ sich kein Zusammenhang zwischen den untersuchten Persönlichkeitsfaktoren und den beobachteten endokrinen, immunologischen oder physiologischen Stressreaktionen auf die akute Belastungssituation feststellen. Es zeigte sich jedoch eine signifikante Korrelation zwischen der Veränderung des Kortisolspiegels nach dem morgendlichen Erwachen und der Stressvulnerabilität in Situationen, die durch Arbeitsüberlastung und Kritik charakterisiert sind. **Schlussfolgerung:** AD-Patienten weisen ein spezifisches Persönlichkeitsprofil auf, das sich jedoch nicht von PSO-Patienten unterscheidet und insofern nicht «Atopie-spezifisch», sondern generell mit einer chronisch-entzündlichen Hauterkrankung assoziiert zu sein scheint.

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Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disorder with increasing incidence characterized by symptoms such as eczematous skin, papules and severe pruritus [Leung, 2000; Boguniewicz, 1997]. There is general agreement that the development and chronification of AD involves multiple factors such as genetic disposition, climate, allergens, or microbial factors (i.e. *Staphylococcus aureus*) [Werfel and Kapp, 1998; Leung, 1995]. Besides, research of the last decade strongly suggests an underlying immunoregulatory abnormality in AD characterized by a hypersecretion of immunoglobulin-E (IgE), elevated levels of proinflammatory, mainly T helper cell type 2 (TH_2) related cytokines and eosinophilia [Leung and Soter, 2001]. In addition, psychological factors such as personality have been assumed to be significant modulators of AD. In this line of research it has been suggested that AD sufferers display an atopy-specific personality profile characterized for example by neuroticism, hostility, anxiety, hypersensitivity, aggressiveness, feelings of inferiority, tension, depression, restlessness, insecurity, emotional lability and rigidity [Greenhill and Finesinger, 1942; Kepecs et al., 1951; Rogerson, 1947]. It should be emphasized, however, that the approach to link a distinct personality profile to AD has been criticized and is still a matter of debate [White et al., 1990]. It has been argued that the personality pattern described in AD patients might not reflect an atopy-specific personality profile but rather a personality structure of the 'chronically ill' which would question the etiological significance of the proposed AD personality pattern. It has further been criticized that most of the studies did not address the question what the underlying (psychobiological) mechanisms of a relation between personality and AD might be.

The specific goal of the present study was to evaluate whether AD patients show a distinct, atopy-specific personality structure that differs from the personality profile determined in non-atopic controls and in patients with psoriasis (PSO), another chronic inflammatory skin disease [Asadullah et al., 2002]. It should further be investigated whether possible atopy-specific personality traits are linked to endocrine and immunological stress responses in AD sufferers. This idea evolved from recent findings of our laboratory showing significantly altered cortisol and catecholamine responses in AD patients when confronted with psychosocial stress [Buske-Kirschbaum et al., 1997, 2002a]. In addition, stress-induced changes of immune functions known to be pathologically relevant were altered in AD sufferers [Buske-Kirschbaum et al., 2002]. Based on these observations we presumed that an atopy-specific personality structure in AD patients may be linked to an altered psychological and biological stress response that may render the person more vulnerable to develop and exacerbate AD pathology.

Methods

Subjects

Patients with AD (n = 36; 18 men, 18 women; mean age 25.0 ± 3.8 years) were interviewed and tested. All AD patients were clinically diagnosed with AD and fulfilled the diagnostic criteria by Hanifin and Rajka [1980]. Patients with current steroid medication or with high-potency inhalant or oral steroid treatment in the past were excluded from the study. Disease severity was assessed by using the Costa score [Costa et al., 1989]. Patient's mean score was 28.9 ± 16.5 indicating a moderate disease activity. As control groups, age and sex matched non-atopic subjects (n = 37; 19 men, 18 women; mean age 24.5 ± 3.4) and patients suffering from psoriasis (n = 23; 12 men, 11 women; mean age 32.7 ± 7.5) were recruited. All control subjects were medication free and all PSO patients were refrained from using topical steroids at least for 3 months prior to the onset of the study. None of the controls had ever suffered from atopy or had a family history of atopy. To control for a potential effect of sex hormones on biological measures, female AD sufferers and female controls were matched for menstrual cycle phases. The experimental protocol was approved by the local ethics committee and written informed consent was obtained from all subjects before participating in the study.

Psychological Assessment

Trait anxiety was assessed by the State-Trait Anxiety Inventory (STAI) [Laux et al., 1981] using the trait component (STAI-T). High levels of trait anxiety are assumed to dispose the individual to experience more situations as being more threatening. The STAI-T includes 20 items to be rated on a 4-point intensity scale (internal consistency: Cronbach's $\alpha = 0.90$). For assessing locus of control and self-concept, the Questionnaire of Competence and Control (FKK) was used [Krampen, 1991]. In the FKK, 'positive self-concept' (e.g. 'Even in difficult situations I usually have many possibilities'), 'internality' (e.g. 'I can determine many things that are happening in my life'), 'powerful others control' (e.g. 'My personal life is determined by other persons in many areas') and 'chance' (e.g. 'Many events in my life happen by chance') are evaluated. The FKK consists of 32 items with 6-point response scales ranging from 'completely disagree' to 'completely agree'. For the FKK, internal consistencies between 0.70 and 0.89 have been described. The Inventory to Measure Stress Vulnerability (MESA) [Schulz, 1995] assesses stress vulnerability/stress proneness and records cognitive, social, emotional and bodily responses to specific stressful situations of everyday life. The MESA consists of 6 scales and 36 items evaluating 'vulnerability against failure', 'vulnerability against work overload', 'vulnerability against social conflict', 'vulnerability against criticism', 'vulnerability against uncertainness' and 'recreation ability'. Internal consistencies of the MESA vary between 0.71 and 0.91.

Psychosocial Stress Test

To investigate whether personality traits in AD subjects were related to biological stress responses, AD sufferers and healthy controls were exposed to the 'Trier Social Stress Test' (TSST) which includes a free speech (5 minutes) and mental arithmetic tasks (5 minutes) in front of an audience (3 persons). Numerous studies have demonstrated that the TSST leads to significant activation of the HPA axis and the sympathetic adrenomedullary (SAM) system as indicated by elevated ACTH, cortisol and catecholamine levels [Kirschbaum et al., 1993].

Biochemical Analyses

To determine free cortisol concentrations, saliva samples were collected 30, 20, 10, and 1 min before, and 10, 20, 30, 40, 50 and 70 min after the

Table 1. Trait anxiety (STAI) in patients with AD or PSO and in non-atopic controls

	AD	PSO	Controls	F	df	p
Anxiety	42.1	41.0	35.2	5.3	93	0.006

TSST. Morning cortisol levels were obtained after awakening and 10, 20 and 30 min thereafter. Cortisol levels were analyzed using a time-resolved fluorescence immunoassay (DELFIA) that has been described elsewhere [Dressendörfer et al., 1990].

Blood samples were obtained 10 min before and 1, 10, 20, and 60 min after the stress test. ACTH was measured by a 2-site luminescence immunoassay (Nichols Institute, Bad Nauheim, Germany). Plasma concentrations of epinephrine and norepineprine were determined after alumina extraction and subsequent reverse-phase HPLC (high performance liquid chromatography) with electrochemical detection [Kringe et al., 1982]. Cytokines (IL-4, IFN-γ) were analyzed by use of enzyme-linked immunoassays (IL-4; OptEIA, Pharmingen, Hamburg, Germany; IFN- γ; Quantigen™, Pharmingen, Hamburg, Germany) as indicated by the manufacturer. Blood cell counts were determined using a hematology analyzer (Technikon H3, Bayer Diagnostics, Germany). A blood sample obtained 10 min before the TSST and at identical time point 24 hrs later was used to determine total serum IgE using and enzyme-linked immunosorbent assay (ELISA; IBL, Hamburg, Germany). Heart rates were monitored continuously at 1-min intervals using a wireless signal transmission device (Sport Tester Profi, Polar Instruments, Groß-Gerau, Germany).

Statistical Analyses

Analyses of variance (ANOVAs) were computed on the overall differences between AD patients and controls (healthy controls, PSO patients) for the different personality dimensions. In the case of significant effects, Newman-Keul's post hoc tests for single comparisons were computed. Greenhouse-Geisser corrections were applied where appropriate. Further, Spearman rank correlations were computed for assessment of associations between the different personality domains and the endocrine, physiological and immunological stress responses. The stress response of the different endocrine (cortisol, ACTH, catecholamines) and immune (number of lymphocytes, basophils, neutrophils, eosinophils, IL-4, IFN-γ) parameters was defined as the increase from baseline level (1 min before the TSST) to the individual peak level (stress response$_{biol}$ = index$_{biol}$ peak – index$_{biol}$ basal) after TSST exposure. Accordingly, the heart rate response was defined as the increase from the mean heart rate during the rest period to the mean heart rate during the TSST (heart rate$_{diff}$ = (mean heart rate t11–t18) – (mean heart rate t1–t10)). The IgE response was defined as the increase from IgE levels on day 1 to the IgE concentrations on day 2 (IgE$_{diff}$ = IgE$_{day2}$ – IgE$_{day1}$). The cortisol response to awakening was defined as the increase of the cortisol level after awakening to the cortisol level obtained 30 min later (Mcort$_{diff}$ = Mcort$_{30}$ – Mcort$_{waking\ up}$).

Results

Personality Characteristics in AD Subjects

An ANOVA of the personality data yielded a significant group effect in trait anxiety (table 1), self-efficacy (table 2) and stress vulnerability (table 3) in situations characterized by failure, job overload, social conflicts and uncertainness.

Table 2. Locus of control/self-concept (FKK) in patients with AD or PSO and in non-atopic controls

	AD	PSO	Controls	F	df	p
Self-efficacy	29.4	32.6	33.8	3.8	73	*0.02*
Internality	30.1	30.8	32.7	2.1	73	0.12
Powerful others control	25.0	24.8	24.1	0.2	72	0.79
Chance	23.1	23.9	22.1	0.9	73	0.40
Σ Locus of control/ self-concept	11.4	13.6	19.9	2.99	72	*0.05*

Table 3. Stress vulnerability (MESA) in patients with AD or PSO and in non-atopic controls

	AD	PSO	Controls	F	df	p
Failure	14.8	14.2	13.1	3.5	69	*0.03*
Job overload	12.9	13.0	10.9	5.3	71	*0.007*
Social conflicts	12.3	12.7	10.6	6.6	70	*0.002*
Criticism	11.4	12.3	10.7	2.8	72	0.06
Uncertainness	12.4	12.8	11.1	4.6	71	*0.01*
Recreation ability	9.1	9.3	7.6	4.0	70	*0.02*
Σ Stress vulnerability	73.8	74.4	64.0	8.3	69	*0.0005*

Post hoc analyses revealed that compared to the healthy control group, AD and PSO patients showed significantly higher levels of trait anxiety and stress vulnerability and a significantly lower level of positive self-concept (all $p < 0.05$). No difference in these personality domains could be detected between the two patient groups, i.e. the AD and PSO subjects (t-tests; all $p > 0.05$).

Association between Personality Characteristics and Biological Stress Responses in AD Subjects

The endocrine and immunological stress responses to the TSST in AD patients and the non-atopic control group are described and discussed elsewhere [Buske-Kirschbaum et al., 2002a, b]. Briefly after exposure to the TSST, the two groups showed a significant increase of cortisol, ACTH, catecholamines and leukocyte numbers (eosinophils, basophils, neutrophils, lymphocytes). However, cortisol and ACTH levels were found to be significantly blunted in AD sufferers, while catecholamine levels, eosinophil number and IgE levels were significantly elevated. In addition, a significant increase of IFN-γ and heart rate responses as well as a significant decrease of IL-4 levels were found, however, there were no between-group differences in these parameters. Finally, a significant rise of cortisol levels after awakening was found in the two experimental groups with no significant between-group difference.

Pearson correlational analysis indicated no significant correlation between the different personality domains and any of the endocrine (ACTH, cortisol, epinephrine, norepinephrine), immunological (leukocyte subsets, IL-4, IFN-γ, total IgE) or physiological (heart rate) stress responses neither in AD pa-

tients nor in the non-atopic control group (all $p > 0.05$). However, stress vulnerability (job overload, criticism) in AD patients was significantly correlated with the cortisol response to awakening in the morning (job overload: $r = -0.52$, $p < 0.01$; criticism: $r = -0.58$, $p < 0.005$).

Discussion

In the present study, it was hypothesized that AD patients present a specific type of personality that may be associated with aberrant immunological and endocrine stress responses leading to the common clinical observation of stress-induced exacerbation of AD pathology. In fact, it was found that AD sufferers show higher levels of trait anxiety and stress vulnerability when exposed to social conflicts, job overload or failure. In addition, a lower positive self-concept was found in these patients. This personality profile is in line with other reports suggesting that, for example, high levels of anxiety are commonly displayed in AD patients [White and Horne, 1990; Rogerson, 1947; Ginsburg et al., 1993; Garrie, 1978; Ahmar and Kurban, 1976]. Jordan and Whitlock [1974] even discuss high anxiety levels in AD patients as a potential key personality characteristic. They reported that differences between AD and control subjects in other psychological test data (i.e., suppression of hostility, aggression) are associated with the differences in anxiety levels and disappear when controlling the anxiety factor by matching the AD and the control group on anxiety scores. Others could demonstrate that AD sufferers show inadequate coping skills and have difficulty in dealing with interpersonal conflicts [Scheich et al., 1993; Ehlers et al., 1994] which may prevent the solution of everyday problems. This may explain our findings of a higher stress vulnerability especially in situations characterized by social conflicts, failure or increased work demands.

It is important to note, however, that in our study, AD patients do not differ in these personality aspects from PSO patients suggesting that the personality type found is no specific *atopic* personality type, but rather represents a personality pattern linked to a chronic inflammatory and disfiguring skin disease. This finding would provide additional support for other studies which also failed to demonstrate a unique, AD-specific personality type [Brown, 1967; Shannon, 1969]. Some authors, however, found increased levels of anxiety, depression, neuroticism and hypochondria in AD sufferers but not in PSO or other dermatological diseases [Ginsburg et al., 1993; Ahmar and Kurban, 1976]. In these studies, the authors argue that in contrast to other skin diseases, AD sufferers have to deal with a torturing and disfiguring skin disease throughout their early developmental years leading to a dysfunctional mother-child interaction. These early stressful experiences may predispose the AD child to develop a distinct personality pattern. Although intriguing, we and others could not provide support for this model.

There is a paucity of research trying to uncover potential associations between personality dimensions and immune or endocrine functions. The few data sets available to date are heterogeneous. Some data suggest that personality dimensions, for example extraversion/introversion, attributional style, or anxiety are associated with altered cellular and humoral immune functions, e.g. reduced natural killer cell activity or a lower T cell helper : cytotoxic (CD4 : CD8) ratio [Segerstrom, 2000]. High anxiety was further reported to be associated with reduced cortisol, but elevated catecholamine responses to stress [Hubert and de Jong-Meyer, 1992; Salmon et al., 1989]. Other studies failed to show effects of personality traits on the immune system, the HPA axis or the sympathetic nervous system response [Segerstrom, 2000; Kirschbaum et al., 1992a; van Eck et al., 1996].

In the present study, personality traits in AD sufferers were not related to any of the endocrine, immune or physiological response to psychosocial stress suggesting that altered endocrine and immune stress responses in AD sufferers are not related to the personality dimensions investigated here. This finding does certainly not deny the existence of a link between personality and atopy-relevant biological parameters in AD patients. A cautious interpretation is necessary due to the selection of only a few personality dimensions and the specific stress paradigm used in this study. In addition, Prüssner et al. [1997a] argue that biological stress responses reflect state measures, that only marginally depend on the subject's personality. They could demonstrate that only with repeated stress exposure the association between personality variables and the cortisol stress response becomes more evident, probably because the impact of novelty on the individual stress response is reduced.

Despite the failure to detect a close relationship between personality dimensions and biological stress responses, a significant correlation between stress vulnerability in situations characterized by job overload and criticism and the morning cortisol levels after awakening was observed. Previous work of our group suggests that the morning rise of cortisol levels after awakening is a reliable marker for the HPA axis activity [Prüssner et al., 1997b]. Interestingly, a blunted response of morning cortisol to awakening appears to be related to high levels of perceived stress and symptoms of burnout [Prüssner et al., 1999]. The same group reported an association between the cortisol secretion in the morning and chronic work overload in students [Schulz et al., 1998].

In order to explain the effect of job overload or burnout on the morning cortisol levels, it may be assumed that individuals with an excessive number of duties may worry not to be able to manage the demands. This may lead to feelings of chronic stress and exhaustion. Waking up in the morning, these subjects may already be engaged in the process of coping with these demands and may anticipate upcoming stressful situations which have been shown to affect the HPA axis activity [Kirschbaum et al., 1992b]. Our finding of a negative correla-

tion between stress vulnerability and the morning cortisol response after waking up in AD sufferers but not in controls may suggest that HPA axis functioning in AD patients may be highly susceptible to the experience or anticipation of stressful situations characterized by job overload and criticism. Interestingly, a decreased activation of the HPA axis can be found in this patient group which would be in agreement with our previous data showing a blunted HPA axis responsiveness to acute stress in AD sufferers [Buske-Kirschbaum et al., 1997, 2002b]. To conclude, AD patients show a distinct personality pattern that is similar to the personality type observed in patients suffering from a non-atopic, inflammatory skin disorder. Our data do not support the idea of an 'atopy-specific' personality type. They rather suggest that suffering from a chronic, inflammatory and disfiguring skin disorder may generally be linked to differences in certain personality traits. Although a distinct personality pattern could be observed in AD patients, none of the personality dimensions was related to atopy-relevant endocrine or immunological stress responses. Future studies are necessary to clarify the specificity of personality in different dermatological patient groups and their association to pathologically relevant biological parameters. In these studies, more complex stress paradigms allowing repeated stress exposure should be used. Moreover, dermatological patients which are not compromised by an ever-present, highly visible pathology should be included.

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