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Distress, depression and coping in HLA-B27-associated anterior uveitis with

focus on gender differences

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Running title: Psychological aspects and gender in HLA-B27 Anterior Uveitis

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ABSTRACT

Background/aims: To evaluate depression, coping with disease and stress, and the subjective impression of distress and/or life events as triggers for recurrences in HLA-B27-associated anterior uveitis (B27-AU), with attention to gender-specific characteristics.

Methods: 171 patients with a history of B27-AU responded to a postal survey performed between January 2006 and April 2008 using standardized psychological questionnaires: Beck Depression Inventory (BDI), Freiburg Questionnaire on Coping with Illness (FQCI), and Stress Coping Inventory (SCI).

Results: Patients with B27-AU differed from healthy controls showing more depressive symptoms (BDI, 31.6%), applying characteristic disease coping as well as negative stress coping strategies. Female B27-AU patients tended to react with depression, males to use negative stress coping strategies. 57.9% of patients believed in psychological distress as a trigger for relapses, 34.5% stated specific life events. Together, this group of patients achieved higher depression scores and used more negative disease and stress coping styles than patients without perception of distress.

Conclusion: B27-AU patients exhibited significant psychopathology concerning depression and disease coping. Distress and life events were subjectively suspected to be a trigger. By imparting knowledge to the patients upon probable development of depressive moods and the role of stress/life events as trigger for relapses, as well as offering behavior therapy to optimize coping may help to better deal with B27-AU.

Uveitis associated with the HLA-B27 antigen (B27-AU) is an acute-onset, painful eye disease with a relapse risk of up to 74%.[1] The treatment consists of antiinflammatory topical and systemic therapy as well as pharmacologic cycloplegia for reduction of pain and prevention of synechiae. At each recurrence the pain, as well as the deterioration of visual acuity due to inflammation and impaired accommodation pose a strain for the patients. Furthermore, they may require sick leave for several days, lose their ability to perform certain tasks (i.e. reading, working on a computer, driving), and face a risk of losing their jobs. The fact that a patient with a history of B27-AU is at permanent risk for a relapse of disease, associated with pain and fear of a transient or even persistent loss of vision, causes omnipresent distress (negative forms of stress, compared to positive forms of stress = eustress) and poses a chronic psychological burden. For rheumatic diseases in general, as well as for ankylosing spondylitis in particular, a higher prevalence of depression has been reported.[2,3] In a pilot study, Franke et al dealt with the psychopathology of patients with various forms of uveitis and pointed out the importance of evaluating psychological interventions for rehabilitation.[4]

But, distress does not only play a role as a consequence of disease. Psychological stress also has been discussed as a probable trigger for uveitis, as patients often report the onset of relapses during or after periods of increased psychological pressure causing a negative mood. Specific life events can cause such distress and therefore have been investigated in this context. So far, clinical studies on uveitis have yielded disparate results.[4-14] Concerning other auto-immune diseases, such as multiple sclerosis or Behcet's disease, stressful life events were shown to represent an aggravating factor , as they resulted in a significant increase in risk of disease exacerbations.[15,16]

The aim of the present study was to evaluate the role of distress as a trigger from the patients' point of view, as well as to objectively evaluate the presence of depressive moods and the strategies used to cope with disease and stress. We decided to include only patients with a history of anterior uveitis associated with the HLA-B27-antigen, to obtain a large and homogenous patient population. A further point of interest was to delineate gender-specific differences. The results could help to gain further insight into the psychopathology of B27-AU and underline the importance of psychological interventions.

MATERIALS AND METHODS

Patient recruitment

This clinic-based, cross-sectional study was performed at the uveitis unit of the Department of Ophthalmology, Medical University of Vienna, from January 2006 to April 2008. A written invitation to participate in the study via a postal survey was sent once to 381 B27-AU-patients who had been treated at the uveitis unit since 1980. 171 patients (45%) with recent and/or recurrent history of acute B27-AU responded with a completed questionnaire and were included in the study. Patients had to indicate whether an acute relapse was present or not. Institutional review board approval and informed consent were obtained in accordance with the Declaration of Helsinki. The booklet containing the questionnaires was prefaced by a general invitation letter explaining the scientific character of the survey and that the participation was voluntary. Patients were informed that the impact of stress on disease coping in patients with AU should be studied, the expressions "gender", "depression" and "trigger" were not used. Normative values were obtained in an ethnicity- and aged-matched control group of 55 healthy individuals (mean $age=45.6\pm10.1 \text{ yrs}, p=0.1$).

The survey consisted of 3 psychometric instruments, listed below, as well as questions related to sociodemographic data (gender, age) and uveitis details (age at onset of uveitis, number of recurrences in total and approx. per year, the approx. duration of attacks and interval since the last recurrence, coexistence of a B27-associated spondylarthropathy). Furthermore, patients were questioned upon the presence of psychological factors before an attack. Patients could indicate specific live events, which subjectively were suspected to be connected with a relapse.

Psychometric instruments

The <u>Beck Depression Inventory</u> (BDI) is a self-report inventory for differentiation of a clinically relevant depressive mood.[17] Twenty questions document the actual severity of depressive moods, indicated by a sum score (0-63 points). The sum score also is allocated to one of 3 clinically relevant groups: "*not depressed*" (0-9 points), "*minimal depressive mood*" (9 to 19 points), and "*clinical relevant depressive mood*" (19-63 points).

Coping was assessed by the <u>Freiburg Questionnaire on Coping with Illness</u> (FQCI).[18] This 35-item questionnaire is used to calculate 5 primary dimensions (subscales): "*depressive coping*", "*problem-solving behavior*", "*distraction and self-revalorization*" (encouraging oneself), "*religiousness/quest for meaning*" (each 5-25 points), and "*cognitive avoidance/ dissimulation*" (trivializing and wishful thinking, 3-15 points). A high score in a FQCI subscale indicates a strong tendency to apply this type of coping mechanism.

Coping was also assessed by the <u>Stress Coping Inventory</u> (SCI) questionnaire, which consists of 114 items.[19] Item scores (each 0-4 points) are grouped to calculate 19 subscales that describe various coping strategies (combination of 6 item scores, 0-24 points). Alternatively, the items may also be

classified into 2 secondary dimensions, namely "*negative*" or "*positive coping*" strategies (0-24 points).

Statistics

The SPSS 16.0 software was used for statistical analysis. For descriptive analysis, data are expressed as total numbers (n), percentage relating to group (%), means \pm standard deviation (SD). The Kolmogorov-Smirnoff-test was used to test for standard distribution, the T-test or Mann Whitney U-test was used as appropriate. The cut-off level for statistical significance was set at p<0.05; all tests were performed in a two-tailed manner. In case of multiple testing within a group (gender-comparisons concerning BDI items, FQCI and SCI), a Bonferroni-Holm correction for adjustment of the p-value was applied.[20]

RESULTS

171 patients with known HLA-B27 antigen-associated uveitis, 64 women and 107 men, returned the questionnaires. The gender distribution was calculated to be female: male = 1:1.7 (p<0.001, table 1).

Table 1 Patient characteristics concerning sociodemographics and history ofB27 antigen-associated anterior uveitis

	Total patient			
	population	Women	Men	
Number of patients	171	64 (37.4%)	107 (62.6%)*	
Current age	48.8 (14.1)	46.6 (14.9)	50.2 (13.4)	
(years±SD)				

Age at onset of uveitis	34.5 (12.6)	33 0 (11 4)	35 5 (13 3)
(years±SD)	54.5 (12.0)	55.0 (11. 4)	55.5 (15.5)
Uveitis relapses†			
Total numbers (n±SD)	12.9 (20.1)	12.6 (18.6)	13.2 (21.0)
Approximate relapses	25(10)	20(10)	2 2 (1 0)
per year (n±SD)	2.3 (1.9)	2.9 (1.9)	2.3 (1.9)
Duration (weeks±SD)	4.9 (4.1)	5.5 (5.0)	4.6 (3.4)
Acute B27-AU at time of			
study participation	13 (7.6%)	5 (7.8%)	8 (7.5%)
(n of patients,%)			
HLA-B27-associated			
spondylarthropathy	78 (45.6%)	27 (42.2%)	51 (47.7%)
(n of patients,%)			

Legend: Data are given as total numbers or means; standard deviation (SD) or percentage relating to groups is given in parentheses; † as subjectively reported by patients; * significance at p<0.05.

13 patients (7.6%) had active recurrence at the time of answering the questionnaire, in 75 patients (43.9%) a B27-associated spondylarthropathy was existent. Altogether, the patients had suffered from approximately 12.9±20.1 uveitis relapses since disease onset, which had been 14.3±9.6 years ago. More information concerning uveitis recurrences is given in table 1. No differences in sociodemographic data were found comparing patients who responded to the survey and those who did not.

Beck Depression Inventory (BDI)

The mean total score obtained in patients with B27-AU was significantly higher than the value obtained from the control group (8.7 \pm 7.0 and 4.4 \pm 4.3 respectively, p<0.001, table 2, figure 1). Patients with an acute relapse scored even worse (11.3 \pm 7.7, p=0.19), the coexistence of an additional spondylarthropathy did not affect the score (9.5 \pm 7.6, p=0.13). 31.6% of B27-AU patients (n=54) were above "*normal range*", as 19.3% were classified to be in a "*minimal depressive*" and 12.3% in a "*clinical relevant depressive*" mood.

36% of women and 28.9% of men exhibited depressive moods (p=0.34), the mean total sum score was slightly higher in the female group (table 2). In female and male B27-AU patients the scores were significantly higher than those of the corresponding healthy comparison groups (table 2, figure 1). Concerning the individual test items women suffered more from "*loss of libido*" than men (w=2.00±1.03, m=1.57±0.76, p=0.002).

Table 2 Results of statistical significance as obtained by the Beck Depression Inventory (BDI), Freiburg Questionnaire of Coping with Illness (FQCI) and Stress Coping Inventory (SCI) in patients with B27-AU and an age-matched, healthy control group.

	Patients (P)	p-value for			
	vs	gender			
	Controls (C)	Total	Women	Men	differences
Numbers	Р	171	64	107	
	С	55	33	22	
BDI -sum score	Р	87(70)	95(76)	84(67)	n.s.
		0 (0)	0.0 (1.0)	0.1 (0.17)	n.s

	С	4.4 (4.3)	4.5 (4.0)	4.1 (4.7)	
		p<0.001*	p=0.004*	p=0.02*	
FQCI					
Problem-solving	Р	16.2 (4.7)	16.5 (5.2)	16.1 (4.4)	n.s.
behavior	С	14.1 (3.7)	14.9 (2.9)	13.0 (4.4)	n.s.
		p=0.004*	n.s.	p=0.004*	
Distraction and self-	Ρ	15.2 (4.2)	15.7 (4.4)	14.9 (4.0)	n.s.
revalorization	С	16.7 (3.7)	17.6 (3.1)	15.5 (4.3)	n o
		n.s.	p=0.030*	n.s.	n.s.
Cognitive avoidance	Ρ	6.6 (2.8)	7.0 (3.1)	6.4 (2.6)	n.s.
and dissimulation	С	4.5 (1.9)	4.3 (1.5)	4.7 (2.4)	n.s.
		p<0.001*	p<0.001*	p=0.005*	
SCI					
Playing down the	Р	10.6 (4.7)	9.4 (4.6)	11.3 (4.7)	n.s.
disease	С	12.3 (4.3)	10.7 (4.2)	13.0 (4.6)	n.s.
		p=0.02*	p=0.030*	n.s.	
Substitutional	Ρ	10.2 (5.7)	12.0 (5.2)	9.0 (5.7)	p=0.002†
satisfaction	С	11.0 (4.4)	12.4 (4.3)	9.4 (4.1)	p<0.001†
		n.s.	n.s.	n.s.	
Attempt to control	Ρ	14.6 (4.4)	14.3 (4.5)	14.8 (4.3)	n.s.
reactions	С	13.4 (3.8)	14.4 (3.4)	13.0 (4.7)	n.s.
		n.s.	n.s.	p=0.02*	
Need for social	Ρ	12.9 (5.6)	15.4 (5.3)	11.3 (5.2)	p<0.001†
support	С	13.5 (5.7)	14.9 (5.3)	12.7 (5.3)	n.s.
		n.s.	n.s.	n.s.	

Avoidance tendency	Р	13.5 (5.1)	14.4 (4.7)	12.9 (5.3)	n.s.
	С	11.3 (5.3)	12.8 (5.3)	9.9 (5.0)	n.s.
		p=0.008*	n.s.	p=0.010*	
Flight tendency	Р	10.6 (4.7)	11.4 (4.8)	10.1 (4.6)	n.s.
	С	9.4 (4.2)	10.8 (4.6)	8.4 (3.6)	p=0.001†
		n.s.	n.s.	p=0.006*	
Social withdrawal	Р	7.6 (5.3)	7.8 (5.1)	7.4 (5.4)	n.s.
	С	5.5 (4.3)	6.5 (4.3)	5.4 (4.7)	ne
		p=0.009*	n.s.	p=0.009*	11.3.
Rumination/	Р	15.0 (5.7)	16.4 (5.1)	14.1 (5.9)	n.s.
pensiveness	С	12.0 (5.5)	13.7 (5.8)	10.0 (5.1)	n.s.
		p=0.002*	p=0.020*	p=0.003*	
Resignation	Р	7.3 (5.2)	8.3 (5.3)	6.6 (5.1)	n.s.
	С	5.7 (4.6)	7.3 (5.0)	4.6 (3.3)	n.s.
		n.s.	n.s.	p=0.010*	
Self-pity	Р	8.9 (5.6)	10.1 (5.8)	8.2 (5.4)	n.s.
	С	7.6 (4.7)	9.1 (4.8)	6.5 (4.0)	n.s.
		n.s.	n.s.	p=0.063*	
Self-accusation	Р	9.0 (4.8)	9.6 (5.6)	8.6 (4.3)	n.s.
	С	7.7 (4.4)	9.0 (4.5)	6.8 (4.7)	n.s.
		n.s.	n.s.	p=0.016*	
Aggression	Р	8.8 (5.5)	8.6 (4.9)	9.0 (5.9)	n.s.
	С	7.9 (4.7)	8.8 (4.4)	7.0 (4.6)	n.s.
		n.s.	n.s.	p=0.084*	
Use of self-	Ρ	2,2 (3,3)	2.0 (2.5)	2,3 (3,7)	n.s.
		(0.0)	()	<u> </u>	n.s.

medication	С	2.9 (3.9)	3.7 (4.2)	3.2 (3.9)	
		n.s.	p=0.005*	n.s.	
Negative coping	Р	9.7 (4.2)	10.6 (4.2)	9.1 (4.1)	p=0.027†
style	С	7.9 (3.9)	9.3 (4.0)	7.3 (3.5)	p=0.008†
		p=0.005*	n.s.	p=0.002*	

Legend: P, patients; C, controls; n.s., not significant. Data are given as means; standard deviation is given in parentheses; * significance between patients- and control group at p<0.05, † significant gender-specific differences after Bonferroni-Holm correction. Test items/ subscales in which no statistical significances were found are not displayed.

Freiburg Questionnaire of Coping with Illness (FQCI)

B27-AU patients exhibited different patterns than controls concerning 3 of 5 coping styles. They tended towards "*cognitive avoidance and dissimulation*" (p<0.001, table 2), women as well as men. Women in particular seemed to lose the ability for "*distraction and self-revalorization*" (p=0.030), men tended to apply a "*problem-solving behavior*" (p=0.004).

German Stress Coping Inventory (SCI)

Compared to healthy controls, B27-AU patients reached higher scores on 4 of 19 subscales, leading to a statistically significant increase of the secondary dimension *negative coping* (table 2, p=0.005). Splitting these findings according to gender, female patients seemed to less "*play down the disease*" (p=0.030), needed more "*social support*" (mean score was significantly higher than in B27-AU males although should have been similar), used less "*self-medication*" (p=0.005), but reacted with more "*rumination*" (p=0.020) than healthy controls. Male patients also tended to use

"rumination" (p=0.003), but in addition exhibited aggravated patterns in 8 more subscales, displayed in table 2. Summarized, these patterns are reflected in an elevated score of *"negative coping"* in males (p=0.002).

Distress and/or life events as triggers for B27-AU relapses

57.9% of patients (n=99, p<0.001) had the impression that psychological factors had an influence in the sense of triggering B27-AU, women more often than men (p=0.045, figure 2). 34.5% could even state specific life events after which an attack had occurred (table 3).

Table 3 B27-AU patients' subjective estimation	s about psychological distress
or life events as triggers for relapses	

	Total	Women	Men
	patient		
	population		
Patients reporting of distress +/-	57.9% (99)	64.1% (41)*	54.2% (58)
life event(s) before an B27-AU			
attack			
Patients stating distress only	23.4% (40)	29.7% (19)	19.6% (21)
Dationts stating distross and	24.5% (50)	24 40/ (22)	24 60/ (27)
Pallenis staling distress and	34.5 % (39)	34.4% (22)	34.0% (37)
specific life events			
Life events (10 most often stated,			
in quantitative order)			
Death in family	18.1% (31)	21.9% (14)	15.9% (17)
Senaration	15 2% (26)	1/ 1% (0)	15 0% (17)
σεραιαιοπ	13.270 (20)	14.170 (8)	13.370 (17)

Common cold	11.7% (20)	15.6% (10)	9.3% (10)
Job cancellation	10.5% (18)	9.4% (6)	11.2% (12)
Occupational change	8.8% (15)	7.8% (5)	9.3% (10)
Divorce	8.8% (15)	10.9% (7)	7.5% (8)
Diagnosis of an illness	8.2% (14)	7.8% (5)	8.4% (9)
Accident	7.0% (12)	6.3% (4)	7.5% (8)
Moving the household	6.4% (11)	9.4% (6)	4.7% (5)
Birth of a child	2.3% (4)	4.7% (3)	0.9% (1)

Legend: Data are given as percentage relating to group (total of patients or gender); number of patients per gender group is given in parentheses. * Significance at p<0.05.

Patients, who had mentioned psychological stress +/- a life event ("distress"-group), exhibited raised and depressive BDI sum scores (distress=10.1 \pm 7.9, no distress=7.1 \pm 5.4, p=0.008). The same finding was true when assessing only women (p=0.042) or men (p=0.056). These patients also reached higher scores for *depressive coping* on the FQCI (distress=11.4 \pm 4.3, no distress= 9.7 \pm 3.9, p<0.001), independent of gender (w=11.6 \pm 3.7, m=11.5 \pm 4.8, p=0.961). On the SCI a difference was found for 3 of the 19 subscales (more resignation, more rumination, less playing down the disease, all p<0.001), together resulting in an elevated score of *negative coping* (distress=10.9 \pm 4.4; no distress= 8.3 \pm 3.6, p<0.001).

DISCUSSION

From the 1960's onwards a number of studies discussed a connection between

distress or depressive tendencies and uveitis (table 4). [4-14]

Table 4 Previous studies on the psychopathology of uveitis

Authors	Year	Questionnaires used (author)	Number of uveitis patients	Uveitis type, number of patients	Results
Schlaegel TF, Levitt EE	1959	Minnesota multiphasic personality inventory	49	AU, AU+PU; granulomatous vs. non- granulomatous; severity staging	Significantly higher values of psychopathology in uveitis patients; the location, type and severity of uveitis or sex are not correlated with psycho-pathology.
Erbaugh JK, Fajardo RV	1962	Personal interview	71	No details given	Uveitis patients report more depressive episodes prior to hospitalization than controls.
Heaton JM	1964	Personal interview	224	AU (n=157) PU (n= 20) Pan (n= 47)	Three potential triggers of the disease: 1) maladaptation to the social environment may act as a predisposing factor because 21% of patients mentioned interpersonal stress 8 weeks before uveitis, 2) influenza in 6.2%, 3) common cold in 3.6%.
Sen DK	1971	Personal interview	48	AU (n=36) PU (n=5) Pan (n= 7)	Stress was reported as a factor influencing the development or progression of uveitis by 37.5% of patients (16.6% reported

					stress in interpersonal relationships).
Kumar A	1981	Modified life inventory scale	40	Patients with controlled uveitis	Correlation between elevated stress scores and uveitis.
Secchi AG, Magni G, Tognon MS et al	1987	Paykel scale for life events (Paykel ES), Symptom distress check list (Derogatis LR)	60	RAAU, (n=60; active n=15, quiescent n=45)	No difference between the uveitis group and a reference group concerning life events or psychological distress.
Mayer H, Kraus-Mackiw E, Barisani T et al	1994	Life change scale (Rahe RH)	21	AU (n= 14) IU (n= 3) PU (n= 4)	Subjective importance of the patients' professional life on their flare-ups; psychological and social factors were perceived as triggers.
Mulholland B, Marks M and Lightman SL	2000	Holmes and Rahe's social readjustment scale (Rahe RH), Spielberger state-trait anxiety inventory (Spielberger CD)	35	Idiopathic RAAU (n=35)	Stress was not involved in triggering recurrences.
Schiffman RM, Jacobsen G and Whitcup SM	2001	SF-36 Health survey (Ware J), NEI VFQ-25 (Mangione CM)	76	AAU (n= 13) IU (n= 17) PU (n= 26) Pan (n= 20)	Scores significantly lower than those of the general US population; the severity of uveitis is correlated with a drop in scores.
Franke GH, Schuette E and Heiligenhaus A	2004	Schedule of recent experiences (Holmes TH), SCI coping questionnaire (Janke W) Essen coping questionnaire (Franke GH), Brief Symptom Inventory (Derougatis LR), NEI VFQ (Mangione CM)	51	Chronic uveitis (n= 51)	Patients with uveitis: more numerous recent life events, poorer coping strategies, greater psychological distress, poorer quality of life. At follow-up patients with recurrence of uveitis had poorer values than did those without recurrence.

Carrim ZI,	2006	General Health	42	AAU (n= 42)	Relationship between
Ahmed TY		Questionnaire			stress and
and Taguri AH		(Goldberg DP),			recurrence of AAU;
		Social			poor general health
		Readjustment			during flare-up
		Rating			
		Questionnaire			
		(Holmes TH)			

Legend: AU, anterior uveitis; PU, posterior uveitis; Pan, panuveitis; RAAU, recurrent acute anterior uveitis; IU, intermediate uveitis; AAU, acute anterior uveitis.

Nevertheless, these studies draw opposite conclusions. Various uveitis entities being grouped together, small sample sizes, and the diversity of evaluation instruments (such as personal interviews versus questionnaires) may have led to these diverse results, difficult to be compared with each other. To overcome these limitations of previous studies we concentrated on a well defined and homogenous uveitis entity and used only standardized questionnaires.

One aim of our study was to evaluate the patients' subjective impression of life events and psychological distress as a trigger for recurrences of HLA-B27 positive anterior uveitis. In our study population, 57.9% of the patients reported life events and psychological distress as a potential triggers. Theories, that distress might negatively influence the immune system via the neuro-endocrine system could be an explanation for a connection between distress and disease exacerbation, but are not investigated closely enough to draw definite conclusions.[22] Distress might play a role before an attack of B27-AU, but definitely plays a role in the time afterwards. Future studies will have to investigate both topics, as too many interactions still remain unclear.

Furthermore, the presence of depressive symptoms, disease and stress coping strategies were analyzed using standardized and validated questionnaires. A

special focus was set on analyzing gender-specific differences. The male:female ratio of 1.7:1 is comparable to the findings of previous studies on B27-AU patients.[21] Test results indicating the presence of depressive moods were found in 31.6% of patients. These results support the data reported by Carrim et al, according to whom patients with acute AU experience an extraordinary burden in terms of their psychological well-being and general health (table 4).[14] The patients investigated in that study achieved higher (i.e. poorer) scores on the General Health Questionnaire (GHQ) than did controls. The GHQ is a psychometric instrument measuring stress, social dysfunction and depression, and is therefore comparable with the BDI used in our study.

With regard to disease coping, we found specific behavior patterns attributable to both sexes ("*cognitive avoidance*"), but also gender-specific ones. Franke et al, who studied psychosomatic aspects of 51 patients with various forms of uveitis in a pilot study, concluded that uveitis patients apply specific coping strategies, have a lower disease-specific quality of life and suffer from greater psychological distress (table 4).[4] Our results thus provide another informative basis concerning B27-AU patients.

Concerning gender-specific differences, women appear to suffer more from the psychological strain caused by B27-AU than men, which is demonstrated by specific behavior patterns. In comparison to males, women exhibited a tendency towards depressive moods, with a strong bodily component as reflected in increased *"loss of libido"*. A possible explanation for these results could be the knowledge that women are more sensitive to pain than men. In diseases associated with chronic pain women achieve higher scores concerning depression and dejection.[23] Behavioral patterns during stressful situations also differed between genders (SCI), although findings in females were not as noticeable as in males. Male B27-AU patients

exhibited predominantly negative coping strategies. This underlines the importance to differentiate between female and male patients, to then be able to offer a gender-tailored supportive approach.

As a probable limitation of the study the participation rate of 45% has to be discussed. According to various authors the response rates to postal surveys rarely exceed 50% [24,25], especially if no factors apply which are known to increase compliance (short questionnaires, complex follow-up procedures such as telephone contacts or re-sending the questionnaire or offering a monetary incentive).[24 26] None of the latter was used in our study, thus explaining the response rate achieved. Other problems in studies using questionnaires are those of social desirability bias and concealment of sensitive information. Besides the fact that these apply rather to personal or telephone interviews than to postal surveys, care was taken to compose an invitation letter without suggestive questions. We therefore believe that patients suffering from more versus fewer symptoms were addressed equally and our results are not biased in that way.

In conclusion, the results of our study indicate that patients with a history of B27-AU are at risk to suffer from depression and tend to use negative coping strategies. According to gender, patients are endangered to encounter specific and sustained psychological problems. A significant proportion of patients believed in psychological distress or life events as a potential trigger for recurrences. These results show that the management of uveitis patients should encompass not only standardized treatment strategies of the ocular disease itself, but also clear information about the relapsing nature of B27-AU, the potential role of distress or life events as triggers, and the disease's impact on psychological well-being. In addition, whenever possible a behavior therapy focused on cognitive styles could be proposed to support the patients' effort and success in dealing with the disease. Through

identification of situations causing personal distress, patients can learn to either fight or "flight" specific situations, depending upon individual coping patterns. To recognize the body's tendency towards highly charged states in distress situations, and to alter behaviour accordingly, can reduce the length of time a person suffers from distress, and reduce the body's continued need to produce adrenaline to cope with danger that does not really exist. Improving coping mechanisms in the therapeutic sense can involve meditation, Jacobson's progressive muscle relaxation, cognitive behavioural therapy, and recognition of the body's inappropriate response to distress (e.g. biofeedback).

Altogether, our findings confirm the need for an interdisciplinary and gendertailored management of B27-AU that combines conventional treatment of uveitis with psychological counseling or guidance.

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LEGENDS FOR DISPLAY ITEMS

Figure 1 Results of the Beck Depression Inventory (BDI)

The BDI sum score was slightly higher in female (9.5 \pm 7.6) than in male B27-AU patients (8.4 \pm 6.7, p=0.34). Both gender-groups reached scores significantly higher than those of healthy controls (females= 4.5 \pm 4.0, p=0.004 and males=4.1 \pm 4.7, p=0.002),

Figure 2 Numbers of B27-AU patients stating psychological distress +/-

specific life events preceding an acute attack

Of 171 B27-AU patients, 99 (57.9%) stated to have felt psychological distress before acute relapses, 23.4% only distress, 34.5% distress and specific life events. Women reported a connection more often than men (p=0.045). Distributions within gender group are given in percentages (equal total).



