ORIGINAL ARTICLE

Emotional experience in patients with clinically isolated syndrome and early multiple sclerosis

T. D. Hälbig[a,b], T. Wüstenberg[c], R. M. Giess[a], H. Kunte[d], J. Bellmann-Strobl[a,e], K. Ruprecht[f] and F. Paul[a,e]

[a]*NeuroCure Clinical Research Center, Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin and Berlin Institute of Health, Berlin, Germany;* [b]*Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY, USA;* [c]*Department of Psychiatry and Psychotherapy, Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin and Berlin Institute of Health, Berlin;* [d]*Faculty of Natural Sciences, MSB, Medical School Berlin, Berlin;* [e]*Experimental and Clinical Research Center, Max Delbrueck Center for Molecular Medicine and Charité – Universitätsmedizin Berlin, Berlin; and* [f]*Department of Neurology, Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin and Berlin Institute of Health, Berlin, Germany*

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Background and purpose: Evidence suggests that there are changes in the processing of emotional information (EP) in people with multiple sclerosis (MS). It is unclear which functional domains of EP are affected, whether these changes are secondary to other MS-related neuropsychological or psychiatric symptoms and if EP changes are present in early MS. The aim of the study was to investigate EP in patients with early MS (clinically isolated syndrome and early relapsing/remitting MS) and healthy controls (HCs).

Methods: A total of 29 patients without neuropsychological or psychiatric deficits and 29 matched HCs were presented with pictures from the International Affective Picture System with negative, positive or neutral content. Participants rated the induced emotion regarding valence and arousal using nine-level Likert scales. A speeded recognition test assessed memory for the emotional stimuli and for the emotional modulation of response time. A subgroup of participants was tested during a magnetic resonance imaging (MRI) session.

Results: Patients in the MRI subgroup rated the experience induced by pictures with positive or negative emotional content significantly more weakly than HCs. Further, these patients were significantly less aroused when watching the pictures from the International Affective Picture System. There were no effects in the non-MRI subgroup or effects on emotional memory or response times.

Conclusions: Emotional processing changes may be present in early MS in the form of flattened emotional experience on both the valence and arousal dimensions. These changes do not appear to be secondary to neuropsychological or psychiatric deficits. The fact that emotional flattening was only found in the MRI setting suggests that EP changes may be unmasked within stressful environments and points to the potential yet underestimated impact of the MRI setting on behavioral outcomes.

Introduction

Controversial evidence suggests deficits in the processing of emotional information (EP) in patients with multiple sclerosis (MS). Reported EP deficits in MS include specific difficulties detecting particularly

Correspondence: T. D. Hälbig, MD, NeuroCure Clinical Research Center NCRC, Charite – Universitätsmedizin Berlin, Charité (Campus Mitte), Sauerbruchweg 5, Charitéplatz 1, D-10117 Berlin, Germany (tel.: +49 30 450 539 705; fax: +49 30 450 539 915; e-mail: halbig.psl@gmail.com; thomas.haelbig@charite.de).

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negative emotional facial expressions [1-3], comprehending affective prosody [4], recognizing emotional compared with neutral visual stimuli and events or defective emotional enhancement of verbal memory [5].

Several studies suggest that deficits in decoding facial emotions of anger and fear might be related to cognitive deficits and in particular to measures sensitive to executive dysfunction and information processing speed [1,6,7] or to depressed mood [8]. Other studies, evaluating emotional prospective memory in patients with MS, did not find deficits [9].

Krause *et al*. [10] in a functional magnetic resonance imaging (MRI) study reported impaired negative emotional facial recognition performance in moderately advanced MS and found decreased anterior insular and ventrolateral prefrontal cortex activation. In contrast, in patients without EP deficits on emotional recognition tasks, enhanced, potentially compensatory brain mechanisms in regions known to be involved in EP appeared to limit the clinical manifestation of EP changes [11,12]. In the same vein, Migliore *et al*. [13] found higher P300 amplitudes in relation to emotional pictures from the International Affective Picture System in moderately advanced MS.

In summary, it remains unclear which functional domains of EP are affected, whether EP deficits in MS are specific to the emotional valence (positive, neutral, negative) and/or arousal dimension and if EP deficits are secondary to other MS-related neuropsychological or psychiatric symptoms.

We ascertained the effects of emotional stimuli on subjective experience, response time and recognition memory performance. To limit the presence of factors potentially impacting EP we enrolled patients in early stages of the disease and controlled for a variety of neuropsychological and psychiatric measures.

Methods

Participants

A total of 29 right-handed Caucasian patients with clinically isolated syndrome ($n = 8$) or relapsing-remitting MS ($n = 21$) [14] within ≤5 years and 29 right-handed matched healthy controls (HCs) (Table 1) were tested. The study was approved by the Charité – Universitätsmedizin Berlin ethics committee and registered at ClinicalTrials.gov (NCT02695394). Written informed consent was obtained from all participants. A total of 32 participants (16 patients/16 HCs) were tested during an MRI session; the remaining 26 participants (13 patients/13 HCs) conducted the experiment in a behavioral laboratory using a personal computer (PC) (Table 1 and Supporting methods, see Appendix S1). The participants were randomized to undergo the testing with or without MRI.

Exclusion criteria were cognitive deficits (Mini Mental State Examination score < 25/30) [15], clinically significant diseases within 7 days before the study evaluations, physical disabilities interfering with the study procedures, depression and anxiety [Hospital Anxiety and Depression Scale (HADS), HADS-D score > 7 and HADS-A score > 7, respectively] [16].

Neuropsychological background testing, health-related quality of life, satisfaction with life and emotional wellbeing

The Brief Repeatable Battery of Neuropsychological Tests [18] was used to test verbal learning and memory, visuospatial learning and recall, attention, sustained attention and speed of information processing, and verbal fluency/executive functioning (Table 1 and Supporting methods, see Appendix S1).

The Modified Fatigue Impact Scale [19] was used to test for fatigue and the Beck Depression Inventory-2 [20] was employed to probe for depression.

Health-related quality of life [Short Form (36-item) Health Survey (SF-36)] [21], satisfaction with life (Satisfaction with Life Scale) [22] and emotional wellbeing (Positive and Negative Affect Schedule) [23] were also examined.

Emotional processing testing

Participants were presented with a series of 54 neutral and emotional pictures (e.g. accident victims, erotica, daily life objects, etc.) from the International Affective Picture System on a computer screen. Pictures differed in valence (18 positive, 18 neutral, 18 negative) and arousal (27 low, 27 high) based on standardized published rating values. Half of the pictures of each of the three valence categories had high and low arousal values, respectively (Supporting methods, see Appendix S1 and Tables S1 and S2) [24]. Each picture was presented for 6 s. After each picture, participants rated the emotion elicited by the picture regarding its valence and arousal using nine-level Self-Assessment Manikin Likert scales (Fig. 1) [25].

After a delay of 15 min, there was a speeded recognition test for the stimuli previously presented ('old') and for distractors ('new'), also comprising neutral and emotional pictures (Supporting methods, see Appendix S1 and Tables S1 and S2). Experiential rating means, percentage of correctly recognized emotional items and modulation of response time by emotional stimulus characteristics served as outcome variables [26,27].

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Table 1 Demographic and clinical characteristics

	Descriptive statistics				Inference statistics (whole 2 × 2 design)
	Patients		HCs		
	PC	MRI	PC	MRI	*P*-value
n[a]	13	16	13	16	0.998
Female/male[a]	7/6	8/8	7/6	8/8	0.999
Age (years)[b]	31.92 ± 7.32	32.63 ± 9.13	33.23 ± 7.12	28.44 ± 7.95	0.356
Education (years)[b]	17.53 ± 3.90	15.57 ± 7.44	17.58 ± 3.35	17.78 ± 2.04	0.545
Disease duration (months)[c]	32.69 ± 21.72	29.19 ± 20.81	N.A.	N.A.	0.663
Disability (EDSS score [17])[c]	1.15 ± 0.94	1.18 ± 0.89	N.A.	N.A.	0.923
Fatigue (MFIS score)[b]	14.23 ± 16.90	13.31 ± 12.97	11.25 ± 9.56	11.93 ± 9.48	0.930
Depression (HADS score)[b]	1.08 ± 1.25	1.75 ± 1.65	1.54 ± 1.51	1.63 ± 1.78	0.699
Depression (BDI-2 score)[b]	4.31 ± 4.66	4.38 ± 4.22	2.54 ± 4.09	3.25 ± 3.80	0.605
Anxiety (HADS score)[b]	3.62 ± 1.66	3.81 ± 2.37	4.62 ± 1.80	4.38 ± 1.75	0.497
Cognition (MMSE score)[b]	29.23 ± 1.30	29.93 ± 0.26	29.54 ± 0.97	29.69 ± 0.60	0.183
Cognition (BRB-N score)[b]					
SRT					
LTS	58.77 ± 14.05	63.50 ± 9.30	61.92 ± 7.47	57.69 ± 10.22	0.389
CLTR	54.92 ± 17.22	60.50 ± 12.01	55.92 ± 10.70	54.00 ± 14.23	0.558
DR	11.00 ± 2.04	11.25 ± 1.57	11.54 ± 0.78	10.87 ± 1.45	0.672
SPART					
Learning	26.77 ± 3.70	25.81 ± 3.31	25.62 ± 3.95	25.00 ± 3.50	0.627
DR	9.54 ± 1.13	8.69 ± 2.24	8.42 ± 2.23	9.19 ± 1.28	0.387
SDMT	62.85 ± 22.82	66.38 ± 14.55	65.85 ± 9.71	59.13 ± 9.88	0.515
PASAT	54.15 ± 4.65	52.19 ± 6.59	51.38 ± 6.25	48.44 ± 9.17	0.179
WLG	32.31 ± 5.71	29.63 ± 5.90	28.54 ± 6.68	29.13 ± 5.28	0.373
Quality of life (SF-36 score)[b]					
PCS					
Vitality	64.62 ± 13.30	59.69 ± 18.30	62.50 ± 13.23	67.67 ± 10.68	0.475
Physical functioning	95.77 ± 7.60	97.50 ± 3.61	97.08 ± 3.34	97.67 ± 5.30	0.773
Bodily pain	89.69 ± 20.77	88.38 ± 19.42	90.42 ± 17.91	88.00 ± 19.13	0.987
General health perception	66.08 ± 15.47	71.44 ± 12.98	71.75 ± 22.52	83.27 ± 13.02	0.042*,**
MCS					
Physical role function	82.69 ± 34.44	89.06 ± 20.35	100.00 ± 0.00	90.00 ± 22.76	0.321
Emotional role function	94.87 ± 18.49	91.67 ± 22.77	97.22 ± 9.62	88.89 ± 20.57	0.686
Social role function	93.27 ± 13.12	94.53 ± 7.86	94.79 ± 8.36	97.50 ± 7.01	0.663
Mental health	79.38 ± 8.46	76.50 ± 10.82	78.33 ± 7.71	78.93 ± 11.16	0.860
Life satisfaction (SWLS score)[b]	25.67 ± 3.23	28.40 ± 4.00	27.00 ± 5.37	27.73 ± 2.99	0.343
Affective state (PANAS score)[b]					
Positive	32.67 ± 7.10	31.53 ± 5.00	32.85 ± 6.84	34.12 ± 7.57	0.760
Negative	11.92 ± 2.81	12.07 ± 3.17	12.00 ± 2.61	13.19 ± 3.56	0.641

Data are given as mean ± SD. BDI, Beck Depression Inventory; BRB-N, Brief Repeatable Battery of Neuropsychological Tests; CLTR, Consistent Long-Term Retrieval; DR, Delayed Recal; EDSS, Expanded Disability Status Scale; HADS, Hospital Anxiety and Depression Scale; LTS, Long-Term Storage; MCS, Mental Component Summary; MFIS, Modified Fatigue Impact Scale; MMSE, Mini Mental State Examination; N.A., not applicable; PANAS, Positive and Negative Affect Schedule; PASAT, Paced Auditory Serial Attention Test; PCS, Physical Component Summary; SDMT, Symbol Digit Modality Test; SF-36, Short Form (36-item) Health Survey; SPART, Spatial Recall Test; SRT, Selective Reminding Test; SWLS, Satisfaction with Life Scale; WLG, Word List Generation. See also Supporting methods, see Appendix S1. [a]Chi-squared test. [b]Group [patients/healthy controls (HCs)] × Experimental Setting [personal computer (PC)/magnetic resonance imaging (MRI)] ANOVA (statistics for whole corrected model). [c]*t*-test for independent samples. **Significant main effect of group ($P = 0.047$).
*Significant at $P < 0.05$.

Statistical analysis

Demographic and clinical variables were analyzed descriptively and differences between subgroups were ascertained by chi-squared tests or ANOVAS for between-subject factors Group (patients/HCs) and Experimental Setting (PC/MRI).

Primary behavioral endpoints were analyzed descriptively and subjected to mixed-model repeated-measures ANCOVAs with between-subject factors Group (patients/HCs) and Experimental Setting (PC/MRI) and within-subject factors Valence (negative, positive, neutral) and Arousal (high, low). To address potential paradigm-unspecific effects on emotional

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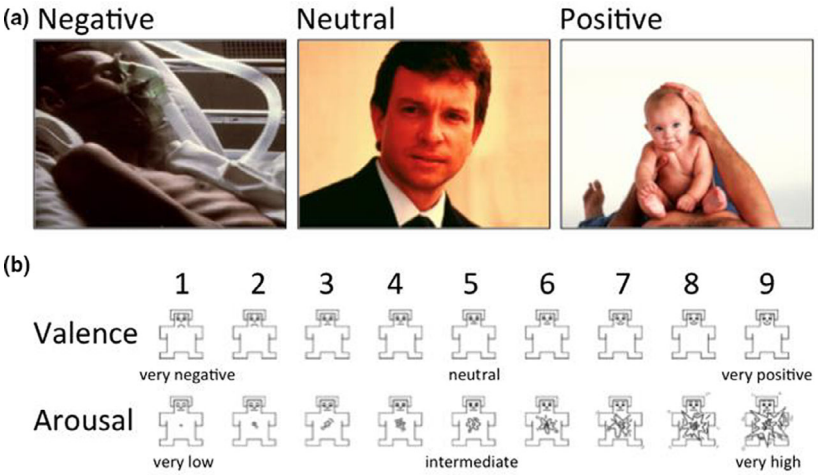

Figure 1 (a) Exemplary International Affective Picture System stimuli. (b) Nine-level Self-Assessment Manikin Likert scales for the rating of the emotion elicited by the picture regarding its valence and arousal. [Colour figure can be viewed at wileyonlinelibrary.com]

processes, we used age, sex and depression severity (Beck Depression Inventory-2) as covariates for the analyses of valence and arousal ratings, recognition performance and response times. The mean values of these primary endpoint variables were used as dependent variables in separate ANCOVAs. In case of sphericity violation, degrees of freedom were Greenhouse–Geisser corrected. Directions of main effects and interactions were *post hoc* assessed via *t*-tests. Two-tailed *P*-values were reported for all effects. The level of significance for all tests was adjusted to $\alpha = 5\%$ and, if applicable, corrected for multiple testing (Supporting methods, see Appendix S1).

Correlations between valence and arousal ratings (corrected for age, sex, Beck Depression Inventory-2 and experimental setting) and health-related quality of life, satisfaction with life, emotional wellbeing and fatigue were analyzed by means of Spearman correlation analysis (Supporting methods, see Appendix S1).

Results

Demographic characteristics, neuropsychological background testing, quality of life, wellbeing and satisfaction with life

There were no significant group- or experimental setting-associated differences, except for the general health perception subscore of the SF-36, which indicated reduced perception of health in patients ($P = 0.047$; Table 1).

Emotional experience

Valence rating

There was a main effect of Valence (Table 2, Fig. 2a, Table S3). *Post hoc* tests revealed that the valence of pictures with positive content was rated higher than the valence of neutral and negative pictures, and that the valence of neutral pictures was rated higher than the valence of negative pictures. Further, there was an interaction of Valence × Group. Patients rated negative and neutral pictures as consistently less emotional than HCs. Finally, there was an interaction of Valence × Group × Experimental Setting. Interestingly, *post hoc* tests revealed that patients from the MRI setting rated negative and positive pictures as consistently less emotional, i.e. more neutral, than HCs (Fig. 2a). In contrast, this effect was not found in the PC group.

Arousal rating

There was a main effect of Arousal, indicating that the arousal of highly arousing pictures was rated higher than the arousal of less arousing pictures (Table 2, Fig. 2b and Table S3). A main effect of Group indicated that, overall, patients were generally less aroused than HCs. However, as revealed by an interaction of Group × Experimental Setting, this effect was found only in the MRI sample. Finally, there was an interaction of Arousal × Group × Experimental Setting. In the MRI setting, patients experienced low and high arousing pictures as less arousing than HCs (Table 2). In contrast, in the PC setting, ratings did not differ significantly between groups. Compatible with this, the patients in the MRI setting rated pictures significantly lower regarding their arousal than patients in the PC setting.

Recognition memory performance and modulation of response time

Our analyses revealed no interactions involving the factor Group (Table 2, Table S3).

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Table 2 Inference statistics

	rmANCOVA			ES	*Post-hoc*	
Outcome variable	Effect	F_{df}	*P*	η^2	Comparisons	*P*
Valence rating	Arousal	$F_{1,51} = 13.84$	<0.001	0.213	H > L	<0.001
	Valence	$F_{1.39,70.96} = 22.83$	<0.001	0.309	NEU > NEG	<0.001
					POS > NEU	<0.001
					POS > NEG	<0.001
	Valence*Group	$F_{1.39,70.96} = 3.62$	0.046	0.066	NEG: HC > Pat	0.036
					NEU: HC > Pat	0.019
	Valence*Group*Exp. setting	$F_{1.39,70.96} = 7.71$	0.003	0.131	NEG(MRI): HC > Pat	0.004
					POS (MRI): HC > Pat	0.038
Arousal rating	Group	$F_{1,51} = 5.98$	0.018	0.105	HC > Pat	0.031
	Group*Exp. Setting	$F_{1,51} = 6.26$	0.016	0.109	MRI: HC > Pat	0.004
	Arousal	$F_{1,51} = 5.10$	0.028	0.091	H > L	<0.001
	Valence	$F_{1.87,95.63} = 4.38$	0.017	0.079	NEG > NEU	<0.001
					POS > NEU	<0.001
					NEG > POS	<0.001
	Arousal*Valence	$F_{1.70,86.87} = 4.67$	0.016	0.084	NEG: H > L	<0.001
					NEU: H > L	<0.001
					POS: H > L	<0.001
	Arousal*Group*Exp. setting	$F_{1,51} = 5.07$	0.029	0.090	MRI: HC(L) > Pat(L)	0.039
					MRI: HC(H) > Pat(H)	<0.001
					Pat: PC(H) > MRI(H)	0.026
Error rates						
Familiar pictures	No effects					
Unfamiliar pictures	Arousal*Exp. setting	$F_{1,51} = 4.10$	0.048	0.074	No significant *post-hoc* effects	
Response times						
Familiar pictures	Exp. setting	$F_{1,51} = 8.58$	0.005	0.144	MRI > PC	0.004
	Arousal*Exp. setting	$F_{1,51} = 6.53$	0.014	0.113	L: MRI > PC	0.028
					H: MRI > PC	<0.001
	Arousal*Group*Exp. setting	$F_{1,51} = 4.15$	0.047	0.075	L: Pat(MRI) > Pat(PC)	0.005
					H: Pat(MRI) > Pat(PC)	0.006
Unfamiliar pictures	No effects					

Results of four-way repeated-measures analyses of covariance (rmANCOVA) for between-subject factors Group [patients/healthy controls (HCs)] and Experimental Setting [personal computer (PC)/magnetic resonance imaging (MRI)] and within-subject factors picture Valence (NEG/NEU/POS) und Arousal (L/H). Covariates were age, sex and Beck Depression Inventory-2. Listed are significant main effects and interactions and associated *post hoc* tests. ES, effect size; H, high arousal; L, low arousal; NEG, negative; NEU, neutral; POS, positive.

Correlation analysis

For patients, but not controls, there was a positive correlation between Satisfaction with Life Scale sum score and valence ratings for highly arousing, positive pictures (Table 3; Supporting results, see Appendix S1). Further, significant between-group differences in correlations between valence ratings and the following three SF-36 subscales were found: emotional role function, physical functioning and physical health (Table 3; Supporting results, see Appendix S1).

Discussion

We here provide evidence that emotional experience in patients with early MS without neuropsychiatric or cognitive deficits may be flattened on the full range of emotional valence and arousal. This effect was only found in patients tested in an MRI setting and suggests that emotional flattening in early MS may manifest only in stressful environments such as in MRI settings.

Previous EP research in MS focused primarily on discrete emotions (i.e. anger, happiness, etc.). For example, studies using emotional facial recognition or classification paradigms provide evidence for altered processing particularly of negative discrete emotions [1,3]. The only previous study in patients with MS that used a dimensional approach [28] evaluated 13 patients using only four International Affective Picture System stimuli per stimulus category. Whereas patients experienced negative but not positive visual stimuli as less arousing than HCs, the experience of emotional valence was not found to be altered. Our behavioral data suggest that EP deficits appear to be broader than suggested by previous research and involve both negative and positive valence as well as the arousal dimension.

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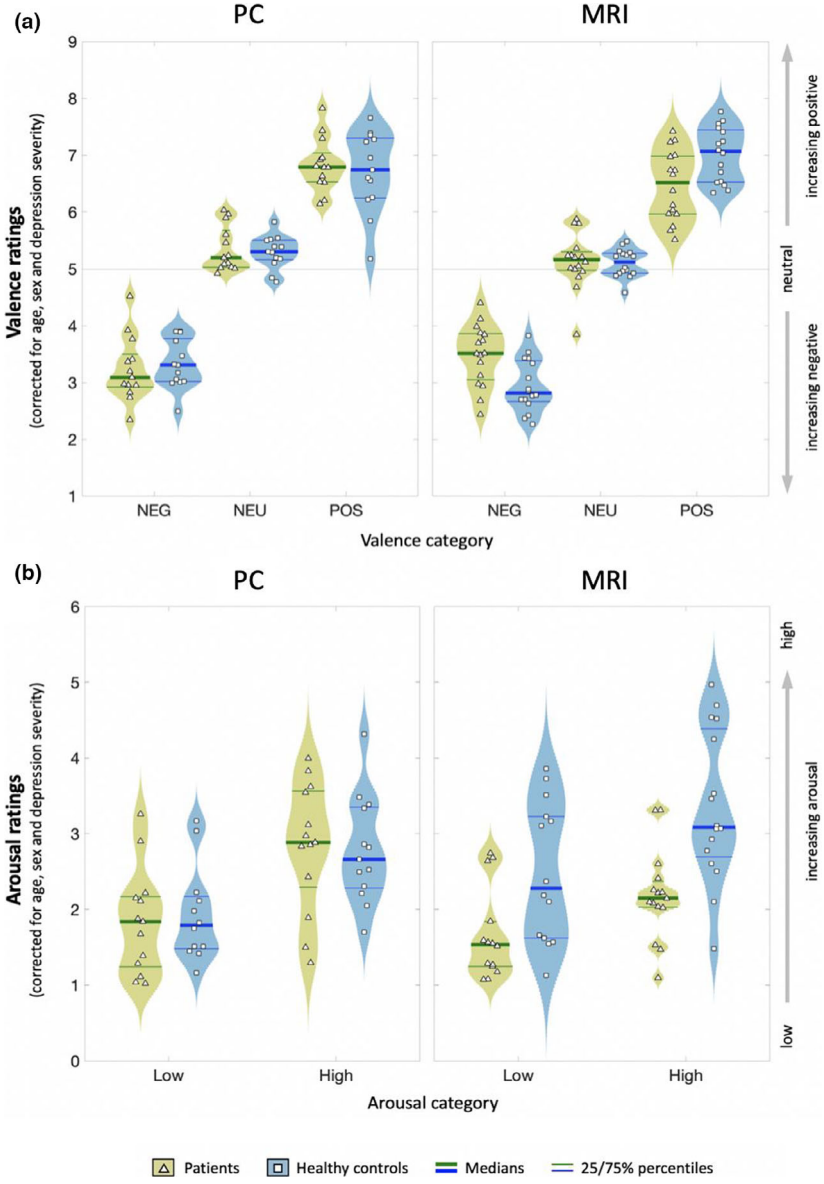

Figure 2 Valence and arousal ratings (n = 58). Displayed are group- and experimental setting-specific rating scores adjusted for the influence of age, sex and depression severity (Beck Depression Inventory-2 score). (a) Valence ratings pooled across high and low arousing stimuli. (b) Arousal ratings pooled across all valence categories. MRI, magnetic resonance imaging group; NEG, negative; NEU, neutral; PC, personal computer group; POS, positive. [Colour figure can be viewed at wileyonlinelibrary.com]

Several rather heterogeneous studies suggest that emotional processing deficits might be related to cognitive deficits [1,2,6] or neuropsychiatric symptoms such as depression [8]. The inclusion of patients with clinically isolated syndrome and early MS without cognitive deficits and mood changes aimed to limit the presence of these and other confounding factors such as relevant disease-related disability or limitations in quality of life. In fact, there were no differences between patients and HCs on demographics and neuropsychological background measures. We therefore deem it unlikely that the flattened emotional responses observed here are secondary to cognitive or neuropsychiatric deficits. The result is rather compatible with the view of a primary deficit in the processing of emotional stimulus information in patients with MS.

The 'flattening' of the experiential response to emotional stimuli in our study was not accompanied by effects on other EP measures such as emotional recognition memory or response time. We cannot exclude the possibility that the power in our study was not sufficient. However, there is evidence that EP relies on

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Table 3 Correlation analyses

Questionnaire	Association: Subscale	Association: Cat(Aro)	Group	Correlation $\rho_{(22)}$ (p 2-tailed)	95% CI: Lower	95% CI: Upper
Valence rating						
Fatigue (MFIS)	Sum score	NEG(L)	Pat	−0.495 (0.016)	−0.755	0.053
			HC	−0.120 (0.595)	−0.536	0.307
Affective state (PANAS)	Positive affect	POS(H)	Pat	0.425 (0.043)	0.119	0.673
			HC	−0.006 (0.977)	−0.497	0.501
Quality of life (SF36)	Emotional role function	NEU(H)**	Pat	−0.447 (0.028)	−0.756	−0.047
			HC	0.572 (0.004)	0.036	0.826
		NEU(L)	Pat	−0.586 (0.003)	−0.818	−0.266
			HC	0.029 (0.897)	−0.414	0.626
		POS(H)	Pat	−0.023 (0.916)	−0.523	0.910
			HC	0.414 (0.049)	−0.123	0.686
	General health perception	POS(L)	Pat	0.513 (0.010)	0.051	0.816
			HC	0.003 (0.988)	−0.457	0.491
	Physical functioning	NEG(L)**	Pat	0.472 (0.020)	0.146	0.781
			HC	−0.312 (0.147)	−0.651	0.032
	Physical role function	NEG(L)	Pat	0.448 (0.028)	−0.037	0.721
			HC	0.248 (0.253)	−0.373	0.741
	Social role function	NEG(L)	Pat	0.593 (0.002)	0.253	0.783
			HC	0.170 (0.437)	−0.271	0.576
	Physical health	NEG(L)**	Pat	0.554 (0.005)	0.213	0.826
			HC	−0.427 (0.042)	−0.837	−0.024
Life satisfaction (SWLS)	Sum score	POS(L)	Pat	0.553 (0.006)	0.143	0.849
			HC	−0.289 (0.192)	−0.641	0.476
		POS(H)	Pat	0.627 (0.001)*	0.068	0.872
			HC	−0.258 (0.246)	−0.638	0.505
Arousal rating						
Fatigue (MFIS)	No associations					
Affective state (PANAS)	Positive affect	NEU(H)	Pat	−0.434 (0.039)	−0.760	0.074
			HC	−0.013 (0.955)	−0.546	0.417
		POS(H)	Pat	−0.020 (0.929)	−0.436	0.440
			HC	0.039 (0.864)	−0.527	0.639
	Negative affect	POS(H)	Pat	−0.441 (0.035)	−0.713	−0.139
			HC	−0.022 (0.924)	−0.419	0.409
Quality of life (SF36)	Vitality	NEG(H)	Pat	−0.047 (0.826)	−0.538	0.399
			HC	−0.565 (0.005)	−0.816	−0.241
	Mental health (sum score)	NEG(H)	Pat	0.066 (0.756)	−0.406	0.564
			HC	−0.456 (0.029)	−0.779	−0.089
Life satisfaction (SWLS)	No associations					

Statistics: estimation of 95% confidence intervals (CI) based on 9999 bootstrapping operations. Aro, arousal category; Cat, picture category; H, high arousal; HC, healthy control; MFIS, Modified Fatigue Impact Scale; L, low arousal; NEG, negative; NEU, neutral; PANAS, Positive and Negative Affect Scale; POS, positive; SF-36, Short Form (36-item) Health Survey; SWLS, Satisfaction with Life Scale. Results of correlation analyses between valence and arousal ratings and fatigue (MFIS), affective state (PANAS), quality of life (SF-36) and SWLS. Ratings adjusted for age, sex, Beck Depression Inventory-2 and experimental setting. *Significant at Bonferroni corrected threshold 0.05/number of tested associations ($P < 0.0021$). **Significant group difference due to CI estimates.

different neural networks with certain processing streams being specifically involved with higher order processing, whereas others mediate the automatic processing of ecologically relevant information enabling the organism to have fast behavioral responses that are not modulated by higher order processing [29]. It is conceivable yet speculative that the disease process at least early in the course of disease progression primarily affects structures involved in higher order EP.

Unexpectedly, EP changes were found only in the MRI subgroup. Patients had been randomized to undergo the experiment in either the MRI or PC setting and the subgroups did not differ on clinical and demographic variables. We therefore hypothesize that the consistent effect of flattened emotional experience seen in patients with MS in the MRI subgroup originates from an interaction of subclinical EP deficits and effects of the MRI environment. Few studies examined the effects of the MRI setting on behavioral task performance. Evidence suggests that supine position, enclosed environment and noise may affect attention, mood or arousal in healthy individuals [30-32]

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with negative as well as positive neuropsychological effects [31,33,34]. Further, the scanner environment is presumably of different psychological significance for patients with MS given the importance of MRI scanning for MS diagnosis, prognosis and therapy decisions. In conclusion, we speculate that EP deficits in our patients with early MS were unmasked within the MRI setting. This hypothesis will have to be confirmed and the underlying specific mechanisms will have to be disentangled by future research.

In addition to the overall flattened experiential responses to emotional stimuli, correlation analysis revealed that patients with higher life satisfaction experience high arousal positive pictures more positively. Further, significant between-group differences in correlations between valence ratings and the following three SF-36 subscales were found: emotional role function, physical functioning and physical health. We interpret these correlations as signals for a potential link of emotional processing capabilities and life satisfaction and health-related quality of life in MS. However, further hypothesis-driven research is needed to substantiate this link, which to our knowledge has not been reported previously.

There are limitations to the present study. Importantly, the overall sample size was relatively small and the finding of EP changes in early MS was observed in an even smaller subgroup of patients. The results of this study will therefore have to be confirmed by future research involving larger sample sizes. Further, the study focused on early MS. No conclusions can be drawn with respect to later stages of the disease. Moreover, the Mini Mental State Examination has severe limitations when used in patients with MS and there are more sensitive alternatives to the Brief Repeatable Battery of Neuropsychological Tests as neuropsychological background evaluation. Finally, we cannot fully exclude a systematic disease-specific picture bias with different relevance of certain picture contents for patients compared with healthy individuals.

Conclusion

Our study extends previous research by demonstrating that EP changes in MS may be present even in early MS and might be unmasked by a stressful environment. Our data suggest that EP deficits are not restricted to the processing of negative information but may affect the full range of emotional valence as well as the arousal dimension. Further, EP changes in early MS do not seem to be secondary to other MS-related neuropsychological or psychiatric symptoms. These observations might have implications for the clinical management of neuropsychological and affective symptoms in MS. The observation that the MRI environment may have a significant yet underestimated impact on behavioral outcome has potential methodological implications given the widespread use of MRI in patients with MS.

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Disclosure of conflicts of interest

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1 Supporting Methods and Results.

Table S1 List of International Affective Picture System pictures used in the present study.

Table S2 Mean normative valence and arousal values for the different picture categories used in the present study.

Table S3 Descriptive statistics: valence and arousal ratings, recognition error rates and response times.

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