

# Stable Asymmetric Interhemispheric Theta Power in Patients With Anorexia Nervosa During Haptic Perception Even After Weight Gain: A Longitudinal Study

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#### ABSTRACT

The aim of this study was to investigate the interhemispheric brain electrical asymmetries during a resting period and during haptic tasks in theta frequency band  $(4-8 \, \text{Hz})$  between healthy controls (N=10) and patients with anorexia nervosa (AN) (N=10). Additionally, AN patients were investigated twice in a longitudinal design  $(T_0-T_1)$  to analyze treatment effects. At rest, a theta asymmetry was observed in the AN group during an acute stage of starvation  $(T_0)$  but not after weight gain  $(T_1)$ . Importantly, theta asymmetry over central regions (C3-C4) was observed in the AN group during the acute stage of starvation  $(T_0)$  as well as after weight gain  $(T_1)$  while performing haptic exploration tasks. In the control group, we found no significant theta asymmetry neither at rest nor during haptic explorations. Results are interpreted as an overarousal of the right hemisphere in AN patients during complex multisensory integration processing which is possibly a result of general functional deficits of the right hemisphere.

Recent advances in the assessment of brain functions in psychiatric disorders were stimulated by the development of several new technologies. One of these technologies is the quantitative EEG analysis (qEEG). Different studies have demonstrated the importance of qEEG in psychiatric diseases. The qEEG analysis is much more independent in comparison to the visual EEG analysis. Further, the data are excellently evaluable using statistical approaches. Accordingly, there are many studies about qEEG changes in depression syndromes (Giles, Perlis, Reynolds, & Kupfer, 1998; Hemmeter, Bischof, Hatzinger, Seifritz,

& Holsboer-Trachsler. 1998; Knott, Mahoney, Kennedy, & Evans, 2001; Schneider, Heimann, Mattes, Lutzenberger, & Birbaumer, 1992), Alzheimers disease (Dierks, Frölich, Ihl, & Maurer, 1995; Elmstahl, Rosen, & Gullberg, 1994; Ihl & Brinkmeyer, 1999), schizophrenia (Lund, Sponheim, Iacono, & Clementz, 1995; Murri, 1991; Sponheim, Clementz, Iacono, & Beiser, 1994; Stassen et al., 1999; Tauscher, Fischer, Neumeister, Rappelsberger, & Kasper, 1998; Wada, Nanbu, Jiang, Koshino, & Hashimoto, 1998a; Wada et al., 1998b). In comparison to these psychiatric applications, there are some

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studies utilizing qEEG in anorexia nervosa (AN) so far (Bradley et al., 1997; Bordallo, Diago, & Alberto, 1986; Crisp, Fenton, & Scotten, 1968; Delvenne, Kerkhofs, Appelboom-Fondu, Lucas, & Mendlewicz, 1992; Hughes, 1996; Lauer & Krieg, 1992; Neil, Merikangas JR, Foster, Merikangas KR, Spiker, & Kupfer, 1980; Rothenberger, Blanz, & Lehmkuhl, 1991; Struve 1986; Torigoe et al., 1999). The different studies investigated, for example, changes of EEG during sleep in AN, or event related potentials (ERP) in patients with anorexia nervosa.

Generally, all studies showed differences in brain electrical activity in patients with anorexia nervosa in the acute stage of starvation. These results point to changes of brain electrical activity in the hemisphere of AN patients. However, it remains unclear whether the observed changes in brain electrical activity in AN patients in the acute stage of starvation are reversible after weight gain or not. Furthermore, it had not been established until now as to whether an interhemispheric asymmetry of electrical brain activity exists in AN patients. Neuropsychological studies by Casper and Heller (1991) suggested asymmetrical brain activation in AN patients.

The question concerning asymmetrical brain activation in AN patients has also occurred in the background of important findings on asymmetric electrical brain activities by several other cohorts. In an attempt to determine the functional differences between the left and right hemispheres, several investigators have made interhemispheric comparisons of spontaneous brain potentials at rest and during various tasks in healthy controls (Autret, Auvert, Laffont, & Larmande, 1985; Kline, Blackhart, & Schwartz, 1999; Miller & Tomarken, 2001; Russo, Persegani, Torlini, Papeschi, & Trimarchi, 2001; Sekimoto et al., 2000; Zhavoronokova, 2000) and different mental diseases (depression, schizophrenia, panic disorders) (Baehr E, Rosenfeld, Baehr R, & Earnest, 1998; Bruder et al., 1997; Debener et al., 2000; Jabbari, Russo MB, & Russo ML, 2000; Kentgen et al., 2000; Knott, Labelle, Jones, & Mahoney, 2000; Merrin & Floyd, 1997). To our knowledge, there have been no related studies on interhemispheric asymmetries in AN patients. However, based on neuropsychological hypotheses (see,

e.g., Casper & Heller, 1991) Kinsbourne & Bemporad, 1984); as well as on EEG data provided by Bradley et al. (1997), it seems valuable to suggest an interhemispheric asymmetry in AN patients. Kinsbourne and Bemporad (1984) suggested that subjects with anorexia nervosa have a dysfunction of the right posterior hemisphere produced by an over-arousal of the right anterior hemisphere. These authors as well as Bradley et al. (1997) suggested that this dysfunction of the right posterior hemisphere, involving predominantly the right parietal lobe, is specific to anorexia nervosa, and that it might be responsible for the "anorectic's neglect" of the patient's starved body. Studies on ERPs found disturbances in patients with anorexia nervosa, particularly when they had a low body weight (Bradley et al., 1997; Rothenberger et al., 1991). Thus, Bradley et al. demonstrated that P3 amplitudes for a non-verbal task are significantly smaller in contrast to a verbal task at a 8-month follow-up in AN patients. This suggests that even after weight gain, anorectics continued to manifest some inefficiency in cortical processing of non-verbal information. From this finding it also could be suggested that there is a more general neurophysiological dysfunction underlying AN. On the basis of these results and of our studies (Grunwald et al., 2001a), which investigated brain electrical changes in the theta band during hypoglycaemia, we expected significant interhemispheric asymmetries in spectral theta power over frontal, central, and posterior regions during rest in AN patients in an acute stage of starvation (T<sub>0</sub>). On the basis of these data, such interhemispheric asymmetries might be expected since different studies have demonstrated strong changes of the cortical glucose metabolism in AN patients during an acute stage of starvation (Delvenne et al., 1996; Herholz et al., 1987). A relationship between changed cortical metabolism and interhemispheric asymmetry has recently been demonstrated by Reid, Duke, and Allen (1998) in patients with depression. Furthermore, on the basis of these data we expect these interhemispheric asymmetries in AN patients to be a consequence of hypoglycaemia. Therefore, it is to be expected that these interhemispheric asymmetries during rest will

disappear after weight gain (T<sub>1</sub>). Moreover, based on data of a study by Delvenne et al. (1996) showing a normalization of cortical metabolism after weight gain, we expect no significant differences of electrical brain activity in the theta band 4-8 (Hz) during rest in patients after weight gain. The choice of EEG theta power for data analysis is based on our own psychophysiological studies that have shown cortical spectral theta power (absolute power in μV<sup>2</sup>) to reflect working memory load during multisensory integrative processing (Gevins et al., 1979; Grunwald et al., 1999, 2001b, 2001c; Klimesch, Doppelmayr, Russegger, & Pachinger, 1996; Klimesch et al., 2001; Mecklinger, Kramer, & Strayer, 1992; Schacter, 1977).

However, it seems to be insufficient to investigate electrical brain asymmetries exclusivedly in unspecific rest conditions. Findings of Günther et al. (1993) support the assumption that EEG measurements during an unspecific rest situation without perceptive-cognitive demand might not be sensitive enough to produce significant differences in spectral EEG parameters. Therefore, the quantitative EEG should be obtained during perceptive-cognitive demands in order to measure the smallest changes in electrical brain activity. Stimulated by these data and by our own previous results on haptic perception in AN patients, we used spectral EEG parameters not only during rest but also during different complex haptic perception tasks (Delvenne et al., 1996; Grunwald & Beyer, 2001e; Grunwald et al., 1999, 2001a, 2001b, 2001c, 2002; Guenther et al., 1993; Herholz et al., 1987; Reid et al., 1998).

Therefore, we hypothesize that brain electrical asymmetry within the theta band in AN patients performing haptic perception tasks changes significantly over central and parietal somatosensory regions at the time of starvation  $(T_0)$  as well as after weight gain  $(T_1)$ . We had expected, on the basis of the postulated functional deficits of the right hemisphere in AN, a more pronounced desynchronization of theta waves over the right than over the left hemisphere. In contrast, no such changes in theta asymmetry were expected in healthy controls neither under resting conditions nor for the haptic tasks.

#### METHODS

# Subjects

### Anorexia Group

Ten patients with AN (females), diagnosed in accordance with ICD-10 criteria (Dilling, 1999), participated in the study. At the time of testing, all group members were being treated as inpatients at the Clinic of Child and Adolescent Psychiatry, University of Leipzig, Germany. Patients with bulimia nervosa or moderate binge eating and/or vomiting were excluded. ICD-10 diagnoses were made by experienced clinicians at the Clinic of Child and Adolescent Psychiatry based on clinical interviews. All patients had normal CT or MRT and no neurological symptoms. Three patients were medicated at  $T_0$  (1 patient with antidepressive drugs, 1 patient with hormones, 1 patient with hormones and neuroleptics). At  $T_1$  all patients were unmedicated.

Eight subjects had already been treated as inpatients in other clinics of child psychiatry and were diagnosed as suffering from anorexia nervosa. Two subjects were being treated as inpatients for the first time. The duration of the illness varied from 8 months to 2 years (mean = 14.5, SD = 5.7).

The demographic data of the participants including intake, body weight, BMI (Body Mass Index) and so forth are documented in Table 1. The mean age (T<sub>0</sub>) was 15.90 (SD = 1.97); (mean age:  $T_1 = 16.90$ , SD = 1.97). The BMI is calculated as: weight (kg) divided by the square of height (m). Whereas a BMI between 20 and 25 is considered optimal, a BMI of less than 16 is considered as an indication of significant undernutrition (Beaumont & Russell, 1982). A questionnaire for the assessment of the own body (FbeK) (Strauß & Appelt, 1983) was used to assess the disturbance of the body image in the patient group. This questionnaire considers changes in the body image on the scales "Attractiveness/Self-Confidence," "outward appearance," "hypochondriac symptoms (Unsureness/ Anxiety)," and "bodily-sexual uneasiness." This questionnaire was used in several studies concerning AN and showed particular sensitivity to body image disturbances in scale 1 "Attractiveness/Self-Confidence" (Lehmkuhl, Flechtner, Woerner, & Masberg, 1989).

Patients were first tested after hospital admission  $(T_0)$  and then again 1 month after being released from the hospital  $(T_1)$ . The time interval between initial testing  $(T_0)$  and follow-up  $(T_1)$  ranged from 8 to 23 months, with a mean of 14.5 months (SD=5.7). The mean BMI for the AN group was 15.24 (SD=1.27) at  $T_0$  and 16.60 (SD=1.71) at  $T_1$ . BMI differed significantly between  $T_0$  and  $T_1$  (t=-3.57, p=.006, paired t-test, two-tailed). Two patients from the initial testing  $(T_0)$  were treated as outpatients at the time of  $T_1$  testing.

Table 1. Data Concerning Age, Body Mass Index (BMI), Quality of Reproductions (QR), Exploration Time (ET) and Intelligence (IQ) for the Control Group (CO) and Anorexia Patients (AN) as Well as Statistical Results of Inter- and Intra-group Comparisons.

	CO $(N = 10)$		AN [T <sub>0</sub> ]	(N=10)	AN [T <sub>1</sub> ]	Statistics	
	Mean	SD	Mean	SD	Mean	SD	
Age	16.14	0.74	15.90	1.97	16.90	1.97	
BMI	22.16	3.01	15.24	1.27	16.60	1.71	a, b, c
QR	1.27	0.22	2.17	0.66	1.92	0.61	b. с
ÈТ	167.58	86.13	136.80	44.15	101.38	41.63	
IQ	114.69	13.52	115.20	7.98	-	_	

*Note.* <sup>a</sup>Intra-group comparison for anorexic patients  $T_0$ - $T_1$  (paired *t*-test): p < .05.

The IQ was measured using HAWIK (Tewes, 1983) at the beginning of testing (mean = 115.20, SD = 7.98). All patients were right-handed according to a test of handedness by Salmaso and Longoni (1985).

# Control Group (CO)

Ten healthy females participated in the experiment. The mean age was 16.14 (SD=0.74) and the age difference between both groups was not significant ( $AN_{T_0}$ -CO: t=0.36, p=.72, t-test, two-tailed). The mean BMI was 22.16 (SD=3.01). The BMI between control group and AN patients was significantly different at both  $T_0$  ( $CO_{BMI}$ -AN $_{T_0}$ -BMI: t=6.68, p<.001, t-test, two-tailed) and  $T_1$  measures ( $CO_{BMI}$ -AN $_{T_1}$ -BMI: t=5.07, p<.001, t-test, two-tailed).

The IQ was also measured using HAWIK (Tewes, 1983) (mean = 114.69, SD = 13.52). There was no significant difference concerning the IQ between CO and AN patients ( $CO_{IQ}$ -AN $_{T_0$ -IQ: t = -0.10, p = .919, t-test, two-tailed). None of the CO participants suffered from any neurological or psychiatric disorder. All subjects were right-handed. The volunteer subjects received a payment of 10\$(US) for each session.

The study was approved by the Ethics Commission of the University of Leipzig. After all human subjects, controls as well as patients, had been fully informed about the aim and content of the investigation procedure, a written, informed consent was obtained from each. All human subjects participated in the investigation of their own free will.

## EEG Recording

A 19-channel digital EEG (linked ears) was continuously recorded during rest and haptic tasks in all subjects. In accordance with the international 10–20 system (Jasper, 1958), Ag-AgCl electrodes were

attached to the scalp in the standard electrode positions (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, T6, P3, Pz, P4, O1, O2). Electrical impedance was measured manually and was kept below  $5 k\Omega$ . Movements of the right eye were monitored by horizontal and vertical electrodes. The signals of these electrodes were recorded on separate channels. The EEG was conducted in a Farady Cage with a digital, non-paper EEGsystem by Walter Graphtek (Bad Oldesloe, Germany). The sampling rate was 333 Hz with a time constant of 0.3 s. All measurements were prepared and realized by the same assistant. They were performed in the same lab with the same apparatus under the same conditions at the same time. All experiments were carried out between 9 and 12 a.m. Volunteers were seated in a comfortable armchair during the whole experiment.

During the data acquisition, EEG signals were displayed on-line on a high-resolution colour monitor and stored on an optical disk (WORM). EEG analytical software from the Institute of Neurophysiology, Friedrich-Schiller-University Jena (Rost, Hansen, Beyer, & Weiss, 1992), was used to segment the raw EEG data and calculate mean spectral power. Artefactfree segments of 1.53 s (512 samples/channel) of the resting condition as well as of haptic exploration intervals were chosen by visual inspection and substantiated by cross correlation analysis between relevant frontal EEG and EOG electrodes ( $r_{crit.} < .5$ ). The remaining segments were submitted to a Fast Fourier Transform (FFT) analysis and smoothed with a 7-point low-pass filter (weights 1/64, 3/32, 15/64, 5/16, 15/64, 3/32, 1/64) in order to balance between resolution of the power spectra and its variance. Mean spectral power density was calculated as the mean amplitude of the spectral lines of the theta band (4-8 Hz). The mean spectral power parameters per channel and subject were ln10-transformed prior to statistical analysis.

Inter-group comparison between controls and anorexic patients at  $T_0$  (unpaired t-test): p < .05.

<sup>&</sup>lt;sup>c</sup>Inter-group comparison between controls and anorexic patients at  $T_1$  (unpaired t-test): p < .05.

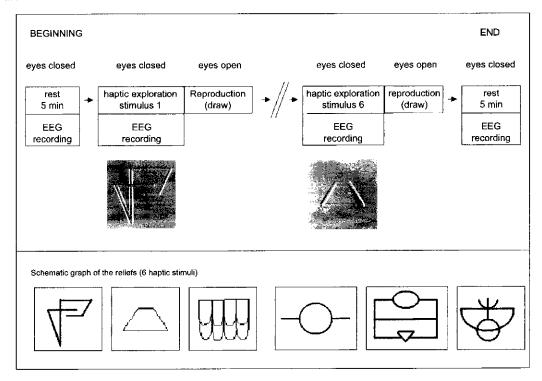


Fig. 1. Test schema. EEG data were recorded from 10 anorectic patients and 10 controls during rest and haptic explorations. The six haptic stimuli were presented to the test subjects in random sequence. The stimuli were explored with both hands and with eyes closed. The upper part illustrates the different intervals (rest, exploration, drawing). The lower part shows two examples of the stimulus material.

## **Haptic Task**

The haptic task consisted of exploring six individual sunken reliefs  $(13 \, \mathrm{cm} \times 13 \, \mathrm{cm})$  (Fig. 1), which were presented to the participants in random order. All participants were asked to palpate the haptic stimuli with both hands while keeping their eyes closed. Following the haptic explorations all participants were asked to reproduce the structure of the stimuli as closely as possible on a piece of paper with their eyes open. Optimal positioning of the stimuli in relation to the fingers was allowed due to an adjustable holder. During haptic exploration the forearms rested on a wide base in order to allow free movement to the fingers only. No arm and shoulder movements were made during haptic exploration.

The exploration time per stimulus was not limited. With the help of a strategically placed screen the participants were prevented from gathering visual information about the stimuli. The participants were not given any feedback on the quality of their reproductions or the stimulus structure. The exploration time per stimulus was registered by means of pressure sensors (in

seconds). The participants were allowed to familiarize themselves with the haptic material by looking at one sample stimulus not included in the following experiment and practicing the haptic exploration task for a duration of 1 min prior to the experiment proper.

### **Statistics**

Spectral EEG data were evaluated with the SPSS statistical package (8.0) for Windows 95. For the statistical comparison of age, BMI, IQ and exploration time (ET) between groups the unpaired t-test were used. The statistical comparison between the  $T_0$ – $T_1$  data in the AN group was undertaken by t-tests for dependent groups. The differences in quality of reproduction (QR) between groups was performed with non-parametric tests (Mann–Whitney test). For the statistical comparison of the quality of reproduction between  $T_0$  and  $T_1$  in the AN group non-parametric tests for dependent group (Wilcoxon test) were used.

For testing theta-power values we used logarithmized (log10-transformed) data separately for each group and situation. To reduce the possibility of Type I

errors, a two-factor analysis of variance for repeated measurements (MANOVA) was used to analyse hemispheric differences. The following factors were included: HEMISPHERE (left vs. right), REGION (frontal: Fp1-Fp2, fronto-central: F3-F4, frontotemporal: F7-F8, centro-temporal: T3-T4, central: C3-C4, parietal: P3-P4, parieto-temporal: T5-T6, occipital: O1-O2). In the case of significant effects in the MANOVA, paired post hoc t-tests were used to identify the sources of variance. For these post hoc tests, a critical  $\alpha'$ -level was adjusted due to repeated testing. Therefore, the critical  $\alpha'$ -level for 48 single paired t-tests was calculated according to Bonferroni ( $\alpha' = 0.05/48 = .001$ ). Only significant differences, at the critical  $\alpha'$ -level, between the left and right sides are documented. Differences in theta power between groups under the different situations are not described in detail here due to the volume of this analysis but they can be found in Grunwald et al. (2001a).

#### RESHLTS

#### **EEG Data**

MANOVA revealed significant interaction effects (HEMISPHERE  $\times$  REGION) in theta asymmetry in AN patients for the first measurement ( $T_0$ ) during rest as well as during haptic perception. No such interaction effects were found for the control group at  $T_0$  and at  $T_1$  nor for the AN patient group at  $T_1$ . The results of MANOVA are displayed in Table 2.

The post hoc analysis of interhemispheric differences revealed exciting results. As expected from MANOVA, significant differences below the critical  $\alpha' = 0.001$  were found only in the patient group. All significant post hoc tests for interhemispheric asymmetries of pairs of electrodes are shown in Figure 2.

Table 2. Results of MANOVA Interaction Between Factors HEMISPHERES × REGION (Dependent Variable: log10-Transformed Theta-Power).

	Controls $(N=10)$			Ano	rexia (N = 1	0), T <sub>0</sub>	Anorexia ( $N = 10$ ), $T_1$			
	df a	F	p	$\overline{df}^{a}$	F	p	df a	F	p	
Rest	2.52	0.72	0.523	1.25	12.85	0.001	4.09	0.33	0.855	
Haptic task	2.55	0.72	0.521	1.66	7.02	0.005	2.54	0.51	0.642	

Note. aGreenhouse-Geisser adjusted.

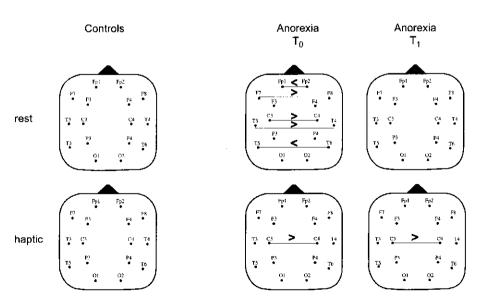


Fig. 2. Significant interhemispheric asymmetries at the critical alpha-level ( $\alpha' = 0.001$ ). A "<" or ">" indicates a significantly lower or higher theta power in the pair of electrodes, respectively.

Table 3a-c. Mean and SD Spectral Power (Theta-Band) of Left Side EEG Channels (Fp1, F3, C3, P3, O1, F7, T3, T5) and of Right Side EEG Channels (Fp2, F4, C4, P4, O2, F8, T4, T6).

Channel	Anorexia nervosa																
	Rest (T <sub>0</sub> )								Rest (T	` <sub>1</sub> )							
	Mean left side	SD	Mean right side	SD	t	p	Mean left side	SD	Mean right side	SD	t	р					
(a) Comp	arison for	Patien	ts With And	rexia l	Nervosa D	uring	Rest (To a	nd $T_1$ ).									
Fp1-Fp2	3.08	3.33	5.79	1.02	-3.413	.008	4.51	1.17	4.65	1.35	-1.546	.156					
F3-F4	6.03	1.19	6.22	1.17	-0.829	.429	5.27	1.03	5.30	1.34	0.177	.864					
C3-C4	7.12	1.22	6.41	1.39	3.158	.012	5.55	1.32	5.34	1.40	2.226	.053					
P3-P4	6.90	1.41	7.22	1.63	-1.755	.113	5.58	1.38	5.64	1.73	-0.013	.990					
01-02	8.37	3.42	8.04	3.06	0.413	.689	5.63	1.16	5.84	1.35	-1.456	.179					
F7-F8	7.22	2.90	4.16	1.09	6.249	.000	3.64	0.64	3.65	1.10	0.223						
T3-T4	4.61	1.20	3.64	0.59	3.213	.011	3.21	0.67	2.93	0.65	1.098						
T5-T6	4.90	2.23	6.02	2.07	-3.219	.011	4.86	1.40	4.82	1.66	0.266						
Channel	Anorexia nervosa																
	Haptic (T <sub>0</sub> )						<u>.                                      </u>	• • • • • • • • • • • • • • • • • • • •	Haptic (	T <sub>l</sub> )	-	p  7  7  7  7  7  7  7  7  7  7  7  7  7					
	Mean left side	SD	Mean right side	SD	t	p	Mean left side	SD	Mean right side	SD	t	р					
(b) Comp	arison for	Patien	ts With And	rexia I	Nervosa D	uring	Haptic Tas	ks (T <sub>0</sub>	and $T_1$ ).								
Fp1–Fp2	4.02	3.05	6.90	1.74	-2.560	.031	6.53	2.83	7.13	3.85	-2.687	025					
F3-F4	6.65	1.26	5.80	0.49	2.733	.023	5.85	1.09	5.71	1.07	1.694						
C3–C4	6.57	0.89	5.48	0.72	4.987	.001	5.67	1.33	5.28	1.31	3.780						
P3-P4	5.58	1.38	5.64	1.73	-0.013	.990	5.44	1.30	5.57	1.65	-0.467						
01-02	5.63	1.16	5.84	1.35	-1.456	.179	5.60	1.94	5.58	1.66	-0.213						
						.828	4.35	1.31	4.32	1.34	0.080	.938					
F7–F8	3.64	0.64	3.65	1.10 0.65	0.223 1.098	.301	3.52	1.22	3.15	0.93	0.986	.350					
T3-T4 T5-T6	3.21 4.86	0.67 1.40	2.93 4.82	1.62	0.266	.796	3.32 4.47	1.24	4.67	2.05	-0.072	.944					
Channel	Controls																
	Rest								Haptic								
	Mean left side	SD	Mean right side	SD	t	p	Mean left side	SD	Mean right side	SD	t	p					
(c) Comp	arisons for	Contr	ols During	Rest ar	nd Haptic	Tasks.			<u>-</u> .								
Fp1–Fp2	6.54	1.32	6.72	1.45	-2.824	.020	6.49	1.08	6.55	1.50	0.070	.946					
F3-F4	7.13	1.53	7.15	1.80	0.168	.870	6.25	0.64	6.34	0.69	-0.847	.419					
C3-C4	7.13 7.60	1.89	7.13	1.60	1.868	.095	6.32	0.74	5.99	0.65	2.397	.040					
P3-P4		2.06	7.34	1.77	-0.383	.711	5.83	0.52	5.89	0.50	-0.714	.494					
	7.35				-0.561	.589	5.94	1.27	5.93	0.84	-0.714 -0.197	.848					
O1O2	8.17	4.05	8.16	3.22													
F7–F8	5.80	1.03	5.31	1.13	2.350	.043	5.08	0.57	4.74	0.94	1.844	.098					
T3- <b>T</b> 4	4.94 6.12	0.90 1.96	4.78 6.58	0.95 3.14	1.388 0.862	.198 .411	3.92 4.71	$0.47 \\ 0.41$	3.71 4.81	0. <b>5</b> 0 0.77	1.628 -0.285	.138 .782					
T5-T6																	

Note. Means and standard deviations (SD) given as log10-transformed theta-power in  $\mu V^2$ . t values and significant levels shown per test between electrodes (t-test for depended samples).

Post hoc tests for stage of acute starvation  $(T_0)$ 

Massive interhemispheric differences were found in AN patients during rest as well as during haptic exploration. During rest, frontal (Fp1-Fp2) and temporo-parietal (T5-T6) theta power was significantly lower on the left than on the right side. Additionally, theta power at fronto-temporal (F7-F8), central (C3-C4), and centro-temporal electrodes (T3-T4) was significantly lower on the right side as compared to the left side. Interestingly, during haptic exploration a significant interhemispheric asymmetry was found at central electrodes (C3-C4) in AN patients. The mean theta power was lower on the right side than on the left side. No differences were found for the control group neither during rest nor during the performance of the haptic exploration task.

# Post hoc tests after weight gain $(T_1)$

No interhemispheric differences in theta power were found during rest neither in the control group nor in AN patients. However, significant results were found for post hoc tests in AN patients during haptic tasks. A significant interhemispheric asymmetry was detected over central electrodes (C3–C4) in AN patients. Mean theta power was lower on the right side than on the left side. Table 3a–c shows all values of mean theta power as well as the *t*-statistics for each of the electrode pairs under investigation.

#### Behavioural Data

Quality of reproduction in the haptic test. The statistical analysis of the quality of reproduction revealed that AN patients showed lower quality of reproduction on the haptic test of  $T_0$  and  $T_1$  as compared to the control group (CO-AN $_{T_0}$ : Z=-3.26, p=.001; CO-AN $_{T_1}$ : Z=-2.78, p=.005, Mann-Whitney, two-tailed). No significant improvement of the quality of reproduction was found in AN patients from  $T_0$  to  $T_1$  (AN $_{T_0-T_1}$ : Z=-1.53, p=.125, Wilcoxon, two-tailed).

Exploration time. No significant differences between groups were found neither on  $T_0$  (CO-AN<sub>T<sub>0</sub></sub>: t=0.917, p=.371) nor on  $T_1$  (CO-AN<sub>T<sub>1</sub></sub>: t=1.992, p=.062). The mean rating score as well as the mean exploration time per group are given in Table 1. A more detailed

description of these data can be found Grunwald et al. (2001a).

#### DISCUSSION

Our EEG data clearly demonstrate significant asymmetric interhemispheric theta power for patients with anorexia nervosa. The main results that will be discussed in detail are: first, during rest theta asymmetry in AN patients was observed in an acute stage of starvation  $(T_0)$  but not after weight gain  $(T_1)$ . Second, theta asymmetry was observed in AN patients over central regions (C3-C4) in an acute stage of starvation  $(T_0)$  as well as after weight gain  $(T_1)$  while subjects performed haptic exploration tasks. Third, in the control group, no significant brain asymmetry has been found neither during rest nor while performing haptic tasks.

These results are in accordance with our above formulated hypothesis that an interhemispheric asymmetry in AN patients under rest conditions might be a consequence of an acute undernutrition in these patients. We propose that the clearly expressed asymmetry in theta power during the acute stage of starvation results from the changed cortical glucose metabolism. Studies on the brain glucose metabolism in AN patients demonstrated that this metabolism is significantly reduced in AN patients but normalizes after weight gain (Delvenne et al., 1996; Herholz et al., 1987). The relationship between brain metabolism and brain electrical asymmetry has been described in detail by Reid et al. (1998). On the basis of these data, it could be suggested that the observed brain asymmetry in AN patients under rest conditions at  $T_0$  disappears after weight gain whereby it seems plausible that the weight gain in AN patients leads to a normalization of brain metabolism and also to a normalized distribution of brain electrical activity during rest.

The second main result confirms our hypothesis; that is, the observed interhemispheric asymmetry over the central C3-C4 remains in AN patients when they perform haptic explorations even after weight gain (T<sub>1</sub>). This stability of interhemispheric brain asymmetry over time points to the fact that this asymmetry is not an

effect depending on patients weight or changed glucose metabolism. Rather we assume that this asymmetry over central cortex regions reflects a general disturbance of the brain's electrical activity in AN patients. This disturbance can be observed only under specific performance tasks and especially in perceptive—cognitive tasks. At least in haptic exploration tasks, AN patients showed a stable asymmetry above central regions of the right hemisphere.

Our data, as well as the data of other studies (Bradley et al., 1997; Casper & Heller, 1991; Kinsbourne & Bemporad, 1984), support the thesis that an over-arousal of the right hemisphere exists permanently in anorexia nervosa. The reasons for this over-arousal are unknown until now and remain to be clarified.

One possible reason might be that a general functional deficit of the right hemisphere during multi-sensory information processing or sensorymotor tasks leads to an unspecific over-arousal of the cortical areas of the right hemisphere; that is, we hypothesize that the over-arousal of the right hemisphere in AN patients might be a consequence of a cortical dysfunction of this hemisphere. As a sign of this dysfunction, AN patients show a strong change in body image (Fernandez-Aranda, Dahme, & Meermann, 1999; Freeman, Thomas, Solyom, & Hunter, 1984; Hsu, 1982; Smeets & Kosslyn, 2001). Also, our results concerning the quality of reproduction in a haptic exploration test of AN patients are in line with a cortical dysfunction of the right hemisphere (Grunwald et al., 2001a). The test revealed substantial differences between AN patients and healthy controls with regard to the quality of reproductions of haptic stimuli. Thereby, the significantly lower quality in reproduction in the AN group depends not on intelligence since both groups had a similar IQ. The lower quality of reproduction of haptic stimuli submitted by patients with AN points to an altered ability in processing perceptions and somatosensory integrations (Fox & Bashford, 1997; Gordon, Halmi, & Ippolito, 1984; Ploog & Pirke, 1987; Szmukler et al., 1992).

Our findings demonstrated that patients with AN, even after weight gain, have greater problems with complex haptic information than healthy controls. Based on studies in the field of

Gestaltpsychology, simple geometric figures are identified on the basis of only a few basic characteristics without comprehensive, perceptual-cognitive operations (Appelle, 1991). With increasing complexity, however, greater demand is placed on somatosensory integration abilities, short-term memory processing, and selective attention (Gibson & Walker, 1984; Grunwald et al., 2001a, 2001b; Klatzky, Loomis, Lederman, Wake, & Fujita, 1993). Thus, it can be deduced that patients with AN are unable to forge the complex relations of individual stimuli elements into an overall concept. The haptic requirements of complex stimuli call for simultaneous sensory integration of a multitude of pieces of information about space and dimensions. We know from neuropsychological studies that these types of tasks are organized in the parietal cortex. Lesions of the parietal cortex can result in disturbances of tactualhaptic perception (i.e., tactile agnosia, tactile aphasia: Kolb & Whishaw, 1993; Reed, Caselli. & Farah, 1996). Additional evidence for an impairment of the right parietal functions was found by our group in another haptic test, the socalled "Angle Paradigm", where AN patients showed a lower performance as well (Grunwald et al., 2002).

Our results allow only limited conclusions due to the relatively small number of patients and an poor control of exploration times. More generally, our results do not allow statements concerning central questions on the genesis of anorexia nervosa. Therefore, it remains unclear whether the suggested functional deficit of the right hemisphere in AN patients is a result of the disease or whether it can be seen as an origin for AN. It is also unclear whether hormonal dysfunctions or genetic factors might lead to the functional deficit of the right hemisphere. Due to the lack of data, we still do not know whether similar functional deficits exist in all anorectic patients; that is, we do not know whether the observed effects are gender specific or not. To answer these questions, large prospective longitudinal studies are required. In these studies, a simultaneous recording of different types of functional imaging (EEG, fMRI, MEG, PET) and different biochemical markers should be applied. It seems important to make use of a relatively long time span of more than 5 years and a pre-adolescent age group, as it is relatively probable that the changes leading to the development of anorexia nervosa take place shortly before and/or during adolescence. Concluding from our study, it seems important for the success of further studies to include such specific tasks as haptic exploration tests.

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