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What Happens to Electrical Brain Activity when Anorectic Adolescents Gain Weight?*

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Summary. We investigated 39 adolescent anorectic inpatients (27 cross-sectionally. 12 longitudinally) and, as controls, 12 emotionally disturbed inpatients with auditory evoked potentials (AEP) of subcortical and cortical origin. Different intensities of the stimuli were applied in an augmenting/reducing paradigm to test the ability to modulate auditory inputs. In addition, cranial CT was performed in each anorectic patient as well as in another group of 12 child psychiatric controls. Three main results were found: (1) anorectics may have difficulty in modulating auditory stimuli adequately at the subcortical level, even after gaining weight. At the cortical level, their modulation did not differ significantly from controls. (2) a systematic dissociation of the AEP amplitude response between subcortical and cortical CNS levels was seen mainly in anorectics when they had low body weight. This may suggest an uncoupling of cortical versus subcortical neuronal systems. After weight gain, anorectics had less subcortical/cortical dissociation of AEP, which was never seen in controls. Thus, to reach regular modulation of sensory information anorectics should gain normal weight and eating behavior in good time. (3) CT results showed no significant correlation with AEP findings. So far, the functional role of pseudoatrophy in anorectics remains unknown.

Key words: Anorexia nervosa – Adolescents – Cranial CT – Auditory evoked potentials – Body weight

Introduction

Looking at the organic background of anorexia nervosa (AN), there is some evidence for the hypothesis of a hypothalamic disturbance (van der Eycken and Meermann 1984). On the other hand, a former study of our group (Kohlmeyer et al. 1983) in 23 adolescent anorectic patients showed that underweight anorectics had cortical pseudoatrophy on their cranial CT, which disappeared in most cases after weight gain. In addition, our recent findings of standard EEG recordings in 100 adolescent anorectic patients showed that about 60% had some disturbances of electrical brain activity, but only in a few patients was there an improvement of the EEG with gain of body weight (Rothenberger 1990).

Thus, we assumed that in AN cortical as well as subcortical levels of the CNS could be affected, probably in close relationship to weight loss. Since spontaneous electrical brain activity was relatively independent of changes in body weight in the anorectic patients examined, we thought that stimulus-related processing of auditory information (i.e., a task which directly addresses the performance of a central nervous subsystem relevant for everyday situations) could possibly better demonstrate the influence of starving on electrical brain activity. Furthermore, we planned to test the functional relationship between cortial pseudoatrophy on cranial CT and cortical AEP (auditory evoked potentials).

With these objectives in mind, we applied the method of AEP and their increase in amplitude with stimulus intensity, the so-called augmenting/reducing paradigm (Bruneau et al. 1985; Garreau 1985). The arrival of the auditory input at the primary auditory cortex occurs, according to Vaughan and Arezzo's (1988) review, at about 9 ms after stimulus onset. Thus, wave V of the AEP derives from a subcortical origin and wave N_1 as well as wave P_2 derive from cortical sources. Therefore, we recorded the AEP at both CNS levels along the auditory pathway in order to examine the subjects' modulation of sensory input. We thought this approach might also shed some light on the question whether a transitory frontocortical disturbance might exist in adolescents with AN, since flexibility of behavioral control, which is closely related to frontal lobe functioning, is disturbed in these patients.

Methods

We investigated two groups of adolescent anorectic inpatients, each including two males only. One group of 27 anorectics examined once had a wide range of body weight (32–51 kg, $\bar{x} = 42$ kg, i.e. 86% ideal body weight (IBW). Those with lower body weight had just started their therapy, while those with higher body weight had already shown some progress during treatment (behavior therapy with controlled diet). Six patients in this group received a ben-

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Table 1. Group characteristics of the three groups studied. In the groups of 27/12 anorectics 23/11 reported none, 3/1 one, and 1/0 two former episodes of their illness

Parameter	Anorexia nervosa ($n=27$)		Anorexia nervosa t1 ($n=12$)		Anorexia nervosa t2 ($n=12$)		Emotionally disturbed ($n=12$)	
	$\bar{x}$	s	$\bar{x}$	s	$\bar{x}$	s	$\bar{x}$	s
Age (years)	16.7	2	16.3	2	16.7	2	15.2	2
IQ (score)	115	14	116	11			100	13
Height (cm)	163	6	162	7	163	6	163	9
Weight-E (kg)	42.2	6	39.1	4	48.3	4	58.3	11
(% IBW)	86.3		77.7		96.0		115.4	
Weight-H (kg)	52.2	7	53.0	7				
(% IBW)	106.7		105.4					
Weight-L (kg)	35.0	6	34.6	4				
(% IBW)	71.6		68.8					
Weight loss (kg)	17.2	7.6	18.4	6.6				
(% IBW)	35.2		36.6					
Duration of illness (months)	17.9	15.7	11.3	7.7				

t1, t2: first and second examinations; IBW, ideal body weight in kilograms according to the following formula: (Height in centimeters minus 100) minus 20% (female) or minus 15% (male); Weight-E, weight at examination; Weight-H, highest weight before onset of illness; Weight-L, lowest weight since onset of illness

zamide (sulpiride) because of compulsive and/or depressive symptoms. As expected (Rothenberger and Eggers 1982), the drug had no significant effect on our measurements: the correlations between weight and AEP data were about the same for both groups of 27 and 21 AN patients, the latter excluding those who received medication. A second group of 12 anorectic adolescent inpatients was investigated twice: during the 1st week of treatment ($\bar{x}=39$ kg, 78% IBW) and 2 weeks after they had reached and maintained their target weight ($\bar{x}=48$ kg, 96% IBW). All patients fulfilled the DSM-III criteria for the diagnosis of anorexia nervosa, were unmedicated and had normal hearing and body temperature. Additionally, a child psychiatric control of 12 inpatients (10 females, 2 males) with emotional disturbances specific for adolescents (according to ICD 313) and normal body weight but without eating disorders or drug treatment was examined once (Table 1). The two groups (anorectics vs controls) differed significantly in body weight ($P<0.0002$) and IQ score ($P<0.01$).

Procedure. All AN patients were submitted to cranial CT and recording of AEP at each examination. In the control group, only AEP were recorded. Cranial CT data were available from a second but similar control group of psychiatric inpatients of 12 teenagers with emotional disorders. All subjects had their body weight measured each time they were tested. Because the cortical sulci are not visible on CT of normal adolescents in this age group, we counted the visible cortical sulci in three slices from the temporal, frontal, and parietal convexity of the brain. Slice 1 was at the level of the frontal horns, slice 2 was at the level of the cella media, and slice 3 was 9 mm above the cella media (Kohlmeyer et al. 1983). The counts could be reliably reproduced by G.L., who was blind concerning diagnoses and time point of investigation.

Auditory brainstem responses (ABR, 1000 artifact-free sweeps) to a left ear rarefaction click of 100 µs duration were recorded from Cz to ipsilateral mastoid at 55 and 75 dBHL (filter: 150–3000 Hz). Auditory cortical responses (ACR, 60 artifact-free sweeps) to binaural tone bursts of 100 ms duration and a frequency of 1500 Hz were recorded at 50 and 70 dBHL (EEG filter: 1–30 Hz). For ACR we used the derivation Cz-Fz to reduce influences from basal brain sources.

Silver/silver chloride electrodes were placed and electrode impedance was always less than 5 kOHM. The stimuli were presented pseudorandomly via earphones at the following rates: ABR 11.3/s, ACR 0.8/s. For each stimulus intensity, AEP were averaged separately. Peaks and troughs were measured by positioning a cursor. To control for vigilance (patients should be relaxed and awake) EEG was recorded on paper. An automatic amplitude guided artifact rejection was used on-line; i.e., EEG sweeps with amplitudes higher than 80 µV were rejected. Additionally, for ACR a prestimulus baseline of 100 ms as well as the option for plus-minus averaging (PMA) was included; i.e., the expected waveform for the ACR was accepted for evaluation only if PMA yielded a curve at about baseline level.

For statistical evaluation of our data we computed Spearman rank correlations and non-parametric tests for group comparisons (Wilcoxon sign rank, Mann-Whitney U).

Results

Cranial CT

For the 27 anorectics group, the mean value for number of countable cortical sulci in CT was very high ($\bar{x}=44.0$, $s=27.5$). The great variability may be related to the wide range in body weight (32–51 kg). In normal adolescents, sulci are not visible, while in anorectics after sufficient weight gain only few sulci can be seen. Cranial CT data showed a high negative correlation with body weight ($r=-0.59$, $P<0.001$), but no significant correlations with the AEP data.

For the 12 AN patients investigated twice there was a clear decrease in number of cortical sulci with weight gain ($\bar{x}$: 43 vs 10, $P<0.001$). Neither at the first nor at the second investigation was there a significant correlation of CT with AEP data. The CT data available for the second psychiatric control group did not show any countable cortical sulci. Only in two cases was the ventricular system asymmetrical and one patient showed mildly enlarged frontal horns.

AEP (Augmenting/reducing)

The chosen peak-to-peak amplitudes (ABR: wave V positive to wave V negative, i.e. Vp-Vn; ACR: N90 to P150, i.e. N_1P_2 could be determined very easily in the individual averages (Fig. 1).

Next, we computed the amplitude differences of "peak-to-peak high" (e.g., N90P150 to 70 dBHL) minus "peak-to-peak low" (e.g., N90P150 to 50 dBHL) stimulus intensity averages (Table 2). These measures showed the following retest stabilities within one session: ABR: $r=0.92$; ACR: $r=0.76$. In pilot experiments with an additional intensity of 30 dBHL it could be seen that AEP curves to this intensity were not reliable enough for our evaluation, and intensities higher than 70/75 dBHL were not tolerated by the patients. Thus, we had to concentrate on two intensities (50/55 dBHL and 70/75 dBHL) which seem to reflect reliably the dynamics of augmenting/reducing (Bruneau et al. 1985; Garreau 1985).

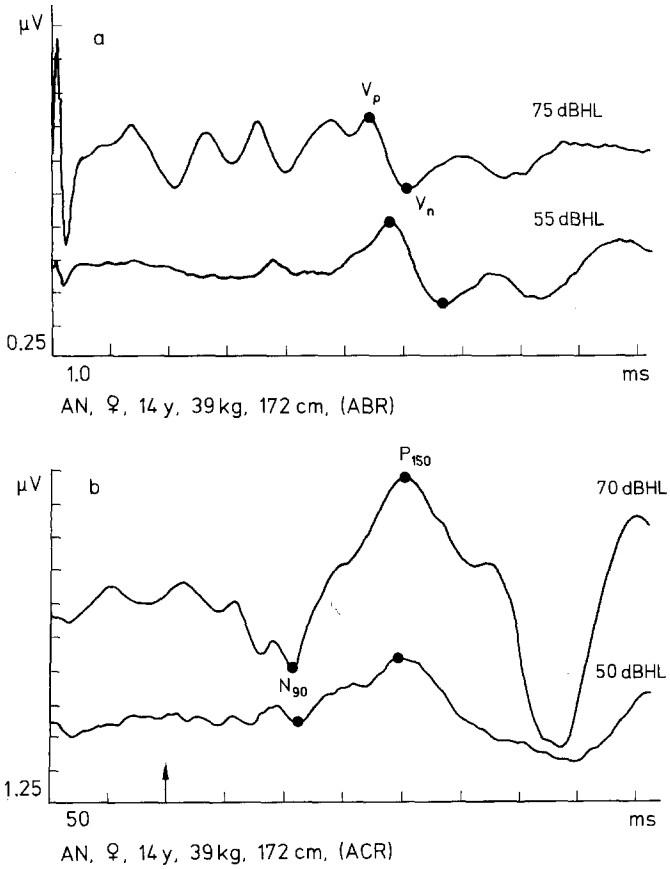

Fig. 1a, b. Auditory evoked potentials (AEP) in response to different stimulus intensities in a 14-year-old female anorectic patient with low body weight. **a** Auditory brainstem responses recorded from Cz/M1, 11.3 stimuli/s; **b** auditory cortical responses from Cz/Fz, 0.8 stimuli/s. With increasing intensity of the stimuli the amplitude of AEP decreases at the brainstem level and, in contrast, clearly increases at the cortical level

Neither the anorectics nor the controls showed significant correlations between AEP and age or IQ score. Comparison of the group of 12 anorectics (first and second examination) with the group of 12 child psychiatric controls revealed significant differences between both groups: the mean augmentation at the subcortical level was more pronounced in the control group, even after anorectics had gained weight (Vp-Vn 75–55 dBHL: 0.37 vs. 0.14 μV, $P < 0.004$). In contrast, there was no significant amplitude difference between the two groups for cortical AEP.

According to the usual definition of AEP augmenters (increase in amplitude of response as stimulus intensity increases) and AEP reducers (decreasing or plateau effect with increasing stimulus intensity), in low body weight AN Table 2 shows for amplitude differences at *short* latencies, fewer augmenters (ABR: 35% and 42%) than reducers and in contrast to this, more augmenters (ACR: 89% and 83%) than reducers at *longer* latencies. After weight gain the group of 12 adolescent anorectics demonstrated an increased number of augmenters (ABR: 64%, ACR: 100%). In the control group there were only augmenters (i.e., at subcortical as well as at cortical level of the CNS). In addition to these effects, 70% of the

Table 2. Results of an auditory evoked potential (AEP) augmenting/reducing paradigm in three groups of patients. Presented are mean values of AEP amplitude differences (high- minus low-intensity stimulus condition), percentage of augmenters (AUG) at cortical (ACR) and subcortical (ABR) brain levels, percentage of patients with divergent subcortical vs cortical AEP patterns (RED/AUG), and Spearman rank correlations between body weight and auditory evoked potentials (WEIGHT/AEP). t1, t2: first and second examinations

Group	AEP	Mean difference (μV)	AUG (%)	RED/AUG (%)	Weight/AEP	
					r	*P*
Anorexia nervosa ($n = 27$)	ACR	4.4	89	70	−0.34	***
	ABR	0.1	35		+0.30	**
Anorexia nervosa ($n = 12$)	ACR					
	t1	3.4	83		−0.18	
	t2	3.2	100		−0.44	**
	t1			83		
	t2			42		
	ABR					
	t1	0.08	42		+0.14	
	t2	0.14	64		+0.33	*
Emotionally disturbed ($n = 12$)	ACR	3.4	100	None	−0.12	
	ABR	0.37	100		+0.05	

*** $P < 0.05$, ** $P < 0.1$, * $P < 0.2$

group of 27 anorectic patients were reducers for the amplitude Vp-Vn of the ABR, but augmenters for N1P2 of the ACR. This value for subcortical vs cortical AEP dissociation was comparable with the 83% of the group of 12 anorectic adolescents at their first examination. Both values are clearly higher than the 42% recorded for the latter group at their second examination. In the control group none of the adolescents showed a dissociation between subcortical and cortical amplitude responses; all were augmenters at both CNS levels.

Finally, in both anorectic groups studied, amplitude differences (high minus low intensity peak-to-peak measures) of cortical responses tended to be higher when their body weight was lower (*r*: −0.34, −0.18, −0.44). On the other hand, amplitude differences of their subcortical responses tended to be lower when their body weight was also lower (*r*: +0.30, +0.14, +0.33). These tendencies were not seen in controls.

There were no significant correlations in any group between the amplitude values of the two different kinds of AEP applied. This is in agreement with the results of other studies (Hecox and Hogan 1982; Garreau 1985).

Discussion

The main symptom that leads to acute treatment of AN patients is their low body weight with all its conceivable complications. The low body weight in AN patients usually is accompanied by a large number of visible cortical sulci on cranial CT, which decreases with weight gain.

This finding was replicated in both groups of anorectic adolescents we investigated.

Furthermore, we could show that there was no significant correlation between cranial CT data and AEP. Thus, there should be an organic basis other than the volume changes of cortical grooves to explain our AEP results. So far, the functional relevance of cortical pseudoatrophy in AN remains unknown.

Nonetheless, we were able to demonstrate that event-related markers of electrical brain activity such as AEP, reflecting neuronal processing of external stimuli, may be influenced by metabolic changes during starving in AN patients. Our study indicated that anorectic adolescents, compared with psychiatric controls, may have difficulties in modulating auditory stimuli adequately, even after gaining weight.

This applied particularly to the subcortical level of the auditory pathways: looking at the ABR amplitudes, this was expressed by a very small augmentation or even reduction of responses to louder stimuli. Since active processing of stimuli in terms of biofeedback occurs already at the level of the brainstem (Finley 1984), one might suggest that the small increments in amplitudes recorded subcortically with increasing stimulus intensity account for a poor modulation capacity, especially in low-weight anorectic patients. Since we observed the above-mentioned amplitude effect in anorectic adolescents even after weight gain to 96% IBW, it may be due, at least partly, to ongoing pathologic eating behavior and its metabolic consequences. To clarify this topic it would be of interest to examine bulimic patients.

Even though there was a tendency for the low-weight anorectic patients to display a cortical hyper-augmenting AEP, no significant difference in ACR amplitudes was observed between anorectics and controls with emotional disturbance. Thus, our assumption of a transient frontocortical deficiency of control (i.e., less ability to modulate incoming stimuli adequately at this level of the CNS) in adolescent anorectic patients could not be supported by means of this investigation. Possibly, full topographical analysis of event-related potentials and, in parallel, recording of behavioral parameters might answer this point more clearly. So far, the PET studies in AN by Herholz et al. (1987), have shown no significant metabolic change in the frontal lobes but increased metabolic activity in the caudate nucleus when these patients had low weight. Given that damage to both areas (frontal lobes and caudate nucleus) may lead to the same sort of functional disorders, it follows that our experimental approach for examining a possible frontocortical dysfunction in anorectic patients should be pursued in the future.

Furthermore, mainly low-weight anorectic patients showed divergent patterns with respect to *cortical versus subcortical* AEP responses. The lower the body weight of the anorectic patients, the larger were the cortical AEP responses and, in contrast, the lower were the subcortical AEP amplitudes. This weight-related dissociation was also expressed in the percentages of individuals with cortical augmenting but subcortical reducing (e.g., t1: 83%, t2: 42% for the group of 12 anorectics examined twice). Thus, we may assume a functional deficit arising from some kind of uncoupling of cortical and subcortical neuronal systems, mainly during starving. A similar dissociation of amplitude responses recorded cortically and subcortically was not found in our control group of emotionally disturbed adolescents, nor was it expected in healthy subjects. The latter have been reported as augmenters for both early and later AEP (Garreau 1985; Rothenberger et al. 1987).

Our uncoupling hypothesis might be viewed in parallel with a study of Malloy (1987) on event-related potentials in obsessive-compulsive patients. He suggested in these patients a frontocortical-subcortical disconnection syndrome with a disturbance at the orbitomedial part of the frontal cortex. Since anorectic patients often show obsessive-compulsive behavior, this factor should be taken into consideration in further studies.

In conclusion, our findings (1) support and specify the clinical experience that in AN there exists a disturbance in CNS functioning which, in general, is weight/starving-related and (2) underline that patients with AN should be treated primarily to obtain normal body weight/eating behavior in good time, to avoid long-lasting disturbances – not only in stimulus processing.

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