Psychophysiological Indices of the Feeding Response in Anorexia Nervosa Patients

R. Hölzl and S. Lautenbacher

Introduction

The Role of Afferent Signals from the Gastrointestinal Tract in Food Intake Regulation

The question as to whether and how afferent signals from the gastrointestinal tract (GIT), and from the stomach in particular, regulate food intake has been a classic issue at least since Cannon and Washburn (1912). Despite later refutations of their concept of "hunger contractions" as the direct stimulus to eat, and some controversy between "centralists" and "peripheralists" in the animal literature, the role of feedback from the GIT in food intake regulation is now generally accepted (Konturek and Rösch 1976; Booth 1978). Neglecting effects of "conditioned hunger" and "appetites" for the moment, it seems that initiation of eating is governed mainly by hypothalamic centers according to humoral factors. Termination of meals, however, is under the control of a "fast feedback loop", in which afferent information from the GIT about gastric filling and nutritional composition of food ingested serves as control variable in conjunction with olfactory and gustatory stimuli arising during oral stages of ingestion. Contents absorbed from the intestines and blood concentrations of nutritional substances provide second- and third-stage feedback signals with longer time constants. They mainly determine the length of interdigestive intervals and not termination of intake.

Local control of stomach emptying and secretion by nutritional contents and other variables contributes to meal patterning and hunger regulation by influencing digestion times. Fatty food, for instance, retards stomach emptying. It enters the small intestine later and at a slower rate. This causes prolonged feedback from the small intestine and in turn a longer feeding pause. In this way retardation of emptying reduces food intake.

Although specific hunger contractions have not been found in more recent studies, more frequent and stronger stomach contractions towards the end of interdigestive intervals have consistently been observed (Konturek and Rösch 1976). It seems probably that this increased GI activity serves as an afferent signal which enhances probability of meal initiation or appetitive behavior (Hollis 1982). In this form, the core of the earlier assumption that GI motility controls food intake by determining not only termination of but also initiation of meals might be worth retaining. A self-stimulation experiment by Ball (1974) at

1 Max-Planck-Institut für Psychiatrie, Kraepelinstraße 10, D-8000 München 40

least clearly shows that afferent signals from the stomach directly influence the activity of the "hunger center" in the lateral hypothalamus: after the gastric branch of the vagus had been severed in rats trained to press a lever and reinforced by electrical stimulation of the lateral hypothalamus, self-stimulation thresholds were raised by magnitudes. This suggests conjunctive operation of hypothalamic and gastrointestinal activity in control of uptake. The particular interpretations of this and related findings are debated, however (Berger 1977; Kupfermann 1981).

In a brilliant integration of ethological and conditioning literature, Hollis (1982) drew attention to a further mechanism by which GI variables, and motility in particular, interact with central factors in eating control. The author shows convincingly that GI activity is an integrated part of appetitive behavior, and that this integration takes place by Pavlovian conditioning of this activity to food-related stimuli and/or species-specific behavior elicited by them or conditioned to them. This learning process also determines the appetitive or reinforcing value of different kinds of food. According to Hollis (1982) and the literature cited by her, the attractiveness of food depends not only on the deprivation state of the animal and stimuli directly correlated with taste, smell, etc. of food itself, but also on various stages of appetitive and consummatory behavior, including GI responses classically conditioned to environmental, internal, or response-produced stimuli.

Gastrointestinal Activity and Eating Disorders

Given the experimental evidence cited above there must be several ways in which altered GI activity could contribute to disturbed eating control in anorectic and obese patients. Stunkard and his co-workers were among the first to discuss the possible role of diminished sensitivity to afferent stimuli from the GIT in eating disorders. In an attempt to corroborate Schachter's findings that obese patients depended more on exteroceptive than on interoceptive stimuli in regulating their food intake, however, they found no evidence for diminished interoceptive sensitivity to spontaneous stomach contractions in obese compared with control subjects, despite a stronger response bias as measured by their signal detection method (Stunkard and Fox 1974). The adequacy of Stunkard's approach was later debated because of the irritating nasopharyngeal tube with which this group tried to measure stomach contractions. Tube-related stimuli may well mask more subtle interoceptive signals. In a preliminary study in our laboratory (Striegel 1978) using noninvasive surface gastrography Stunkard's results were replicated, however. Obese *and* anorectic patients were compared with controls. Differences from controls were found only with subjective hunger ratings and motility base rates and not in interoception indices. The methods and paradigms used were primitive, and the issue is by no means settled. On the contrary, work by Bruch (1973) and Garfinkel et al. (1978) (Garfinkel and Garner, this volume) still supports the notion of altered interoception in eating disorders, but the precise mechanism remains to be investigated.

The measurements of fasting activity and its perception may not be relevant to the understanding of dysregulation of food intake at all (Crisp 1965). At present, therefore, investigation of the *feeding response* in anorectic patients at the physiological, behavioral, and subjective levels seems more promising. Little is known about the range of variations in GI and other autonomic changes to a meal requirement in these patients, how these changes are reflected on the subjective level, and whether this pattern undergoes systematic alterations during weight gain procedures. Only the background of a more thorough knowledge of these responses would make it possible to interpret perceptional differences. Differences in base rates or the contribution of conditioned feeding responses could then be separated from alterations in interoception proper.

Dubois et al. (1979) seem to have been the first to measure gastric emptying rates in anorectic patients with sufficient precision. Their method ("fractional emptying") simultaneously measures gastric secretion and takes its contribution to stomach contents into account. The authors found retarded emptying and changes in acid output in their patients. On the assumption that this was a significant factor in maintenance of the disorder if not in its etiology, Saleh and Lebwohl (1980) attempted acceleration of gastric transit in anorectics by oral administration of metoclopramide and found apparent improvement in some of their patients. Although Dubois et al. (1981) could not generally support these results in a similar study using bethanechol, the importance of gastric function in maintaining dieting seems to be established (cf. Dubois et al., this volume).

Whether the results on emptying also extend to motility records remains to be tested. An earlier investigation by Crisp (1965) revealed no differences in motility compared with controls, but the author used an intragastric tube in fasting subjects. Nothing can be said about postprandial motility and possible inhibitory side-effects of the tube. They may prevent detection of differences from controls by reducing base rates of contractions in both groups to near zero level, thus giving rise to a "floor effect". In fact, this is exactly what was found in the studies cited. Therefore it would be advisable to investigate this question by noninvasive techniques such as surface gastrography. Reliable and valid techniques for certain periodic motility components are now available.

The present chapter reports preliminary data on the measurement of the feeding response in anorectic patients by means of a variant of surface gastrography reported elsewhere (Hölzl 1983; Müller et al. 1983). The method produces reliable and valid indices of specified periodic components of electromotor activity of the stomach without the adverse effects of intragastric pressure probes. In addition it is not negatively affected by nonfluid gastric contents. It therefore allows undisturbed recording before, during, and after a realistic test meal, in contrast to Crisp's fasting records or Dubois' method, for which a test drink of water was necessary.

Changes in motility parameters after a test meal have been described by several researchers. Those were related to emptying in healthy subjects and certain clinical groups other than anorectics. Usually a typical biphasic change in frequency of periodic contractions (Fig. 4) and a postprandial increase in

amplitude is seen (e.g., Kohatsu 1970; Konturek and Rösch 1976; Smout 1980). From Dubois' results on emptying one might conclude that the time course of motility changes after a meal will also be delayed. This would be related to an increased and prolonged subjective feeling of "fullness" if visceral perception remained undisturbed. Frequency and amplitude of postprandial contractions, however, are not correlated with emptying rate in a simple linear fashion. Pyloric resistance, regularity of pressure waves, and antropyloric coordination also influence emptying. Sometimes "functional stenosis" has been connected with retarded emptying in anorexia nervosa. Therefore more complicated alterations of motility patterns might also exist in these patients.

If retardation of the feeding response as measured by motility records was mainly an adaptation to chronic dieting but had no primary etiological significance for anorexia the delay would systematically decrease with weight gain during behavioral treatment. On the other hand, if alterations of the feeding response played a role in initial pathogenesis it would be distinguishable from simple adaptations of the GIT to malnutrition. And lastly, the degree of recovery of a normal feeding response through treatment would be inversely related to risk of anorectic relapses. If these relationships could be shown to hold for the feeding response indices chosen, they could be used not only for diagnostic and research purposes but also to guide therapy and reduce relapses by timely booster treatments. The practical implications of this type of psychophysiological assessment are obvious.

To distinguish direct GI components of the feeding response from autonomic correlates of emotional responses to the meal requirement which in these patients presumably is aversive, recording of other autonomic variables such as heart rate and ratings of task-related subjective states is mandatory. The recording of cardiovascular components of the feeding response has further advantages. Evoked heart rate responses to a meal were earlier found to be correlated with its motivational significance. Eisman (1966), for instance, showed that only thirsty rats showed phasic heart rate increases to the presentation of water, while rats with free access to water did not change their heart rates. Similar results were reported in a comparison of hungry and satiated human subjects. Evaluation of evoked heart rate responses to a test meal in anorectics might thus give important additional and "objective" information on the motivational state. Furthermore, a particular cardiorespiratory parameter, the degree of cardiac-respiratory coupling, has been shown to be a useful and selective index of parasympathetic heart control or "vagotonus" (Hölzl et al. 1983). This index will be used as a measure of autonomic activation by the feeding test in the patient.

Method

To test some of the hypotheses listed above, and the question of retarded feeding responses in anorexia patients in particular, so far 14 patients taking part in the MPIP Anorexia Project, 12 females and two males, and 10 healthy controls have been studied. For six patients and nine controls

an ininterrupted series of three test sessions at 2-week intervals is available at present. Control subjects belonged to two groups: K1 consisted of five nonanorectic persons at least 15% below normal in weight (4 females, 1 male). This group was chosen to control for possible effects of low body weight and corresponding changes in body build on measures of motility. Such relations had been found in previous studies (Skambraks 1981). K2 contained five healthy subjects volunteering in a weight reduction program (Pirke et al., to be published). K2 was included in the experimental design to compare anorectic feeding responses with feeding responses in dieting subjects according to the rationale discussed in the *Introduction*. Weight ranges at the start of the study were 48.9%–77.0% of normal weight for the patient group, 70.0%–85.9% for K1, and 80%–92.6% for K2. For inclusion in group K2 subjects were required to have body weight within 5% of their ideal

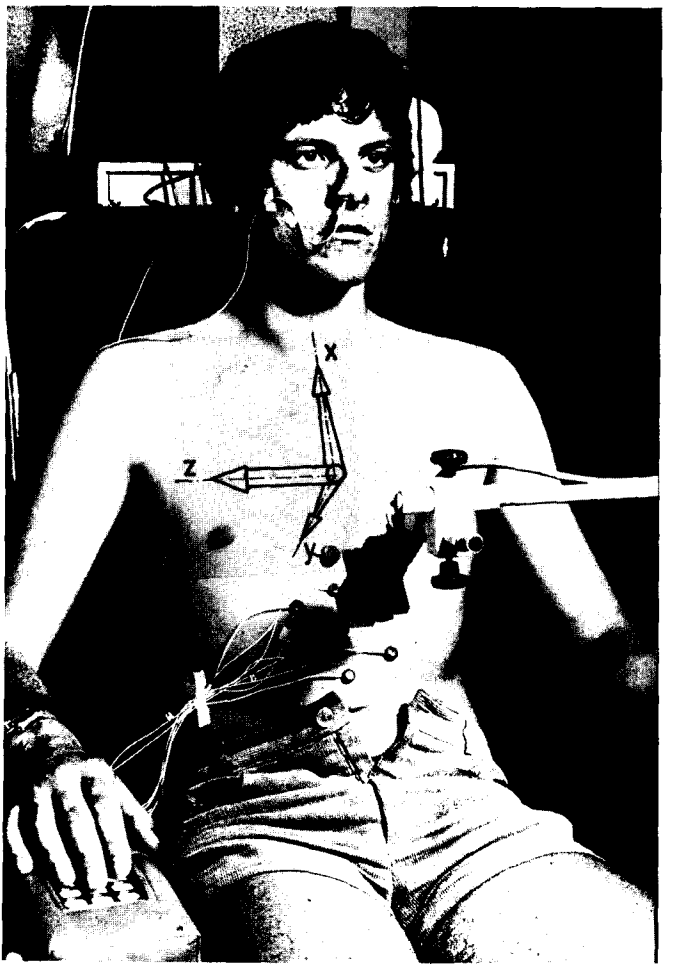

Fig. 1. Experimental subject for conjoint gastrography in situ. A Develco three-axes fluxgate magnetometer is placed over the epigastric region, orthogonal to the abdominal plane. Axes are indicated by *arrows*. Beneath the magnetometer head the hexagonal electrode configuration for bipolar electrogastrograms can be seen. In addition ground and ECG electrodes are placed on the sternum but only partially shown. The probe in the nose contains a thermistor to measure respiration. Technical details are described in Müller et al. (1983), from which this illustration is reproduced with kind permission of Plenum, New York

weight (= normal weight −15%) at the initial sessions. Subjects in this group were paid to reduce this initial weight by 10% within 6 weeks. The average ages of groups were not matched exactly, patients being somewhat younger than controls (21 vs 25); ranges were comparable.

All subjects had fasted overnight since 10 p.m. the previous evening before testing. Sessions started invariably at 7.30 a.m. They consisted of six epochs each 10 min in length and an additional preliminary adaptation period of the same duration. The six recording periods also served as analysis epochs in biosignal evaluation (see below). At the beginning of the second recording period a test meal of 250 g yoghurt was given, which was followed by 40 min of postprandial recording. Subjective reactions to the meal were evaluated by five-point ratings of "fullness", "hunger", and general "tension" at the end of each 10-min interval.

Gastric motility was measured by "conjoint spectral gastrography" (CSG) (Müller et al. 1983). This method consists of simultaneous multichannel recordings of six channels of bipolar and one channel of unipolar surface electrogastrograms (EGGs) and of three channels of magnetogastrograms (MGGs). The latter are obtained with a three-axes fluxgate magnetometer. It senses stomach contractions via magnetic field changes induced by a small teflon-coated magnet which the subject swallows before the recording. EGGs and MGGs are jointly subjected to Fourier analysis. The

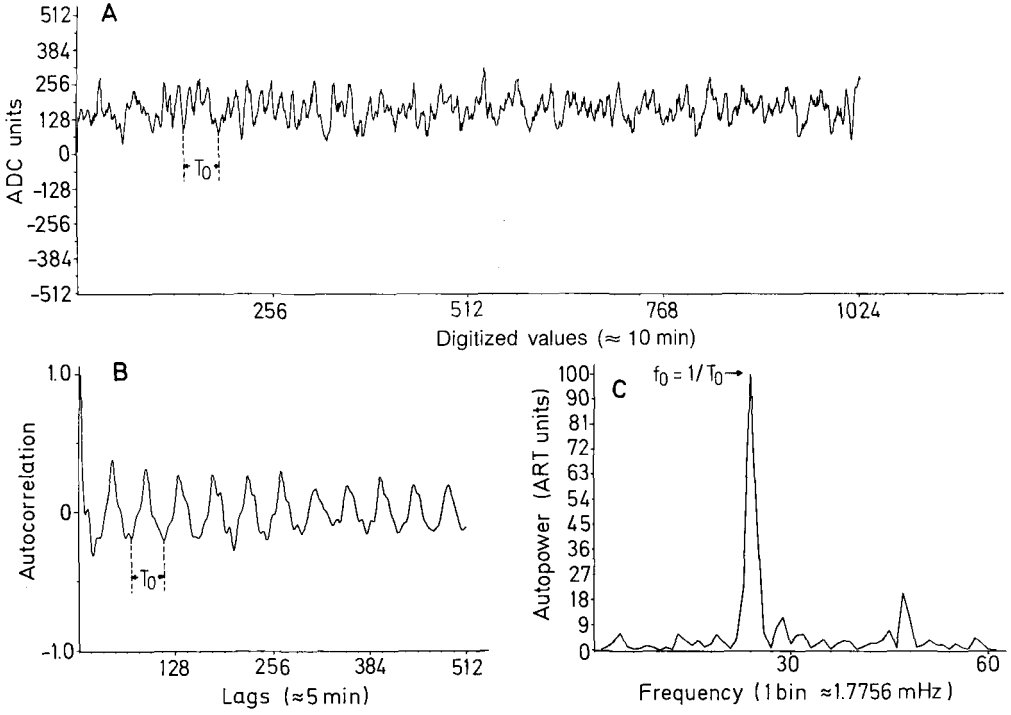

Fig. 2A–C. Sample of surface electrogastrogram, its autocorrelation function, and corresponding power density spectrum. **A** Original recording with respiratory artefact and noise as digitized by the A-D converter (512 ADC units = 500 μV). Sampling intervals is 550 ms; recording period = 1,024 samples or approx. 10 min; T_0 = slow wave period = approx. 20 s. **B** Autocorrelation function (ACF) of the data in record **A** with lags extending up to 5 min. The ACF accentuates the periodic slow wave component and reduces noise. Again T_0 = slow wave period. **C** The auto-power spectrum of record **A** shows a pronounced peak at the frequency of the slow wave component, $f_0 = 1/T_0$ = 2.6 cpm, a smaller peak at the first "harmonic" ($2f_0$), and only minor noise energy at other frequencies. The absolute or relative height of the slow wave peak gives an estimate of slow wave intensity. See also Müller et al. (1983) for technical details

analysis produces reliable and valid measures of frequency and amplitude of specified periodic components of gastric smooth muscle activity for each 10-min analysis epoch. Particularly two frequency bands, the basal gastric rhythm (BGR) at 3 cpm and the ultraslow gastric rhythm (UGR) at 1 cpm, are evaluated in this way. Changes of frequency and amplitude of these rhythms during and after meals are interpreted as the gastrographic feeding response.

A detailed description of the method, its rationale, and relevant validation data have been published elsewhere (Müller et al. 1983). Therefore a short illustration of the method will suffice here. Figure 1 shows an experimental subject with the positions of abdominal electrodes for hexagonal bipolar EGG recordings. The magnetometer is positioned orthogonal to the abdominal plane just over the middle electrode. Magnetic axes are indicated by arrows. The thermistor probe in the nose senses respiratory air flow. Sternal electrodes are used to record the ECG from which heart rate is calculated. Figure 2 shows a sample of a typical gastrographic recording together with its autocorrelation function and corresponding power spectrum. The pronounced peak in the spectrum corresponds to the BGR at 3 cpm, which is the clear periodicity in the raw record. The periodicity is even more pronounced in the autocorrelation function. The frequency and amplitude of these peaks are evaluated for each 10-min epoch and enter analysis of the feeding response.

In addition to gastrographic changes, cardiac and respiratory activity were measured during feeding test. Signal parameters entering statistical analysis for each 10-min epoch were average heart rate, respiratory frequency and amplitude, and Porges' index of cardiorespiratory coupling, i.e., the "weighted coherence" (C_w) between heart rate and respiratory air flow (Hölzl et al. 1983; Porges et al. 1980).

Psychophysiological variables and subjective ratings were analysed as individual and group reaction patterns over number of epoch (1–6) as the independent variable. Raw values and absolute and percentage cumulative feeding responses were considered. The relative or percentage cumulative feeding response is of particular value in comparing the time course of feeding responses in anorectics and controls without confusion caused by differences in absolute reaction levels. Group data analyses are therefore mostly based on relative cumulative records (further explanation below).

Results

Individual Response Patterns

Because little is known about the variation range of postprandial motility changes as measured by gastrography, individual response patterns were studied on a descriptive level first. Typical examples of this descriptive analysis of a) amplitude (or root-power) spectra changes during the feeding test; b) BGR frequency patterns; c) BGR amplitude responses; d) cardiorespiratory effects; and e) subjective ratings are given below.

Figure 3 illustrates the type of change in gastrographic spectra to be observed after a test meal of yoghurt in an anorectic patient and a comparable control subject more than 20% below normal body weight. Each spectrum represents the periodic content of 10 min of gastrographic recordings, and has characteristic intensity maxima at the frequency of the BGR component (approx. 3 cpm). Their height was normalized to make the positions of relative maxima in time more obvious. There are also pronounced peaks in the UGR range (1 cpm, to the left of the BGR peaks). They will not be analysed here. In the present example a clear delay of the BGR maximum by two epochs or about 20 min in the anorectic patient compared with the control was found. Systematic group data on this delay will be presented below.

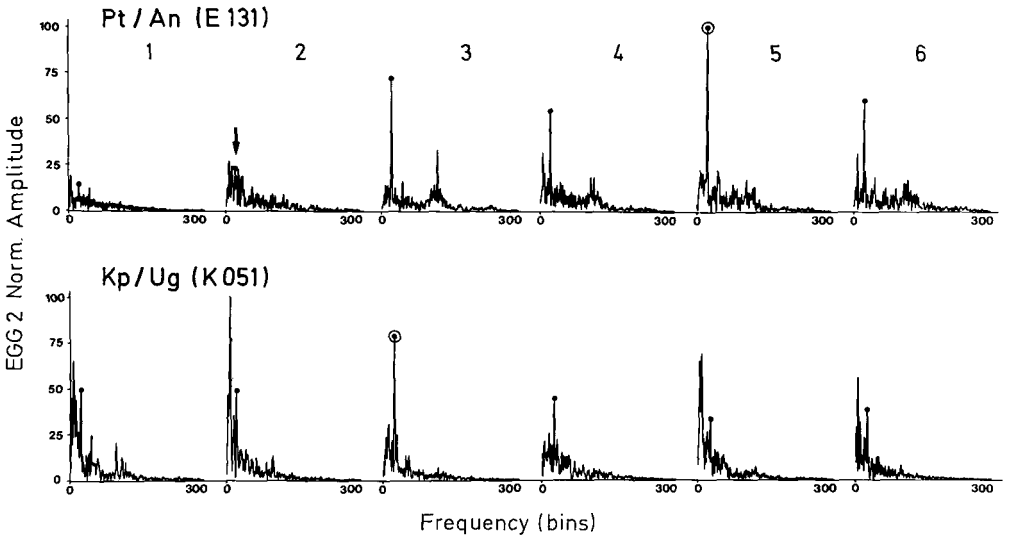

Fig. 3. Gastrographic "feeding response". Amplitude spectra of surface gastrograms show systematic changes in subsequent 10-min epochs of measurement during the feeding test. Spectrum 1 corresponds to preprandial, spectra 3 through 6 to postprandial periods. The test meal is ingested at the beginning of the second 10-min period. Examples show the feeding responses in session 1 of a control subject from group K1 *(lower half, Kp/Ug)* and a patient *(upper half, Pt/An)*. Amplitude peaks are normalized relative to the maximal peak within the individual feeding test. Frequencies are displayed as bins: 1 bin = 1.78 mHz. BGR components are marked with *dots* (●), maximum BGR peaks with *circles* (○). Current body weights were at 61% of normal for the patient and 70% for the nonanorectic control. The maximum postprandial rise of BGR amplitude is delayed in the patient by two epochs or approx. 20 min despite the relatively small difference in body weight

While amplitude changes of certain gastrographic rhythms can easily be seen in this type of data representation, frequency patterns are more difficult to detect. They are displayed separately in Fig. 4. Systematic biphasic changes of BGR frequencies are observed consistently by way of EGGs and of MGGs exemplifying the reliable detection of significant periodic components by CSG methods. The typical drop in BGR frequency during the meal and the subsequent rise over baseline shown in Fig. 4 is in good agreement with gastroenterological literature on direct recordings from implanted electrodes (Kohatsu 1970; Smout 1980). However, this is more difficult to show in anorectic subjects, because the detection logic of CSG depends on MGGs, which are frequently noisy. At present reproducible data on postprandial frequency changes of gastric rhythms are therefore difficult to obtain. Refinement of signal analysis will probably solve this problem. At this stage more reliable differences between patients and controls are seen in the postprandial BGR *amplitudes*. Figure 5 illustrates a biphasic pattern of BGR amplitude changes during feeding test in the control subject. The feeding response of the anorectic patient is different. It shows a sluggish onset, prolonged response, and late maxima in postprandial BGR amplitudes. In addition, the drop in amplitude during eating

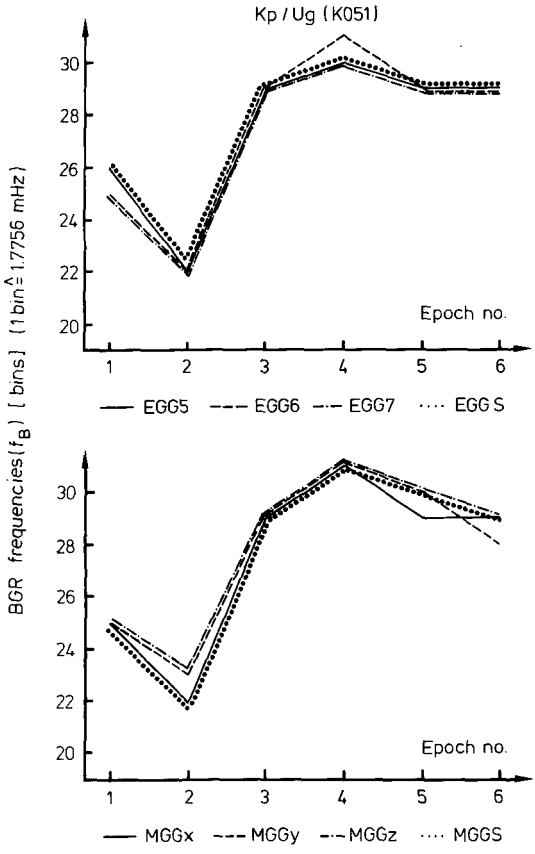

Fig. 4. Frequency changes of BGR components during feeding test. Data are from the same control subject as in Fig. 3. BGR frequencies of two bipolar EGGs (EGG 5 and 6) from the hexagon in Fig. 1, one unipolar EGG (EGG 7, leg reference), and a summated EGG (see Müller et al. 1983) are plotted in the *upper half* of the figure. The *lower half* shows BGR frequencies of MGGs. x, y, and z are the three axes in space, as explained in Fig. 1, MGGS is a summated MGG score

is not seen in the patient. But interindividual variability is still high, and other data representations will be used in later sections.

A comparison of subjective ratings with the gastrographic responses shows that common expectations about psychological covariates of delayed feeding responses may be wrong. As Fig. 6 demonstrates, subjective ratings of fullness are low throughout the session in the anorectic patient, whereas the control reports fullness after relatively rapid ingestion of 250 g yoghurt within first 3 min of the second epoch. This is really the opposite of what would intuitively be expected and of what gastrographic feeding responses would suggest. Hunger ratings shed some light on this paradox perhaps: the anorectic patient shows a surprisingly high hunger rating at the beginning of the session, which goes down after the test meal. This is not the case in the control subject, who shows constant low hunger throughout the session. A possible explanation would suggest that the patient's rating reflects what she considers socially desirable rather than her actual hunger or fullness. But more systematic data on larger groups are needed to corroborate these anecdotal findings.

The difference in tension ratings between patient and control is also interesting (Fig. 6). The control subject reports moderate activation, which only

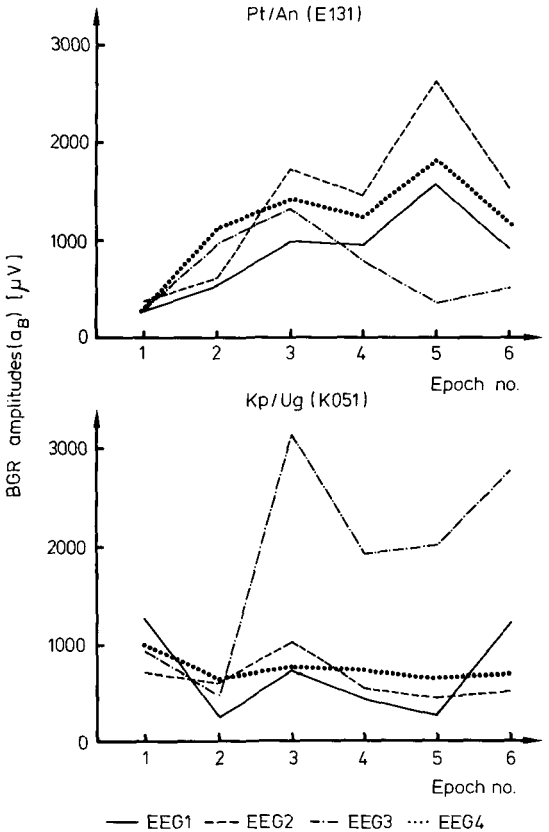

Fig. 5. BGR amplitude changes during feeding test. BGR peak heights from the same subjects as in Fig. 3 are shown for consecutive 10-min periods. Four bipolar EGGs are shown. Biphasic amplitude responses are observed in the control subject. The anorectic patient exhibits more or less monotonic increases in BGR amplitudes with sluggish onset and no inhibition during the meal

increases briefly during eating requirements. In contrast, the anorectic patient is tenser initially and only calms down later. Cardiac-respiratory responses parallel this pattern (Fig. 7). Respiratory frequency in the control subject shows only a phasic drop during the eating period. The same parameter drops monotonically in the patient. Average heart rate and cardiac-respiratory coupling, i.e., "vagotonus" measured by the C_w value, change phasically in both subjects. Despite subjective tenseness ratings suggesting no particular activation during the eating period a specific emotional effect of the eating requirement seems to be uncovered by the much larger drop in C_w in the patient. If this can be reproduced on a larger data base evaluation of parasympathetic heart control via C_w estimation may prove a valuable tool in elaborating the autonomic response pattern of anorectic patients to eating situations. Estimation of respiratory frequency in the eating period is unreliable, however, so that some precautions have to be taken in the future.

The illustrations of individual response patterns in the feeding test presented so far show several features worth studying in larger numbers and over longer intervals. Instability of gastrographic feeding responses over subjects, however,

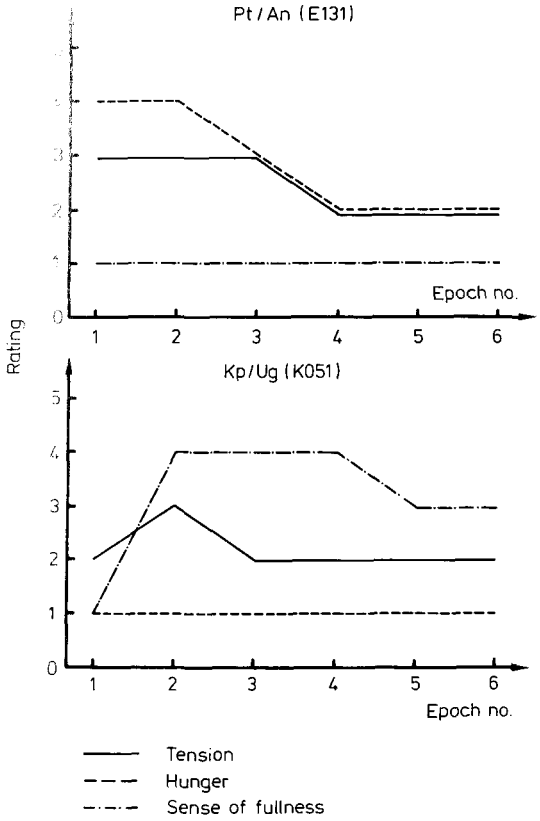

Fig. 6. Subjective ratings of hunger, tension, and fullness during the feeding test. Data from the same subjects as in previous figures

demands further developments in defining suitable indices of the feeding responses. One source of interindividual variation is large differences in initial values of physiologic variables which confound differences in response size. In group analyses *relative cumulative response graphs* are used below to account for initial level differences in physiological variables and thereby accentuate differences in the time course of the feeding response rather than absolute differences. For this purpose the cumulative values of physiologic parameters such as BGR amplitudes in each 10-min period are expressed as percentages of the final cumulative level of responses. Figure 8 exemplifies this kind of data representation for the patient and the control subject whose individual autonomic and subjective responses patterns were described above. The electrogastrographic curve shows changes in the electrical activity and the magnetogastrographic curve shows the contractile activity of gastric smooth muscles. The characteristic difference in the time course of the feeding response measured by cumulative BGR amplitudes is much enhanced, and the expected delay in gastrographic response to the meal is clearly demonstrated. Whether this holds for the group data is investigated in the next section.

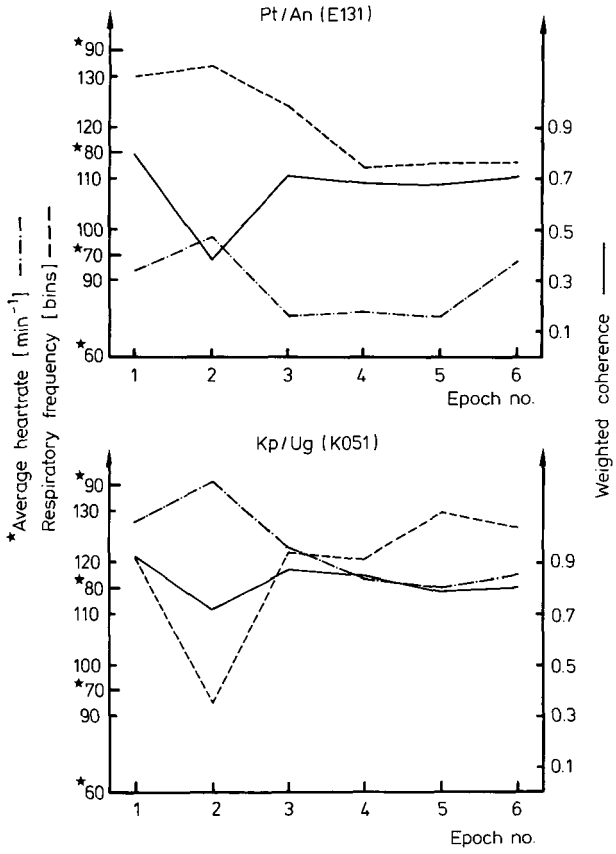

Fig. 7. Averaged heart rates, respiratory frequency, and cardiac-respiratory coupling during feeding test. Data stem from the same subjects as in previous figures. Analysis periods are 10 min as before. *Bold ordinates* on the *left* refer to heart rate, *fainter ordinates* to respiration frequency. Ordinates on the *right* indicate the dimensionless measure of cardiac-respiratory coupling, i.e., weighted coherence values, C_w, varying from 0 to 1 (explanation in text)

Group Differences in BGR Amplitude Changes to the Test Meal

Comparison of the *averaged cumulative response graphs* in the first session of anorectic patients and K1 and K2 controls combined reveals characteristic initial differences in the speed of feeding responses (Fig. 9). Cumulative response graphs express this in differences of slopes: cumulative feeding curves of control groups rise much faster and with negative acceleration, whereas the curves for anorectic patients start more slowly and have positive acceleration. As expected, the two control groups do not differ in the first session, because K2 subjects have only just started dieting at this point. K1 and K2 were therefore pooled for this graph and statistical testing. Percentages of total cumulative feeding response reached at the end of 3rd and 4th 10-min periods (1st and 2nd postprandial period) are used in the statistical testing as indices of the "time constants" of

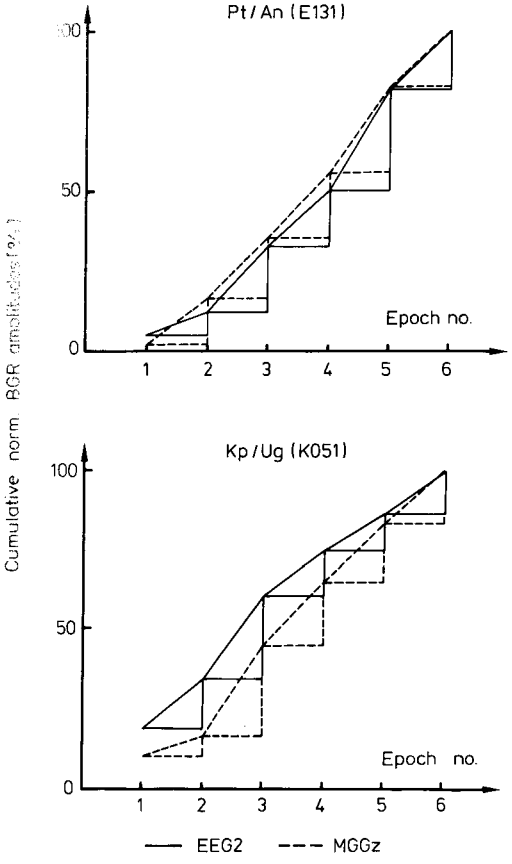

Fig. 8. Normalized cumulative feeding response. To enhance differences in the time course of BGR amplitude during the feeding test normalized cumulative plots are used. One EGG and one MGG are shown for illustration. Data stem from the same subjects as in previous figures. BGR amplitude values are cumulated over consecutive measurement periods and expressed as percentages of the final value of the cumulative series. Data are drawn in as polygon as well as step functions. The latter facilitates comparison of individual contributions of consecutive 10-min intervals

feeding responses. Group differences in these parameters are significant at the 5% level for some gastrographic channels but not for all (*t*-tests; see Table 1).

In addition to these initial differences in gastrointestinal effects of the test meal, the pattern of differences shows systematic changes over sessions which parallel weight gain in anorectics, weigth loss in dieting subjects, and constant weight in K1 subjects. Retardation of anorectic feeding responses gradually diminishes with weight gains, which range from −2.0% to 8.1% of normal weight from the 1st to the 2nd, and from 1.0% to 24.4% from the 2nd to the 3rd session. The simple explanation of the retardation as an adaptation to prolonged dieting is made improbable, however, by the feeding pattern in K2, i.e., nonanorectic subjects voluntarily reducing weight for a money fee. Weight reductions in this group range from −3.7% to −7.0% of normal weight from the 1st to the 2nd, and from −2.0% to −3.8% from the 2nd to the 3rd session. Instead of retardation of gastrographic feeding response, cumulative graphs of 3rd sessions after at least 6 weeks of low calory intake (see Pirke et al., to be published) indicate accelerated postprandial reaction patterns (Fig. 10). Because of the small numbers in this study differences do not reach conventional

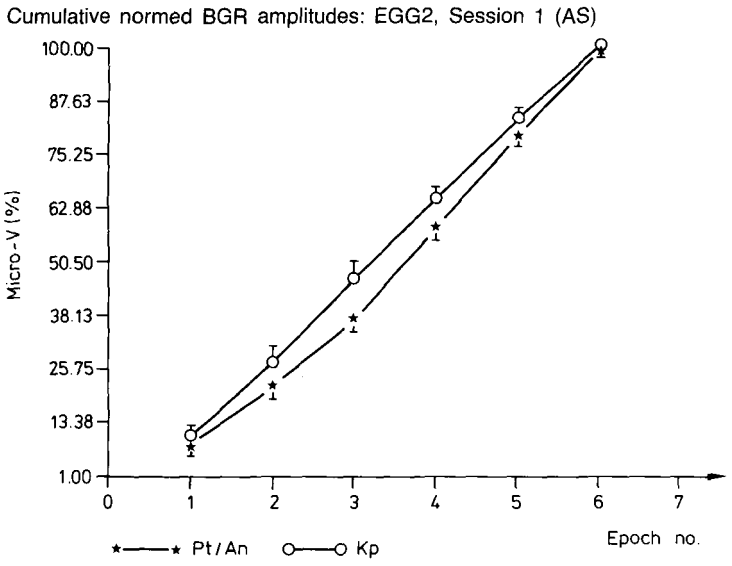

Fig. 9. Average group cumulative feeding responses in first session for anorectic patients and controls. All patients (PT/AN, $n = 14$) and control subjects from K1 and K2 (KP, $n = 10$) are included. Differences in the 3rd and 4th intervals are significant (t, 5%). *Vertical bars* indicate standard error of mean. See text and previous figures

Table 1. Group means, standard deviations, and significance testing of relative index of feeding response speed during first session (cumulative percentage of BGR amplitude, EGG2; see text)

Measurement period	Patients ($n = 14$)	K1: Thin controls ($n = 5$)	K2: Diet controls ($n = 5$)	K1 and K2 ($n = 10$)
1	7.86 (4.24)	12.80 (5.54)	6.20 (1.92)	9.50 (5.23)
2	21.36 (8.60)	34.20 (8.93)	19.60 (6.69)	26.90 (10.70)
3	37.00 (8.17)	50.80** (9.04)	41.60 (11.22)	46.20* (10.76)
4	58.21 (7.80)	65.60^{+} (8.08)	63.60 (6.88)	64.60* (7.15)
5	79.07 (4.95)	84.40 (4.77)	81.80 (4.32)	83.10 (4.51)

Statistically significant differences in control subjects as against anorectic patients: $^{+}$ $P < 0.10$; * $P < 0.05$; ** $P < 0.01$ (t-test)

significance levels in the 3rd sessions, and further experiments will be necessary. Group differences are better accentuated in the time constant indices defined above. But group differences are significant at the 5% level only for the first session (t-tests; see Table 2 and Fig. 11).

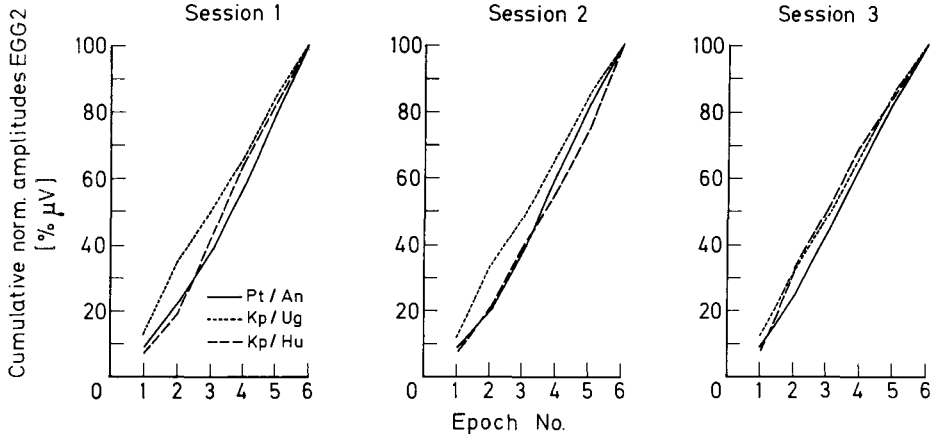

Fig. 10. Changes in cumulative group responses over three sessions. *PT/AN,* patients; *KP/UG,* K1; *KP/HU,* K2. See text and previous figures for further explanation

Table 2. Group means, standard deviations, and significance testing of relative index of feeding response speed over three sessions (cumulative percentage of BGR amplitude, EGG2; see text)

Session	Patients (n = 6)	K1: Thin controls (n = 5)	K2: Diet controls (n = 4)	K1 and K2 (n = 9)
(a) 1st Postprandial interval				
1	38.17 (6.52)	50.80* (9.04)	42.00 (12.91)	46.89 (11.17)
2	38.17 (14.08)	47.40 (12.66)	39.00 (7.75)	43.67 (11.06)
3	42.83 (10.98)	48.00 (14.61)	48.75 (15.33)	48.33 (48.33)
(b) 2nd Postprandial interval				
1	57.33 (6.02)	65.60** (8.08)	63.75 (7.93)	64.78 (7.56)
2	61.00 (11.24)	66.00 (10.70)	55.75 (9.03)	61.44 (10.82)
3	63.33 (7.37)	66.20 (9.26)	69.00 (9.93)	67.44 (9.06)

Statistically significant differences in control subjects as against anorectic patients: * $P < 0.05$; ** $P < 0.10$ (t-test)

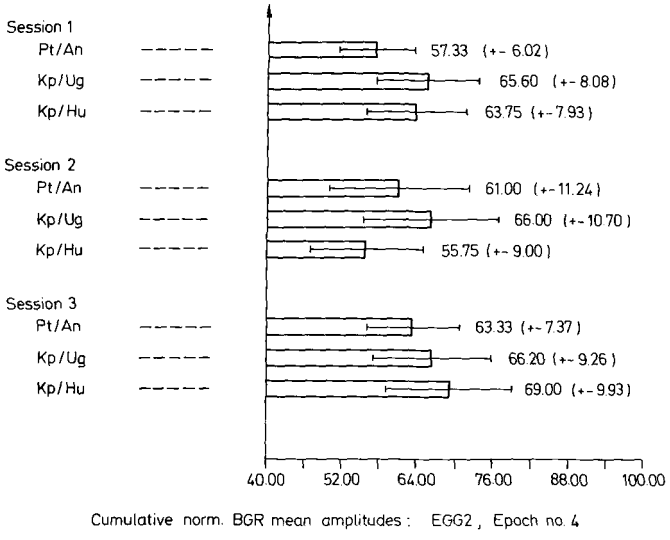

Fig. 11. Changes in "time constants" of group feeding responses over three sessions. *Bars* indicate group mean with standard deviation of raw scores. *PT/AN,* patients; *KP/UG,* K1; *KP/HU,* K2. Explanation in text

Discussion

Data on gastrographic feeding responses in anorexia nervosa patients presented in this report apparently confirm Dubois' results on retarded emptying in this group. It has to be kept in mind, however, that his method of fractional emptying with an intragastric tube directly measures *emptying,* albeit of an unrealistic "meal", i.e., plain water. How serious (inhibitory?) effects of the intragastric tube on motility could influence measurements of emptying is not clear at the moment, but this has to be considered when data are compared. The method used here measures postprandial changes in *motility* by indirect surface techniques, and with a more realistic test meal. That these studies seem to replicate each other at least partially is significant. But the differences also deserve discussion.

Motility of GIT segments and the stomach in particular is not related to emptying rates in a straightforward manner. It is only one of several factors contributing to net transit rate. Except for Dubois' reports this was sometimes not considered in earlier publications (e.g., Crisp 1965, 1967). The present data therefore have to be interpreted with caution. On the other hand, emptying of water may not be a valid indicator of stomach emptying times for non-zero-calorie meals and meals of different of other consistencies. Furthermore, motility is an important variable of GI function in its own right. With the method used the study of visceral perception in anorexia is easily possible under realistic conditions.

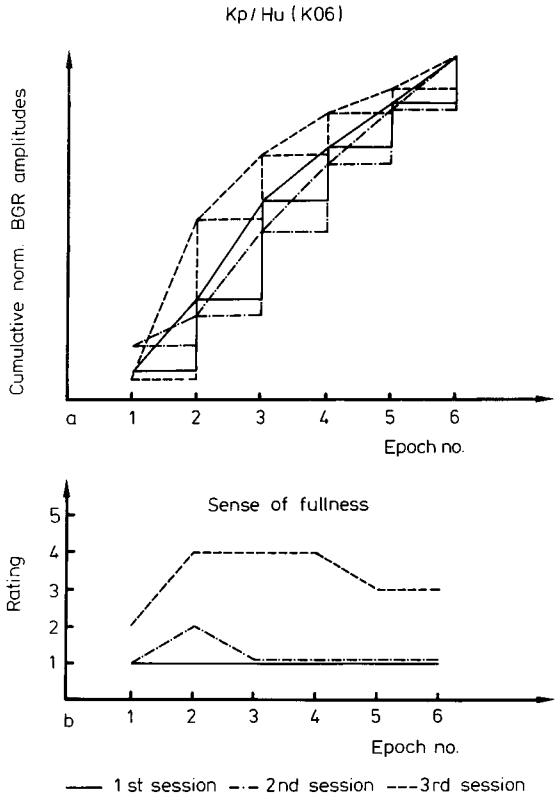

Fig. 12. Individual pattern of changes in feeding response and subjective ratings over three sessions in a dieting subject. Data from a dieting control subject (group K2, K/Hu) are displayed similar to previous figures. Weight at 1st session 93%, at 2nd session 89%, and at 3rd session 85% of normal weight. *Upper half:* Cumulative BGR amplitudes as previously explained. *Lower half:* Subjective five-point ratings of fullness. Further explanation in text

The fact that the retardation of the feeding response is diminished during later stages of treatment might suggest that it is a secondary effect of malnutrition. However, dieting volunteers do not show this retardation. On the contrary, their postprandial motility pattern is accelerated. Thus delayed motility increases after ingestion of a test meal seem to be a genuine feature of the anorectic feeding pattern. The covariation of subjective variables gives important hints for the interpretation of this feature. Figure 12 shows individual cumulative feeding response curves of a subject from group K2 together with subjective ratings of fullness from the 1st to the 3rd session. There is some similarity with the group results in that a clear acceleration of the feeding response is seen after 6 weeks of dieting. But subjective ratings show a pattern which one would expect from an anorectic patient. Individual data on subjective ratings in anorectic patients, on the other hand, do not show this plausible effect. It appears, then, that dieting control subjects with *accelerated* or back-to-normal feeding responses feel "stuffed" after a test meal of reasonable size, while anorectic patients do *not* report subjective fullness with *retarded* feeding responses! This could be just another consequence of disturbed interoception in this group, which has been postulated by several investigators in the field (cf. Garfinkel, this volume). Group analysis of subjective data on our feeding tests

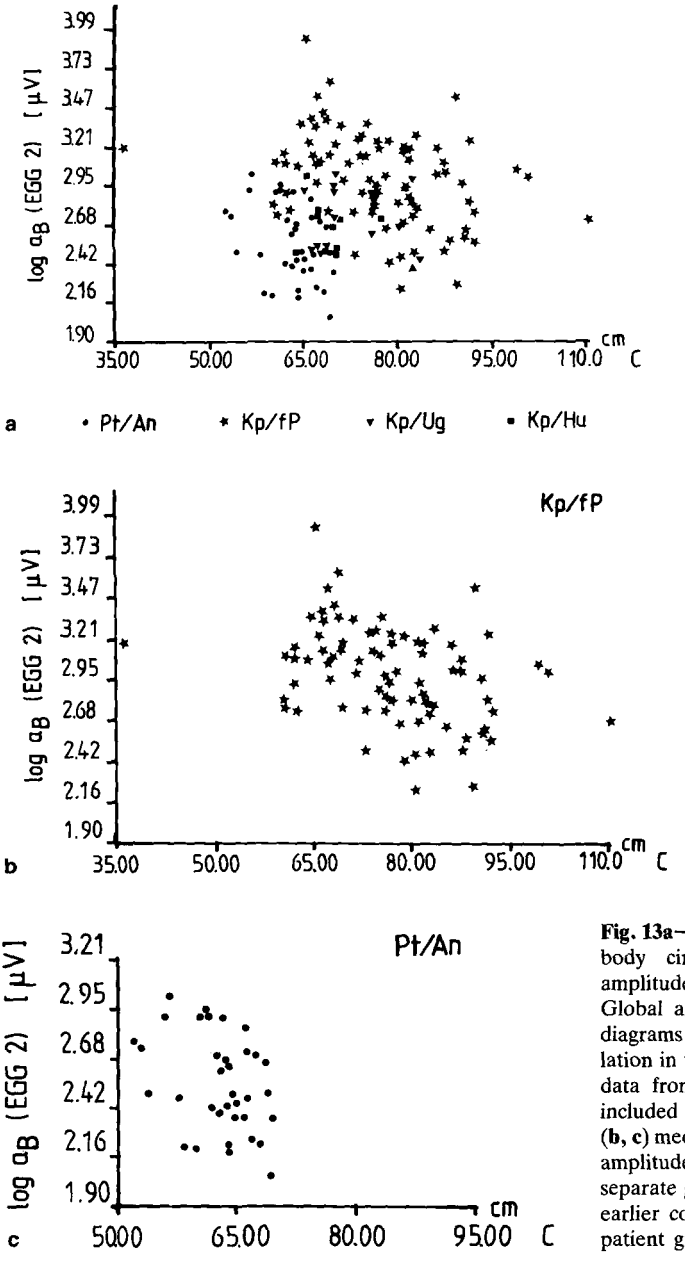

Fig. 13a–c. Correlations between body circumference and BGR amplitudes as measured by CSG. Global and group-specific scatter diagrams exemplify (**a**) zero-correlation in the total sample in which data from an earlier study were included (Skambraks 1981), and (**b, c**) medium correlations of EGG amplitudes and body measure in separate groups, i.e., −0.45 in the earlier controls and −0.37 in the patient group

should clarify this question. Because of the limited number of cases included in this preliminary report these data were not analysed here.

Whether a retarded feeding response of motility and emptying variables has major etiological significance or even relevance for risk of relapse will have to await appropriate follow-up studies. The same is true for a possible therapeutic

implication of this finding: it is feasible to include retraining of normal feeding response patterns by psychophysiological techniques analogous to pharmacological attempts to speed up emptying (see *Introduction*). This might enhance effects of behavioral treatments and/or increase their persistence.

A possible artefact contaminating surface gastrographic recordings of the feeding response must be discussed at this point. In earlier studies negative correlations of EGG amplitudes and body circumference as well as thickness of abdominal fat layer were found. The correlations are only of medium height (-0.30 to -0.60), but high enough to account for some of the amplitude variance. With extremely thin abdominal walls in anorectic patients this may be an important variable, especially in repeated measurement designs with body measurements changing during weight gain. In the present study body measurements, in particular circumference and fat layer, were taken before each session. The scatter diagrams in Fig. 13 show part of the results of this correlational analysis. On the whole there seems to be no sizable dependency of gastrographic amplitudes on body measurements. But correlations within groups are significant if low. This is especially true for the anorectic patients and may influence changes in absolute response measurements by changes in body parameters during therapy. The use of relative and not absolute feeding curves such as our normalized response characteristics therefore seems advisable. In this way changes in the initial level of gastrographic amplitudes will not contaminate changes in response speed.

Confusion of primary gastrographic feeding response by vegetative correlates of emotional consequences of the meal requirements has not yet been considered at this stage. Analysis of the corresponding cardiac-respiratory group results will be reported elsewhere. A number of other problems must also be solved before one can generally recommend surface gastrography for measurement of feeding response in patients with eating disorders. While the reliability of the feeding scores may be sufficient to show significant differences even in small group designs this seems to be not enough for individual diagnostic use. Unreliability of MGGs with fasting subjects in whom frequent magnet loss into the duodenum in early phases of the feeding test can be observed presents further problems. In addition, it is difficult to relate our motility scores to emptying. A possible solution to both problems may be the use of a variant of the magnetogastrographic technique originally introduced by Frei et al. (1970). Instead of a small magnet, magnesium ferrite suspension is used as a magnetic agent. Any change in ferrite concentration during gastric emptying is measured by a susceptibility probe and used as an index of emptying. In a pilot study (cited in Hölzl 1983) we were able to show that with sufficient sensitivity of the measurement system not only emptying but also motility can be measured with this procedure, because contractions deform the ferrite bolus and give rise to transient field changes. An improved version is currently under test in our laboratory.

At present signal analysis in CSG is not well suited to detect transient events in the records like single contractions with sufficient signal-to-noise ratios. This would be needed in the study of visceral perception of patients suffering from eating disorders. The gross subjective ratings used so far can be of only limited

value. The pilot study conducted by Striegel (1978) showed this very clearly. It was confirmed by the variability of subjective response patterns in the present study. Assessment of Pavlovian conditioned feeding responses, which according to the pioneering work by Hollis (1982) seem to play a major role in the regulation of eating behavior, would also demand transient detection. The so-called interdigestive migrating complex is another important transient feature of GI activity. Its inhibition seems to be an important part of the feeding response, especially of those elements controlled by humoral factors and gastrointestinal peptides (Wingate 1981; Dockray 1982). Partial solutions to these problems are conceivable to date. The psychophysiological study of eating disorders may now be integrated with established fields of study.

Acknowledgements. A number of colleagues from the MPIP have assisted the work reported here. We would like to acknowledge their help and at least mention a few. Dr. Pirke not only provided the opportunity to test the feeding responses in volunteers dieting in his endocrinological project (see references below). He also stimulated much of the present research by suggesting the use of conjoint gastrography within the MPIP Anorexia Project. Secondly we honestly admit that no single measurement of the study would have been successfully completed without Inge Riepl's psychological and technical skills. Inge's competent guidance of patients and "experimenters in charge" alike prevented impending disasters more than once if not always. She also assisted in data analysis and preparation of figures. Kurt Löffler and Gerd Müller (Department of Psychology) helped us with biosignal analysis and statistical computation. Dr. Pahl from the Department of Clinical Chemistry was responsible for arranging session dates with patients from the psychiatric wards. He also assisted in several test sessions. Lutz Erasmus and Michael Sladeczek from the Psychophysiology Lab took part as experimenters in charge and helped with the equipment.

References

Ball GG (1974) Vagotomy: effect on electrically elicited eating and self-stimulation in the lateral hypothalamus. Science 184: 484–485

Berger R (1977) Psyclosis. The circularity of experience. Freeman, San Francisco

Booth DA (ed) (1978) Hunger models. Computable theory of feeding control. Academic Press, London

Bruch H (1973) Eating disorders. Basic Books, New York

Cannon WB, Washburn AL (1912) Explanation of hunger. Am J Physiol 29: 441–454

Crisp AH (1965) Some aspects of the evolution, presentation, and follow-up of anorexia nervosa. Proc R Soc Med 58: 814–820

Crisp AH (1967) Some aspects of gastric function in anorexia nervosa. Atti 1 Congr Nazion Soc Ital Med Psicosom 3–9

Dockray GJ (1982) The physiology of cholecystokinin in brain and gut. Br Med Bull 38: 253–258

Dubois A, Gross HA, Ebert MH, Castell DO (1979) Altered gastric emptying and secretion in primary anorexia nervosa. Gastroenterology 77: 319–323

Dubois A, Gross HA, Richter JE, Ebert MH (1981) Effect of bethanechol on gastric functions in primary anorexia nervosa. Dig Dis Sci 26: 598–600

Eisman E (1966) Effects of deprivation and consummatory activity on heart rate. J Comp Physiol Psychol 62: 71–75

Frei EH, Benmair X, Yerushalmi S, Dreyfuss F (1970) Measurements of the emptying of the stomach with a magnetic tracer material. IEEE Trans Magn MAG 6: 348–349

Garfinkel PE, Moldofsky H, Garner DM, Stancer HC, Coscina DV (1978) Body awareness in anorexia nervosa: disturbances in "body image" and "satiety". Psychosom Med 40: 487–498

Hölzl R (1983) Surface gastrograms as measures of gastric motility. In: Hölzl R, Whitehead WE (eds) Psychophysiology of the gastrointestinal system: experimental and clinical aspects. Plenum, New York, pp 69–121

Hölzl R, Lautenbacher S, Brüchle H, Müller G (1983) Vegetative Reaktionen in operanten Leistungstests. In: Vaitl D, Knapp TW (Hrsg) Klinische Psychophysiologie. Beltz, Weinheim (Experimentelle Ergebnisse der Klinischen Psychologie, Bd 1)

Hollis KL (1982) Pavlovian conditioning of signal-centered action patterns and autonomic behavior: a biological analysis of function. In: Rosenblatt JS, Hinde RA, Beer C, Busnel M-C (eds) Advances in the study of behavior, vol 12. Academic Press, New York, pp 1–64

Kohatsu S (1970) The current status of electrogastrography. Klin Wochenschr 48: 1315–1319

Konturek SJ, Rösch W (1976) Gastrointestinale Motilität. In: Konturek SJ, Classen M (Hrsg) Gastrointestinale Physiologie. Witzstrock, Baden-Baden, S 3–61

Kupfermann I (1981) Hypothalamus and limbic system II: motivation. In: Kandel ER, Schwartz JH (eds) Principles of neural science. Elsevier, New York, pp 450–460

Müller GM, Hölzl R, Brüchle HA (1983) Conjoint gastrography: principles and techniques. In: Hölzl R, Whitehead, WE (eds) Psychophysiology of the gastrointestinal system: experimental and clinical aspects. Plenum, New York, pp 123–159

Pirke KM, Lemmel W, Schweiger U, Berger M, Krieg C (to be published) Influence of caloric restriction on LH and FSH secretion pattern in healthy adult women

Porges SW, Bohrer RE, Cheung MN, Drasgow F, McCabe PM, Keren G (1980) New time-series statistic for detecting rhythmic co-occurrence in the frequency domain: the weighted coherence and its application to psychophysiological research. Psychol Bull 88: 580–587

Saleh JW, Lebwohl P (1980) Meoclopramide-induced gastric emptying in patients with anorexia nervosa. Am J Gastroenterol 74: 127–132

Skambraks M (1981) Psychophysiologische und psychologische Unterschiede zwischen Patienten mit Ulcus ventriculi aut duodeni, Personen mit vegetativen Magenbeschwerden und normalen Kontrollpersonen. Thesis, University of Munich

Smout AJPM (1980) Myoelectrical activity of the stomach. Gastroelectromyography and electrogastrography. Delft University Press, Delft

Striegel R (1978) Hungerattribution. Ein psychophysiologisches Experiment zur Hungerwahrnehmung normalgewichtiger, übergewichtiger und anorektischer Personen. Thesis, University of Tübingen

Stunkard AJ, Fox S (1974) The relationship of gastric motility and hunger. Psychosom Med 33: 123–134

Wingate DL (1981) Backwards and forwards with the migrating complex. Dig Dis Sci 26: 641–666