

III.2. THE SIGNIFICANCE OF GASTROINTESTINAL AND  
SUBJECTIVE RESPONSES TO MEALS IN ANOREXIA NERVOSA

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*This paper describes gastrointestinal dysfunctions in patients with anorexia nervosa. Their significance as prerequisite to and consequence of the disturbed eating behavior is discussed. Conditioned food aversion/preference and adaptation to malnutrition are postulated to be the underlying mechanisms of that reciprocal relationship. The reduction of reinforcement value of normal-size meals might, then, be explained by inconspicuous interactions between gastrointestinal and behavioral factors. Therapeutic and diagnostic implications of such a point of view are mentioned.*

## INTRODUCTION

Anorectic behavior alters - in contrast to other behavioral disturbances - the individual physiology directly. The reduction of food intake and its often bizarre shape do not only lead to adaptation attempts contingent on it, but also to deficient stimulation of some organ systems, which is usually triggered by food intake. Though all this affects the gastrointestinal tract (GIT) first - because of the principles of feeding - research on these pathophysiological reactions and their impact on behavior was rather scarce. Infrequent gastroenterologic findings of importance might be one reason for this. This lack of interest is the more surprising as signals from the GIT have been proved significant for the motivations regulating feeding, such as hunger, appetite and satiety. These signals are determined by the food itself and/or by pre- and postprandial patterns of activity in the GIT.

One does not have to consider anorexia nervosa (AN) to be a consequence of GI disorders to see the evidently reciprocal relationship between disorders of feeding and dysfunctions of the GIT. Especially within the framework of behavioral medicine, these initial-

ly inconspicuous interactions between behavioral and physiological factors have to be observed, because reinforcement of disturbed behavior can be their result (Lucas, 1981). In this context, the question about a disorder like AN has to be: to what extent do GI dysfunctions, caused by starvation, reduce the reinforcement value of food and thereby render the disturbance chronic?

Some examples of the behavioral effectiveness of GI signals in the regulation of feeding will now be presented. Then follow some hypotheses about the role of the GIT in the etiology of AN. Finally the implications for assessment and therapy will be discussed. First, however, some empirical findings about GI dysfunction in AN will be reported.

#### GASTROINTESTINAL DYSFUNCTIONS IN ANOREXIA NERVOSA

Despite the relatively small and late interest in GI dysfunctions in AN, evidence has recently accumulated that at least the gastric phase of digestion is impaired. Beside alterations of the gastric secretion, delay of gastric emptying - in some cases with corresponding symptoms like early satiety, sense of fullness, abdominal discomfort, epigastric pain, belching and spontaneous vomiting - is reported as main condition (Dubois et al., 1984; McCallum et al., 1985). Both solid and liquid meals are concerned (Holt et al., 1981). In one study metoclopramide-induced acceleration of gastric emptying was not only accompanied by a decrease of the above mentioned symptoms but also by weight gain (Saleh & Lebwohl, 1980). The connection between delayed gastric emptying, clinical symptoms associated with feeding-related complaints, and anorectic conditions is sometimes also found in cases of diabetic gastroparesis (Lautenbacher et al., 1986). These observations furnish indirect proof that signals important for the regulation of feeding and its dysfunction are generated already in the gastric phase of digestion. It is therefore feasible that they at least may contribute to the maintenance of a disorder like AN.

#### THE SIGNIFICANCE OF THE GASTROINTESTINAL TRACT FOR FEEDING

Preload experiments, in some of which the gastroduodenal transit was prevented, and studies with artificial gastric distension have already

established the significance of gastric distension for the short-term regulation of food intake (Houpt, 1982). The existence of chemo-sensitive structures in the stomach wall, which produce satiety signals, is highly probable (Deutsch & Gonzales, 1980). Particularly the afferent pathways of the nervus vagus and the release of GIT hormones such as bombesin are discussed as mediating mechanisms. During the duodenal phase of digestion, the composition of the ingested food is analyzed by chemo-sensitive enteroceptors, which generate satiety signals consisting mainly in the duodenal release of cholecystokinin or CCK (Smith & Gibbs, 1978).

With regular digestion, however, gastric and duodenal phase do not stay isolated, but shortly after reaching the stomach, part of the ingested food is advanced into the duodenum to be analyzed (Thompson, 1980). Depending on food amount (gastric phase) and food composition (duodenal phase), transit rates can be regulated by local mechanisms for which CCK again is of special importance. Transit, in its turn, influences the satiety signals generated on the different parts of the GIT (McHugh & Moran, 1985). Feeding-dependent GIT reactions - e.g. antral contractions - also reach the CNS through afferent channels.

By influencing feeding (generating satiety signals) and GI transit time, this coordination of the different parts of the GIT makes possible an adjustment of digestion and resorption to specific nutritional situations. This shows clearly that consequences of reduced feeding can be counteracted by a number of mutually dependent adaptation mechanisms (local and central) on the level of the GIT.

#### THE ETIOLOGIC SIGNIFICANCE OF GASTROINTESTINAL DYSFUNCTIONS FOR ANOREXIA NERVOSA

The alteration of GI functions under starvation conditions must be seen - as shown above - not only as a pathophysiological reaction but rather as an attempt to optimize digestion and resorption during malnutrition. Such processes might, however, complicate the therapeutic remediation of malnutrition.

These considerations have led to the formulation of the following hypotheses about the etiology of AN:

- (1) The malnutrition encountered in AN leads to preabsorptive adaptation processes of the GIT, which aim at optimizing digestion and

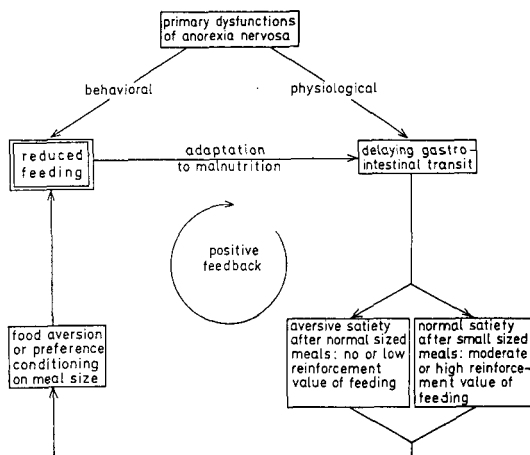
resorption of the reduced quantity of food. The emptying and transit times increase thereby through locally or centrally mediated GIT mechanisms, in order to prolong the digestive and resorptive phases.

(2) As a consequence, small-size meals evoke already the subjective, vegetative and behavioral components of normal satiety, because the food stays longer in any part of the GIT. Normal size meals lead to greater satiety as well as to aversive reactions on subjective and vegetative levels. The latter occur normally only when food ingestion is excessive.

(3) These changes of postprandial effects now modify in turn the reinforcement value of food. Normal-size meals lose their reinforcement value in favor of small meals. This process gains control over behavior by being repeated constantly at feeding. It can be seen as a form of conditioned food aversion and conditioned food preference respectively, the critical feature being food quantity. With the support of the adaptive GIT reactions, this kind of conditioning favors reduced food intake, i.e. deficient food ingestion in AN.

(4) In order to distinguish AN from forced starvation as well as from experimental starvation states, and to explain the variability in therapeutic outcome and relapse risk, predisposing alterations of the GIT functions have to be assumed.

The hypotheses posited here are presented schematically as a positive feedback-loop in figure 1.



**Figure 1:** Reduced feeding in anorexia nervosa as consequence of (a) positive feedback with gastrointestinal and behavioral components and (b) primary dysfunctions

Hypothesis 1 and 4 are supported by direct empirical proof, since gastric emptying is prolonged in AN (Dubois et al., 1984; McCallum et al., 1985) as well as during forced and experimental starvation conditions (Keys et al., 1950). This prolongation occurs in AN patients even after weight gain. Hypothesis 2 and 3 are supported on the one hand by GI complaints (like early satiety, strong sense of fullness, epigastric pain etc.) found in some ingestion (Garfinkel, 1974). Some of the above made statements, however, can only be verified by experiments collecting the relevant variables for the postulated food aversion/preference conditioning directly at feeding. But this kind of experiment has yet to be conducted.

The following anecdotal information from the experience of an anorectic patient will emphasise the important role of food quantity (Graf, 1985): "When I wanted to eat an apple, for example, I chose the smallest. But when there were many equally small ones, it always took all my strenght to finally decide".

#### THERAPEUTIC IMPLICATIONS

If aversive reactions to normal-size meals in AN are caused by the mechanisms outlined above, the following conclusions have to be drawn:

(1) Weight gain should be attempted through small meals, whose size is increased during the course of therapy.

(2) Especially at the beginning of treatment, large meals must be prevented in order to avoid renewed conditioning of aversive reactions to meals.

(3) The treatment of the GI dysfunction - in this case acceleration of GIT transit - removes the mediating visceral components of the learned reduction of food ingestion (see 4.) and allows perceptions influenced by visceral feedback, such as taste and odor, to act again as incentives for food intake (García, 1977).

Whereas most therapy programs take account of point 1 and 2 without explicit reference to GI dysfunctions, the treatment of the GIT malfunctions is still in the experimental stage. Such therapeutic approaches do not really want to influence overt behavior towards normalizing food ingestion by changing visceral variables, but try to remove just the dysfunctions of the GIT in AN. For the treatment of gastric emptying malfunctions, substances like metoclopramide and

bethanechol have been used with success up to now. This medication also reduced the symptoms up to now. This medication also reduced the symptoms associated with feeding and resulted in weight gain (Dubois et al., 1980; Saleh & Lebwohl, 1980). Similar results were obtained in a single case study using domperidone (Russel et al., 1983). Methods of treating impaired emptying without medication are not available as yet.

From what has been said so far, the treatment of dysfunctional gastric emptying disorders appears to be a promising addition to the therapeutic tools in AN.

#### THE DIAGNOSTIC SIGNIFICANCE OF PSYCHOPHYSIOLOGICAL STUDIES

To determine the significance of GI variables for the primary and secondary etiology of AN (in the sense previously outlined), tools for the assessment of psychophysiological functions have to be established, which investigate - in addition to the GI functions in question - other processes directly associated with feeding. A suitable experimental strategy must also take into account highly mediated interrelations, since subjective, behavioral and physiological variables must be expected to interact intricately in AN (see 4.). Thus the correlations must be studied between gastric and intestinal transit, subjective and vegetative variables of the postprandial state as well as the reinforcement value of food-related exteroceptions like taste and odor. Failure to find visceral perceptions of an unmistakably aversive nature does not indicate the unimportance of GIT variables; rather, the search for relations was conducted on too simple a level.

Initial endeavours to study the subjective and vegetative processes involved in feeding were made in our laboratories (Hölzl & Lautenbacher, 1984). For now, only the employed experimental strategy and its justification shall briefly be described in order to show the feasibility of investigating the above mentioned functions. A detailed description of results is given elsewhere (Hölzl et al., 1986).

The objectives of experimental strategy were:

(1) Measurement of postprandial gastric motility: this variable was chosen, because gastric motility has its own afferent innervation and represents a postprandially reactive variable in its own right; for gastric emptying, by comparison, coordination of several GIT functions is necessary. Moreover, gastric motility is one of the conditional factors of gastric emptying (Hölzl, 1983).

(2) Measurement of subjective and other vegetative variabls as indicators of postprandial state: as shown above, the search for negative and positive consequences of feeding - usable to explain conditioned food aversion and conditioned food preference respectively - must be carried out on the subjective, vegetative and behavioral level. Therefore, cardio-respiratory measures were taken in addition to rating of postprandial state.

One example shall illustrate the connection between postprandial gastric motility and subjective indicators of postprandial state. With AN patients, the amplitude of the basal gastric rhythm (BGR) - being the electric correlate of antral motility (Hölzl et al., 1985) - showed a sustained rise of postprandial motility. The ingested food, then, serves as a stimulus enhancing motility over a longer period of time. These findings are compatible with those reporting delayed gastric emptying and indicate a prolonged gastric digestive phase. This rise of the BGR-amplitude was observed at all three sessions, although weight gain was achieved in the meantime. Only at the first session, the groups (12 AN patients, 9 sex- and age-matched controls without GI dysfunctions) differed from each other in the rating sense of fullness (higher levels in AN patients). This difference was already present before and during meal, but increased postprandially (20 to 40 min. after the meal). Since the patients were tested after an overnight fast, this proves that normally food-related perceptions of an aversive quality can occur in anorectic patients even without an adequate stimulus. Nevertheless, the connection between functional parameters of the GIT and visceral perceptions is preserved. That the group differences regarding the subjective variable disappeared while the differences in postprandial gastric motility remained unchanged across sessions, also indicates that the effect of the physiological changes on the subjective variables is mediated by other variables.

Therefore, it is necessary to look for response patterns of satiety

specific for AN. The etiologic significance of such response patterns can be tested by means of the established experimental methods of food aversion conditioning, whereby the relevance of the above mentioned hypothesis concerning causes and therapy of AN can be ascertained. The results obtained so far concerning feeding-related processes support the importance of such an assessment in AN patients whose reactions to a test meal might be of both diagnostic and therapeutic significance.

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