The Eating Disorders

Medical and Psychological Bases of Diagnosis and Treatment

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Dedication

The editors dedicate this volume to Hilde Bruch, M.D., and Albert Stunkard, M.D., whose scientific contributions and educational endeavors have enriched the field.
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Preface


Our aim is to present the beginnings of a comprehensive psychobiologic curriculum for the eating disorders; to foster the education and encourage the interest of the widest possible readership in general medicine, psychiatry, psychology, nutritional science and nursing; and promote both the highest level of informed treatment of patients who suffer from eating disorders and advance the research contributions to our basic clinical knowledge.

This work can serve also as an organized reference for clinicians and researchers with the hope of promoting cross-fertilization between the neurobiologic studies of appetite and eating, and clinical practice.

Conveyed in the sections and chapters of this book are the exciting advances in knowledge, diagnostic concepts and clinical accumen over the past decade that contain the promise of comprehensive treatment in the future.

There is expanded coverage in the text to include rumination and pica; special interests: oncology, eating disorders in the menstrual cycle, eating disorders and affective disorders, and eating disorders and other psychiatric conditions. Treatment techniques described in the text emphasize a broad coverage of principles directed toward the rehabilitation of the patient in the direction of competence, self-awareness and self-regulation.

The hope of the editors and contributors to this volume is to stimulate teaching and research in the eating disorders over the next decade and to establish the guidelines of a pertinent curriculum.

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The Eating Disorders

Medical and Psychological Bases of Diagnosis and Treatment
Section I

Neurobiologic Foundations of Appetite and Eating: Basic and Applied Studies

John E. Morley

The regulation of appetite and eating is an extremely complex process. The decision to eat or not to eat is based on the interaction of a variety of external and internal cues. Overriding all else is the availability of food: During a famine there are few fat people! Food availability interacts with social attitudes and the knowledge of the value of the available foodstuffs. Thus, survival for the moose on the shores of Lake Superior depends on the knowledge that it needs to graze not only on the high-energy-containing deciduous leaves but also on aquatic plants to obtain its salt requirements. The central role of social mores in the regulation of feeding is demonstrated by the sharing of food as a gesture of peace by the hunter-gatherer and typified by the modern business lunch. The next process in the decision to eat involves the hedonic qualities (sight, smell, and taste) of the food. We all have eaten our fill in a restaurant but found it impossible to refuse those extra calories we clearly don’t need when the waiter wheels the dessert cart in front of us. The applied studies in this section deal predominantly with the factors enhancing or decreasing the acceptability of a particular food.

Thus, with the increasing affluence of a society, overeating becomes a natural way of life. At first this is accepted as a just reward for hard work, as in Isaiah 55:2: “...and let your soul delight itself with fatness.” However, with time, the organism becomes aware that gluttony and obesity are just as detrimental to species survival as was the marasmic status. This leads to the need to develop a variety of inhibitory systems to decrease food intake.

Basic animal studies have tended to concentrate on these inhibitory factors, and this is reflected by the general content of the chapters in this section on basic studies. Early studies spent much time debating the role of different absorbed nutrients as appetite regulator. This led to the development of a variety of “appetostat” theories in which various authors vied to establish their nutrient (eg, glucose, fatty acids, amino acids, or purines) as the factor responsible for inhibiting feeding (the Holy Grail Hypothesis).

More recently it has become clear that a variety of gastrointestinal hormones that are released during a meal are capable of decreasing food intake. Whether these peptide hormones are true satiety agents or merely produce a mild state of aversion if being hotly debated. However, it seems reasonable to suggest that in the end it will prove to be an interaction of these hormones and the physicochemical properties of the absorbed nutrients that leads to the termination of a single meal. In addition, the state of glycogen repletion or depletion of the liver, the production of energy (heat) by tissues such as brown fat, and the effect of fat depots on the circulating concentration of fatty acids and insulin all appear to be capable of modulating feeding.

Finally, all this information needs to be coordinated, and the organism has to make the decision whether to eat. This integrative process appears to take place within the central nervous system (predominantly but not entirely in the hypothalamus). There is growing evidence
that this integrative process involves a variety of neurotransmitters (monoamines, neuropeptides, prostaglandins, and amino acids) interacting on a backdrop of hypothalamic interneurons. The putative role of these neurotransmitters is discussed in two of the chapters in the basic studies section.

If after reading the chapters on the Neurobiologic Foundations of Appetite and Eating the neophyte is left somewhat bemused by the multitude of factors involved and theories invoked to explain them, heart can perhaps be taken from the words of the English philosopher, Emerson Pugh: "If the human brain were so simple that we could understand it, we would be so simple that we couldn't." The chapters in this section clearly demonstrate that despite the tremendous progress in our knowledge of the neurobiologic foundations of appetite in the last decade, we are just emerging from medieval times, hopefully to enter the Renaissance Period of insights into appetite regulation. Despite our present limitations, I believe that the future development of viable treatment modalities for eating disorders will be based in the knowledge gained from the neurobiologic foundations of appetite and eating.
Chapter 1

The Development of Feeding Behavior

Elliott M. Blass

Feeding is unique among mammalian behaviors. It is the only behavior that can be practiced successfully in total isolation yet almost always occurs in a social milieu. The meal is a setting for intense social interactions, for joy, and for pain. The meal has become incorporated into religious and national festivals such as the Passover seder or Thanksgiving dinner. It has become an integral part of Western and Eastern cultures alike in the form of coffee breaks and other social interactions.

Feeding is also unique in the sense that it changes developmentally. Mammalian infants cannot feed alone, and they derive their sustenance from breast or bottle. Over time the infants' repertoire of ingesta eaten and of consummatory motor patterns expands from their limited base of suckling milk, and the adult ingestive profile of independent feeding and drinking emerges. The social aspect of group feeding continues, however, and this serves as an opportunity for cultural transmission.

Things can go awry in feeding settings, however, and pathology can develop. If the feeding history is sufficiently traumatic and the other aspects of the psychosocial milieu are not sufficiently supportive, pathology is presented as in anorexia nervosa, bulimia, severe obesity, and other behavioral disorders.

There are major difficulties in identifying the causes of feeding disorders, however. Among the stumbling blocks are lack of time, lack of proper experimental control, and documentation of aberrant feeding situations.

Animal studies circumvent some of these problems. Accordingly, this chapter focuses on the development of feeding in animals, mostly laboratory rats. In this chapter I will document the physiological bases of early ingestive behavior, especially suckling, and the influences that the suckling setting can exert on future noningestive and ingestive behaviors.

SUCKLING

Developmental psychobiologists have come to appreciate the richness and complexity of the suckling act only during the past decade [2,3,4,5]. What appeared at first to be a simple reflex [6] is now appreciated to be under the influence of diverse physiological, social, and experiential factors. Moreover, the influence of these factors changes during development. It is now appreciated that suckling cannot be equated with feeding [4,7]; that the earliest determinants of suckling—more specifically, nipple attachment—are social [8], not physiological; and that internal factors start to exert their influences at about two weeks of age in developing rats [2,3,4,5]. Yet even after physiological factors come into play, they do so against the background of social deprivation until weaning is almost complete [8]. During the postnatal period [9], indeed even prenatally [10], the stimulus that will elicit nipple attachment and milk withdrawal is influenced by various experiences. In short, as will be more fully documented, the nest setting offers a remarkably rich opportunity for conditioning and learn-
ing that are influential during and beyond the nursing period [11].

During the first 10 to 12 days after birth, nipple attachment appears to be an end in and of itself. Rats remain attached to a nonlactating dam for up to 12 hours without milk delivery [12]. Attachment latencies are not influenced by deprivation very much [13]. Indeed, rats younger than 12 days of age continue to suckle despite receiving up to 22% of their body weight in infusions through a tongue cannula [14] or by actually withdrawing milk from the milk-laden nipples of dams that had not nursed their own young overnight [15]. This is a remarkable testimony to the lack of adultlike control over milk intake. Rats that obtain these large volumes of milk detach from the nipple only after milk has refluxed into the nares from the bloated stomach and caused respiratory distress. This changes by Day 15, when normal amounts of milk are taken (ie, within the volume of milk found in the stomachs of rats continuously with their dam [14,15]).

Even though volume intake does not appear to be determined by internal factors in rats younger than 15 days of age, the rate at which milk is ingested via suckling is. Cramer and Blass [15] confirmed earlier reports of Houpt and her colleagues [16,17] that demonstrated differential intake according to differential deprivation length. Cramer and Blass [15] showed that this differential intake was directly related to the frequency with which rats shifted from nipple to nipple after each milk letdown, with more deprived rats shifting more frequently. This is an important infantile strategy, because it allowed deprived pups to sample more nipples before the ducts constricted, thereby making milk unavailable until the next letdown. Thus, there is control over ingestive activity in the sense that increased deprivation leads to increased nipple-shifting, yielding additional opportunities to obtain milk, and this is probably under vagal control [18]. However, given that a rat is attached to a nipple, then deprivation does not seem to affect the likelihood of extracting the available milk in rats younger than two weeks of age.

Deprivation to suckling infants is very different than adult deprivation. Until rats are about 25 days of age, it is lack of suckling opportunity per se that determines responsiveness to the internal signals affecting rate of intake. By Day 25, it is the energetic consequence of deprivation that allows the physiological signals to gain control in older rats. Cramer and Blass [8] studied six groups of rats. One group was deprived of maternal contact and suckling for eight hours. Another group was not deprived. The remaining groups had different components of privation imposed during the eight-hour period. One group was deprived of suckling and its concomitant nutritional and hydrational benefits by living with a thelectomized (nipples surgically removed) female that was maintained in a maternal state. These animals, therefore, enjoyed maternal contact during privation. Another group was allowed to suckle a maternal female whose nipples were sutured, preventing milk letdown. A third group was deprived of female contact but received three, intubations (2% of body-weight) of “half and half creamer” to help offset the caloric deficit encountered during suckling abstinence. The final group was allowed to suckle nonnurtitively and also received the three preloads. As can be seen from figure 1, nonnutritive suckling per se was sufficient to cause levels of milk intake in 15-day-old rats that did not differ from those of nondeprived rats. Intake was not due to energy or caloric deficit, because intubation did not reduce intake. Much the same holds true for Day 20 rats. It is clear that contact without suckling opportunity (thelectomized dam) was not enough to ward off the consequences of privation. By Day 25 missed suckling opportunities exerted rather little effect on milk derived from suckling. The critical factor appears to be the lost nutrients, because the preloads fully restored intake to baseline levels. In short, for suckling rats younger than two weeks of age, nipple attachment appears to be the motivating factor as a determinant of the highly specialized suckling act [19]. By two weeks, physiological controls of gastric distention [14], cholecystokinin, and dehydration [20] are operative. These controls in rats 15 and 20 days of age affect both the frequency of nipple shifting as well as volume intake. They appear to become activated in the context of the animals having been separated from the dam and not because of physiological consequences of separation. By Day 25 the factors affecting intake from the nipple appear to be similar to those affecting both feeding away from the dam and adult feeding.

Privation affects motivational as well as consummatory systems. According to Amsel et al [21], infant rats’ running speed accurately reflects the quality of the maternal interaction that is awaiting the infant at the end of a runway. That is, rats run fastest when allowed to suckle nutritively, slower for nonnutritive sucking, and slower yet to only establish contact. Stoloff and Blass [22] showed that 2- or 24-hour deprived 17-day-old rats prefer to suckle rather than eat, even if the sucking is nonnutritive. By Day 21 sucking is preferred to eating a liquid diet only if the nipple is lactating, and by Day 28 feeding is always preferred over sucking. These results are in complete accord with the Cramer and Blass [8] findings concerning milk intake determinants in rats during the weaning period.

Thus, in rats, at least, a prolonged period of suckling
is strongly favored by the infant, even after it has started feeding and drinking independently and even at an age when rats are often weaned in the laboratory (Day 21). The implications of this protracted period of contact are of considerable interest, because during this period the infant much prefers the odors of its mother to that of other female or male rats [23]. This contact during the late weaning and early juvenile stage provides the unique biological opportunity for the infant to learn from its mother directly and indirectly about various facets of the environment in which it is about to enter independently. I will shortly return to this issue of what is learned in the next setting, but first a discussion of infantile feeding is in order.

FEEDING DURING DEVELOPMENT

The first hint that adultlike ingestive behavior could be obtained in suckling infants was provided by Wirth and Epstein [24], who observed increased water and milk intake in dehydrated rats that were held to a tube that delivered a continuous flow of liquid. This has been extended by Bruno [25], who observed increased water intake in rats that could initiate drinking by lowering their heads onto a fluid-soaked mat and drink in a very warm test chamber. In the interim, however, Hall and his colleagues [26,27,28] demonstrated that under certain conditions of high ambient temperature and deprivation, and when the infant rat pups' limited motoric capacity is taken into account, feeding could occur. Remarkably, feeding in 1-to 9-day-old rats had many of the major characteristics of normal adult feeding. That is, it was sensitive to the factors that enhanced food intake as well as to those that decreased it. Specifically, intake of a liquid diet, whether infused through an anterior mouth cannula or taken from a moist mat at 33°-34°C; eating a mash diet directly from the floor of a 34°C container; or ingesting sucrose were all linearly enhanced by
privation [26-28]. Moreover, as feeding progressed, pups showed a progressive sequence of satiety similar to that of adults, suggesting that satiety mechanisms were in place for the feeding system at a time when they did not appear to affect intake derived from suckling. These behaviors could only be obtained in rats that were tested in the heat. When milk was infused into the mouths of pups kept at room temperature, the pups allowed the milk to dribble out of their mouths.

This feeding had another salient characteristic of adult ingestive behavior: Johanson and Hall [29] observed that 1-day-old rats receiving milk through an anterior cannula (it opened into the rostral portion of the lower jaw) became extraordinarily activated, displaying a wide variety of postures that even included lordosis. The researchers capitalized on the fact that these pups also did a lot of thrusting upward along the sides of the container. They placed a paddle on the wall of the test container and trained infant rats to push the paddle to obtain food. The increased operant rate was contingent upon the animals' receiving food for their efforts. Yoked control rats did not increase operant rate. Moreover, when tested with two paddles in the cage, the rats tracked a reversal of the rewarded paddle, showing further the properties of a motivated behavioral system. Clearly, major facets of the ingestive system are in place before ever being used by the animal under natural circumstances. Indeed, if the system were used, it would probably be lethal to the animal given the immaturity of the gastrointestinal tract. These data can be taken as another example of motor systems being fully available before their use. This is a conservative evolutionary approach that provides a safe margin of error for meeting early feeding demands [30]. Another phylogenetic interpretation may shed greater light on the evolutionary significance of suckling behavior. I will return to this issue after discussing learning that may occur in the nest.

**LEARNING THROUGH MOTHER-INFANT CONTACTS**

In addition to Johanson and Hall's demonstration of instrumental learning by Day-1 rats, there have been a number of demonstrations of both instrumental and classical learning outside of the nest area. Moran, Schwartz, and Blass [31], for example, used the major features of the Johanson and Hall technique to demonstrate that Day-3 rats would push a lever to obtain electrical stimulation to the medial forebrain bundle (MFB). It is of considerable interest that the rats in the Moran et al. study behaved similarly to those studied by Johanson and Hall in terms of the broad spectrum of activities that were elicited by MFB stimulation.

Classical conditioning has also been obtained away from the nest. Johanson and her colleagues [32,33] demonstrated that rats would come to prefer an otherwise aversive odor if that odor was paired with the delivery of food to the mouth. Thus, both classical and instrumental conditioning can be obtained in infant rats, and the parameters of this conditioning have been elucidated by Rudy and Cheattle [34]. It is remarkable that these animals that bear only the slightest physical, sensory, and motoric similarity to adults differ only subtly in their abilities to be conditioned under the right circumstances.

It turns out that the right circumstances are exactly the ones that are present in the nest. The nest is kept warm by the dam, and she vigorously activates her pups on her return to the nest to nurse. In fact, according to Shair et al. [35], the EEG indicates an awake state only at the initiation of sucking and after a milk letdown, when rat pups exhibit the hyperextension response for milk withdrawal and then shift to another nipple. Thus, the circumstances necessary for conditioning away from nest and dam are routinely present in the nest itself. The infant can be really conditioned under these circumstances. Brake [36] for example, has shown that Day-10 rats will come to prefer an odor that is specifically paired with milk delivery through a nipple. Pedersen and Blass [10] and Pedersen et al. [9] demonstrated that prenatal and postnatal stimulation, the latter mimicking that which is delivered by the dam to her nestlings, determines the stimuli that will elicit sucking. Prenatal conditioning, both appetitive and aversive, have been reported by Smotherman [37] and Stickrod et al. [38] in a series of remarkable experiments. Indeed, according to DeCasper and Feifer [39] human infants appear to respond to their mothers' voices on the basis of having heard them in utero.

There is now considerable indirect evidence that classical conditioning during the nesting period determines the expression of vital behaviors during adulthood. Alberts [40], in an extensive series of studies on huddling behavior, demonstrated that after two weeks of age, huddling occurs in albino rats with animals bearing a familiar scent, and that this scent becomes familiar by virtue of the infants' contact with the dam. Also, Leon [23] demonstrated that infant rats learn about certain characteristics of the mother during the weaning period by virtue of an attraction to the potent odor of the dams' bacteria-rich excreta. Likewise, Galef and Clark [41,42] found that rats, at weaning, ate the foods that adult rats, especially the mother, ate. This is a very important finding in the context of feeding ontogeny. Galef and Clark [42] discovered that familiarity with safe foods was conferred by virtue of the infants' obtaining information...
concerning that food via suckling and possibly by eating the mother's excreta. The weanlings learned about poisons by following adults to the feeding station and observing avoidance by the adults, who spilled and contaminated the poisoned food by urinating on it. Thus, the bond formed during development appears to have allowed the infants to venture from the nest to learn about the features of the external world in low-risk setting accompanied by the adults. It is important to note that the infants are not learning how to eat. Hall's [43] experiments had shown first that infants reared away from the dam ate normally upon their very first presentation of food, and as indicated above, the feeding system according to Johanson and Hall [27] is functional, albeit normally unavailable, during infancy.

PHYLOGENETIC CONSIDERATIONS

Precocity of feeding, even on the day of birth, in otherwise altricial mammals is remarkable. It may simply represent an example of a complex behavioral system being available before it is called upon (ie, to ensure its availability when the mother can no longer guarantee sufficient calories for growth because of the increased litter biomass) [7,30]. I find it difficult to envisage, however, how this would be selected phylogenetically, especially given the fact that the immature gastrointestinal system could not handle food directly ingested from the environment. I would like to speculate that this early feeding system represents the regression of a phylogenetically older system of infantile ingestion that has become subserved to the phylogenetic suckling system as the sole mechanism of infantile ingestion.

The question presents itself, therefore, as to why has suckling evolved. It requires extensive morphological, physiological, hormonal, and behavioral modifications on the part of the mother and the young. Nursing is extremely costly to the mother. She endures a hyperphagia that is so severe that it can not be exaggerated by ventromedial hypothalamic destruction [44]. She is also markedly hyperdipsic and spends considerable metabolic energy converting food to milk for the young. The hyperphagia and especially the hyperdipsia are particularly noteworthy, because mothers make themselves more vulnerable to predators to obtain sufficient food and water, and this vulnerability is exaggerated when moving about saddled with an infant. Obviously, these risks had to be offset by phylogenetic gains in inclusive fitness. The remarkable abilities of newborn altricial mammals to be conditioned at birth, indeed in utero, raise the possibility that altricial mammals may use the suckling period to learn from the dam about the rules of the external world in a relatively protected setting. (It also allows for rapid growth because of the low energy expenditure by nested animals with very few physiological heat-producing obligations or capacities). That such learning takes place has been documented [11,40]. The means through which these experiences can enhance inclusive fitness are just now starting to be appreciated [45].

The hypothesis can be stated specifically. A protracted period of contact between mother and offspring has evolved that increases inclusive fitness. Central to this is the infants' ability to form associations between intrinsically rewarding maternal features (eg, warmth, milk) and her arbitrary features (eg, odor, sound, color, and behavior patterns). This association is positive and causes infantile patterns of behavior that maintain maternal proximity. Through this proximity, the mother teaches her young before and during the weaning process [41,42,46]. She does not teach how to eat, for example, so much as what and where (and whom) to eat. The infant, therefore, benefits from parental experience rather than discovering major environmental traps directly, at considerable risk.

This invites speculation on the mandatory phylogenetic changes for nursing and suckling to have evolved. Recent paleontological literature suggests that certain reptilian groups lived in relatively close contact with their young [47,48], a trait that is seen in today's crocodilians. Accordingly, one means of encouraging a prolonged contact is to reduce thermal capacity and regress body size so that, relative to adults, the surface-to-mass ratio is high, leaving the infant in a state in which body contact is necessary to ensure normothermia. These alterations in themselves are not sufficient to ensure protracted contact. The situation is abetted, over time, by making the mother the infants' exclusive food source. There is a problem here. Given that the starting point is the reptile with its well-developed (at birth) dentition, digestive system, and behavioral response systems for procuring food, then morphological, physiological, and behavioral regression is in order. My thesis is that this has been achieved over the course of phylogenetic time. The suckling response is unique; the digestive system can only handle mother's milk, and the mammalian dentition emerges slowly. One may add to this the change in articulation that allowed for a more complex facial neuromusculature to ensure the seal on the nipple for milk withdrawal, and the pieces are all in place for protracted infant contact with the mother. The parallel changes in maternal morphology and hormonal and physiological controls attendant to the nursing setting completes the picture. Accordingly, one possible means of viewing feeding systems, at least in infant rats, is as a vestige of an earlier system that became increasingly less available, so that the infant could form a bond with the mother that allows it to learn from her in a low-risk set-
CONDITIONING DURING HUMAN INFANCY

Pioneer work in this area has come from the laboratory of Lipsitt [49] at Brown University. Lipsitt demonstrated under a variety of circumstances that infants can modify rooting and orienting behaviors that are rewarded with the presentation of sweet solutions. From Sameroff's [50] studies, we learn that infants can modify their sucking rate during the first week of life in order to have sucrose injected into the mouth via a special nipple. Despite these and other unequivocal demonstrations of instrumental behavior in human infants during the first postnatal week [51], there have not been unequivocal demonstrations of classical conditioning. With Judith Ganchrow and Jacob Steiner of the Hebrew University in Jerusalem, I attempted to obtain classical conditioning in infants 2 to 48 hours of age [52]. We accomplished this by stroking the infant's forehead for ten seconds every two minutes and immediately following this delivery of 0.2cc of 0.037M sucrose solution within ten seconds. The infants avidly accepted the sucrose, making sucking movements and orienting toward the source of delivery. Over the course of conditioning trials, the infants came to make many orient and suck responses during the stroking period itself. This is shown in figure 2, where the number of orient responses of the experimental and control infants are presented for each ten-seconds bin of the two-minute trials. Control infants were treated in a manner identical with that of experimental infants except that a 10-, 20-, or 30-second delay was interposed between stroking and sucrose delivery. These data demonstrate the capacity of the newborn human infant to be classically conditioned in an appetitive setting that has certain characteristics of the nursing setting. Moreover, when extinction was instituted, seven of the eight experimental infants cried, whereas only one of sixteen control infants did so. This suggests that the experimental infants...
were responding to the violation of the predictive relationship and not strictly to the withdrawal of sucrose.

DISCUSSION
These data have made it clear that conditioning in nonhuman mammals can readily take place in the nest situation. Conditioning occurs when certain features of the mother, such as her arousing qualities, her touch, and warmth stimulate the infant in a highly predictive and biologically significant setting. Through this, affectional systems are formed, behavioral patterns are developed, and biologically significant information is acquired. In humans, and presumably in nonhuman mammals, sometimes things go wrong, and in humans, clearly identifiable syndromes of pathology develop. I am not claiming that the etiology of these problems can be attributed necessarily to faulty nursing. I do suggest, however, that the learning capabilities in the infant have been selected for, and that opportunities are present to acquire harmful patterns of coping during suckling and early stages of mother-infant interactions. That is, the phylogenetically old associational mechanism may lead the individual to formulate an appropriate affectional bond with an inappropriately behaving parent. To maintain the bond, the proximity-seeking behavior of the child is expressed pathologically to seek inappropriate rewards. During normal development, normal and presumably adaptive patterns are obtained from a stable and supportive setting that is marked by physiological pleasure and contact comfort [53]. In the pathological setting, presumably through the same processes, the same physiological stimuli may be associated with parenting patterns that are highly inappropriate. To the extent that the etiology of behavioral feeding disorders such as marked obesity, anorexia nervosa, and bulimia are poorly understood, it behooves us to assess the earliest feeding histories of these patients to see if classes of ineffectual or harmful parenting emerge.

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REFERENCES
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