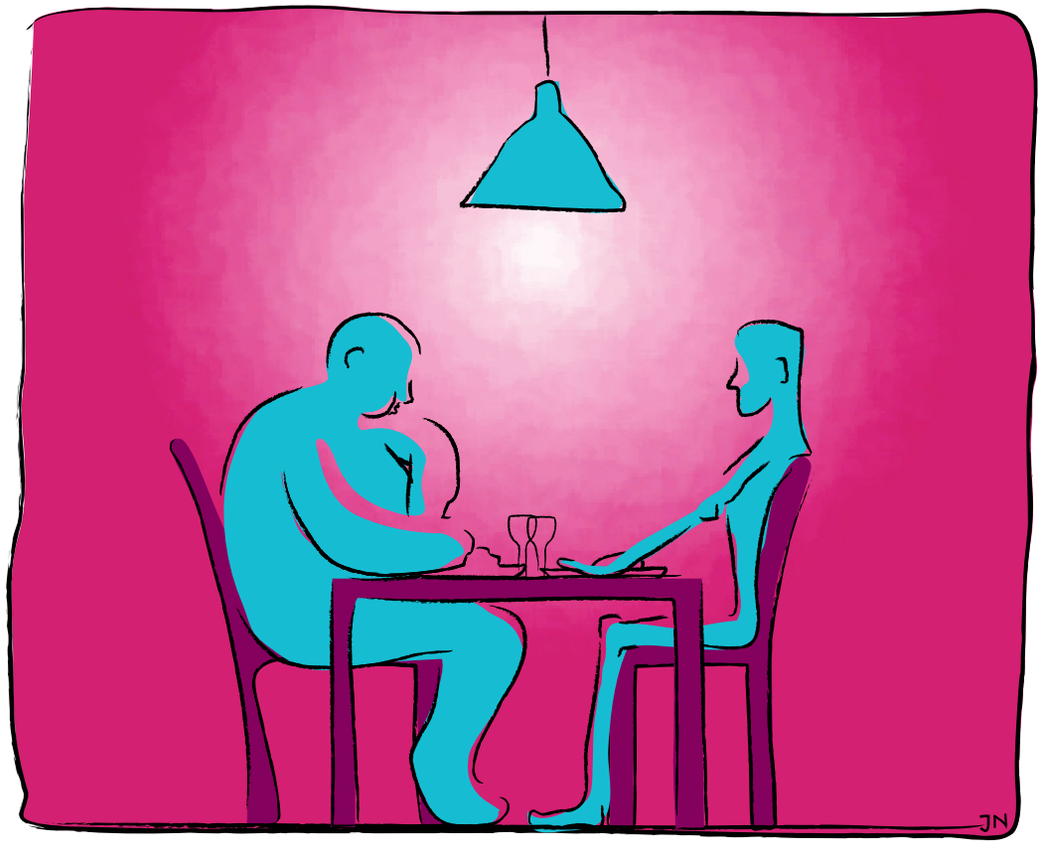
Thesis for doctoral degree (Ph.D.)
2009

YOU ARE HOW YOU EAT

Decelerated eating may prevent obesity and eating disorders



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YOU ARE HOW YOU EAT: Decelerated eating may prevent obesity and eating disorders
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To my family with love

for the things we have to learn before we can do them, we learn by doing them
-Aristotle

Contents

Abstract

On a new framework for anorexia nervosa, learning to eat is central intervention; as patients regain a normal pattern of eating their problems dissolve. Mandometer®, a development of previous methods, allows simultaneous recording of eating rate and the development of satiety as well as experimental manipulation of eating rate. By measuring eating behavior during the course of a meal with this method, women were divided into those eating at a decelerated rate and those eating at a constant rate. Decelerated eaters are able to resists experimental challenges such as eating at an increased or decreased rate, but linear eaters eat more or less food in these experimental conditions. Satiety develops similarly in both decelerated and lineal eaters. Linear eaters develop a pattern of eating similar to that of anorexic patients when eating at a decreased rate, they eat less food yet experience an increase in satiety. Linear eaters can learn to eat at a decelerated rate and if they do they can resist overeating when tested to eat at a high rate. As a result of the learning, they also score lower on restrained eating, a cognitive construct thought of as a cause of eating behavior. Skipping dinner increases the linearity of eating and reduces food intake in women but has the opposite effect in men; these changes in eating behavior can be reversed by feedback on how to eat during the meal. The conditions of the school dinner in secondary schools are such that the speed of eating increases by 50% and food intake gets distorted from its normal pattern. The change can be reversed by eating in a relaxed condition or by feedback on how to eat during the meal. It is suggested that linear eating is a risk factor for eating disorders and that the risk can be reduced by practicing eating using feedback on how to eat properly.

List of Publications

The present thesis is based on the following papers.

I Zandian, M., Ioakimidis, I., Bergh, C., & Södrsten, P. (2007). Cause and treatment of anorexia nervosa. *Physiol Behav, 92*(1-2), 283-290.

II Zandian, M., Ioakimidis, I., Bergh, C., Brodin, U., & Södersten, P. (2009). Decelerated and linear eaters: effect of eating rate on food intake and satiety. *Physiol Behav, 96*(2), 270-275.

III Zandian, M., Ioakimidis, I., Bergh, C., & Södersten, P. (2009). Linear eaters turned decelerated: Reduction of a risk for disordered eating? *Physiol Behav, 96*(4-5), 518-521.

IV Zandian, M., Ioakimidis, I., Bergh, C., & Södrsten, P. (2009). Linear and decelerated eaters: Women eat less, men eat more after fasting. *Physiol Behav, (Submitted).*

V Zandian, M., Ioakimidis, I., Bergh, C., Bergström, J., & Södrsten, P. (2009). The school dinner should not be eaten quickly: an observational-experimental study of eating behavior among children in secondary school. *BMI, (Submitted).*

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Introduction

Since the so called ”obesity epidemic” emerged, abruptly about 25 years ago (Bergh, Brodin, Lindberg, & Sodersten, 2002), research on eating behavior and body weight regulation has exploded. Studies on animals and humans have explored neurobiological mechanisms in admirable detail (Shin, Zheng, & Berthoud, 2009) but this research strategy has yielded very little, if anything that can be used clinically to manage eating behavior and body weight¸ except in the rare cases of a monogenetic cause of obesity (Farooqi & O'Rahilly, 2009). This may be because our knowledge of genotype-phenotype-environmental interactions is far from complete; flexible genetic networks interact to cause patterns of phenotypic expression, as reflected in behavior and disease, and these networks are very far from being identified more than partly (Altshuler, Daly, & Lander, 2008; Robinson, Fernald, & Clayton, 2008). An interesting new paradigm for brain research in this scenario has emerged according to which the role of the brain is to “mediate” rather than “determine” behavior which allows the individual to adapt to changes in the environment. This would appear particularly true in conditions where there is no brain damage, such as in obesity and anorexia. Add to this the recent vogue of research on epigenetics (e.g., Keverne & Curley, 2008) and the “determinants” of behavior, including eating behavior appear more flexible than ever before. The days of orthodox genetics and neuroscience when behavior was analyzed merely as the outcome of neural activity may be over, the brain is no longer thought of as a machine than produces behavior, but as an organ that responds to changes in the environment. However, this point of view is actually not all that new, recall that Ramón y Cajal (1897) pointed to the possibility of neural plasticity long ago; he even suggested that anyone can become a scientist merely be participating in scientific work, the brain gradually adapts and changes to become indistinguishable from the brain of a scientist after all the work!

With the emergence of the cognitive revolution, a wealth of cognitive “processes” is now thought to explain behavior (Wansink, 2006); behaviorism is at bay. However, cognitive causation of behavior is by no means “correct” a priori, the mind is easily misled (Wansink, 2004, 2006); in addition, cognitive science does not always meet the demand of being

neurobiologically realistic, and if it is not, explanatory models fail (Crick, 1989; Marshall, 2009). Cognitive processes in the control of eating behavior have even been thought of as emancipated from biology (Polivy & Herman, 1985). One is reminded of William James (1890): there is "no 'mind-stuff' out of which the emotion can be constituted". It is time to rescue the analysis of eating behavior from obvious dualistic mistakes. Yet cognitive factors in eating are important, most obviously so in the analysis of eating disorders; anorexia nervosa and bulimia nervosa are always associated with cognitive, or perhaps better, psychological change.

Because the neurobiology of eating has been reviewed so many times recently (e.g., Shin et al., 2009), another review is redundant. Also, paper I provides a review of the conventional analyses of the behavioral, psychological and neurobiological changes in eating disorders and so there is no reason to expand on these topics here. Instead, some selected aspects of the study of human eating behavior will be discussed, in particular those that led to the hypotheses of this thesis. In brief, this thesis is an attempt to restore behaviorism in the context of eating.

The motivation to eat

What initiates eating? What encourages us to continue eating? What makes us stop eating? These questions are often thought to be answered by the physiology of hunger and satiety. However, real life reveals that eating, both in humans and in animals, usually takes place when the individual is presented with the opportunity to eat, even in the absence of hunger (Yeomans, Blundell, & Leshem, 2004), and eating can continue after satiation (Lowe & Levine, 2005). These motivational aspects of eating suggest that homeostasis is easily overshadowed by cue conditioning (de Castro & Plunkett, 2002; Petrovich & Gallagher, 2007).

Homeostatic versus learned eating

Undoubtedly, the most important paper on the neural control of feeding was published by Stellar (1954), who suggested that "the amount of motivated behavior is a direct function of the amount of activity in certain excitatory centers of the hypothalamus". In this model, food intake is assumed to be a result of a reciprocal interaction between an excitatory and an inhibitory center in the brain. Thus, internal and external stimuli processed by these centers in hypothalamus are necessary for the production of motivated behavior; this model of eating behavior remains

essentially the same today, the modification is that excitation and inhibition are now thought to be chemically mediated by partially overlapping neural networks, which extend beyond the classical hypothalamic regions and include some cortical, limbic and brainstem areas as well (Shin et al., 2009). The hypothalamocentricity of the model, however, remains in focus (e.g., Woods & D'Alessio, 2008). However, the influence of hedonic and learned factors on food intake put behavioral measurements into a broader context (Berridge & Kringelbach, 2008; Shin et al., 2009; Volkow, Wang, Fowler, & Telang, 2008). Thus, food intake has been shown to be positively correlated with learned properties related to palatability (Yeomans et al., 2004). For example, the habitual consumption of palatable food can generate positive valence and generate eating regardless of energy need (Yeomans et al., 2004). Accordingly, two separate eating motivations have been outlined, one at the neurophysiological and one at the behavioral level (Levine & Billington, 1997). Hedonically learned eating is thought of as generated in the absence of energy need by the presence of palatable food and terminated by removing or consuming the food, as opposed to biological or homeostatic eating which is based on energy depletion and ends by energy repletion. These appetitive motives are generated by overlapping systems in the brain (Lowe & Levine, 2005) and interact in maintaining energy balance (Shin et al., 2009). A real life example is the "dessert effect"; the individual continues to consume palatable foods even after energy requirements have been met and homeostatic satiety signals have been engaged. This scenario has been referred to as hedonic hunger (Lowe & Butryn, 2007); consumption is driven by pleasure rather than by homeostatic mechanisms. Therefore, body weight should be explored through the study of these interactions and not merely as the result of homeostatic mechanisms.

In an elegant review, Woods (1991) analyzed the relationship among the neuroendocrine system and food intake in a reciprocal manner. Thus, while neuroendocrine factors associated with onset of eating are most often thought of as causes of the eating, Woods (1991) suggested that it may be the other way around. Hence, an animal may need to adapt to the upcoming challenge of a meal by eliciting responses in preparation for the consequences of eating, such as reducing its body temperature to counteract the thermogenic effect of eating; in Woods´s (1991) analysis release of e.g., neuropeptide Y in the paraventricular hypothalamic nucleus may be an effect of eating food at the same time of day rather than the cause of that daily eating (Drazen, Wortman, Seeley, & Woods, 2005). This perspective may be particularly important in states of functional change when there is no evidence of brain damage or dysfunction, such as obesity and anorexia.

Absence of hedonic eating is perhaps a rare condition today, when tasty foods are abundant, but may have been prominent in evolution when homeostatic motives were at work to properly maintain energy balance. Starvation as a result of enforced food shortage is the human condition and is the obvious example (Sodersten, Nergardh, Bergh, Zandian, & Scheurink, 2008). Interestingly, the capacity to eat large amounts of food persists in starvation and is in all probability essential for promoting storage of energy thus buffering against starvation (Sodersten et al., 2008). This behavioral adaptation does not exclude the possibility that inhibition of food intake can also occur in times of shortage favoring foraging at the expense of eating so as to prevent depletion of energy stores ((Sodersten et al., 2008).

In addition to learning and homeostasis, factors such as stress (Gluck, 2006), socio-cultural context (De Castro, 1990), environment (Wansink, 2004) and physical activity (Nergardh et al., 2007) affect eating behavior. Additionally, responsiveness to eating cues and internal/external orientation toward food impact on body weight (Wansink, Payne, & Chandon, 2007). Long ago, Schachter (1971) pointed out an interesting similarity between the eating behavior of obese humans and rats, both of which refuse to work hard for food; external factors, and in particular ease of availability, were thought to be important in maintaining a high body weight among obese individual humans as well as rats. Experiments in which the effort to obtain food was manipulated demonstrated that as the cost of food is decreased food intake in a single meal is substantially increased (Schachter, 1971). Subsequent experiments have verified this "economic" hypothesis of eating in both rats (Collier & Johnson, 2004) and humans (Wansink, 2006). Recently, it was suggested that the main cause of the "obesity epidemic" is the reduction in the price off high caloric "junk" food (Drewnowski, 2000; Norman, Temple, Steyn, & Myburgh, 2006); the present economic crisis may increase body weight further because economic constraints force people into eating even more "junk" food and so gain even more weight (Ludwig & Pollack, 2009). The nervous system, apparently, offers no protection against the influence of such external factors in the control of eating.

Cognitive control of eating

Today, behaviorism has lost explanatory priority to cognitive science. However, cognitive research has provided little, if anything that can be used to change eating behavior and body weight. The intention to diet, for example, may cause weight loss in the short term, but fails to achieve

weight loss in the long term (Vohs & Heatherton, 2000), relapse is the decided norm. However, the mental/cognitive responses to dieting and starvation are quite conspicuous (Wadden, Brownell, & Foster, 2002). "What I was not expecting was the effect it would have on the mind, the total feeling of depression and the total occupation with the idea of food, food for thought", commented one of the participants in Ancel Keys´ landmark experiment on starvation in normal men (Keys, Brozek, & Henschel, 1950). Unsurprisingly, the obsession with the idea of food is well connected with starvation (Södersten et al., 2008); but the causal relationship between the two is not altogether clear. Studies in the neurobiology of mental causation suggest that state of mind and action can be disassociated experimentally (Wegner, 2003).

Interestingly, it has been observed that behavioral factors, such as slow eating, greatly influence nutritional status (Keller, 1993). For example, Berkhout et al. (1998) investigated the cause of unintentional weight loss in demented patients and found a strong positive relation between weight loss and behavioral aspects of eating, such as choosing food, bringing it to the mouth, and chewing. This relation was seen in both demented patients and in patients with other disorders, suggesting that it is the deficits in eating that cause the weight loss, rather the factors related to the dementia per se (Hickson, 2006). In addition, the starvation study by Keys et al. (1950) indicated that eating behavior and, more specifically the eating pattern is affected by dieting. Keys et al. (1950) noted that starving people eat very slowly: "Toward the end of starvation some of the men would dawdle for almost two hours over a meal which previously they would have consumed in a matter of minutes".

The cognitive concept of dietary restraint refers to the control of body weight by the use of strategies to limit food intake, such as avoiding special foods or eating small portions (Polivy & Herman, 1985). The concept of restrained eating has been quite influential in the analysis of eating behavior (Bryant, King, & Blundell, 2008). Dieting occurs periodically among restrained eaters, it is not a permanent behavior, but an attitude manifest by rules and intensions to restrict food and losing weight (Heatherton, Herman, Polivy, King, & McGree, 1988). Previous studies have shown that dietary restraint is related to self-reported pathological eating behavior and influences both perceived hunger and actual eating behavior measured by calories consumed, and rate of intake was unrelated to dietary restraint (Smith et al., 1998). Thus, the term 'dietary restraint' or 'restrained eater' does not actually describe the way an individual eats, but instead refers to the attitude or intention the person holds toward eating and food (Bryant et al., 2008; Lowe & Levine, 2005).

Another influence on food consumption is disinhibition, e.g., inhibition of dietary restraint, which is the tendency toward over-eating in the face of a challenge. Disinhibition is reflected in excessive eating at an increased rate and is thought to be the result of loss of control (Bryant et al., 2008).

Eating disorders

Eating disorders, including anorexia nervosa, bulimia nervosa and eating disorders not otherwise specified are considered chronic psychiatric disorders which are difficult to treat; outcome remains poor, anorexics and bulimics have about a 10% chance of recovering in ten years (Von Holle et al., 2008) and most treatments have minor or unknown effects (Bulik, Berkman, Brownley, Sedway, & Lohr, 2007). The analysis of eating disorders conforms to the cognitive model; both anorexia and bulimia are considered effects of mental predispositions. This explanatory model is discussed in paper I. In the context of eating behavior it is interesting to note that eating disorders are thought of a mental disorders rather than eating disorders and perhaps for this reason relatively few attempts to examine how anorexics and bulimics actually eat have been reported. While individual bulimics may eat at a higher than normal rate (Kissileff, Walsh, Kral, & Cassidy, 1986), there are no reports of e.g., the rate at which anorexics eat.

A method to treat eating disorders was developed at the Section of Applied Neuroendocrinology, Karolinska Institutet. The method is based on a neurobiological framework (Bergh & Sodersten, 1996; Sodersten et al., 2008) and uses eating behavior as an intervention. Patients practice eating using Mandometer®, a development of the method for recording food intake, described in the method section. The treatment was found to be effective in a randomized controlled trial, brought an estimated 75% of eating disorder patients into remission in 14 months on average and had a relapse rate of about 10% within a year after discharge (Bergh et al., 2002). The central intervention in this treatment is Mandometer®, a device that assists patients as they practice eating. On the view that eating disorders are eating disorders it is hypothesized that eating behavior is the cause of the psychological condition of the patient (paper I) and a detailed study of human eating behavior is therefore the focus of this thesis.

Measuring eating behavior

The study of eating behavior in animals and humans shows that much can be learned by detailed and sensitive measurements of the ingestive process (Brunstrom, 2005; Cottone, Sabino, Steardo, & Zorrilla, 2007). Thus, the microstructural analysis explores the details of eating responses within a single meal; the "how" of eating. Studying eating behavior within this framework has contributed to our understanding of the learned properties of eating, such as palatability (Yeomans, 2000, 2006) and satiation (Bellisle, Guy-Grand, & Le Magnen, 2000; Guss & Kissileff, 2000; Westerterp-Plantenga, 2000).

The first objective measure of the time course of eating during the meal in humans in the laboratory was made by Jordan and colleagues (1966); in this test the subjects ingested a solution via a straw connected to a hidden container. The technique was further developed by Meyer and Pudel (1972), who first suggested an association between the pattern of eating and the development of biological satiation. After pioneering theoretical and technical (Kissileff, Klingsberg, & Van Itallie, 1980) contributions by Kissileff, computerized methods were developed. Also, an interest in the relationship between the structure of eating behavior and the behavioral treatment of obesity emerged with the control of meal size in focus (Kissileff et al., 1986; Westerterp-Plantenga et al., 1990; Yeomans, 1998).

Pudel et al. (1971) and Kissileff et al. (1980) described the now standard method for continuous recording of food intake in man. The subject places a plate on a scale and puts food on the plate and a computer records the weight loss of the plate during the meal. Mandometer®, a further development of this method, provides instant feedback on how much and at what rate to eat via a computer screen during the meal (see method section).

Cumulative Food Intake Curve

Data on food intake and meal duration are obtained from the eating monitor during the meal and yield the cumulative food intake curve (CIC), first suggested by Pudel and Meyer (1972) and confirmed by Kissileff et al. (1982). Thus, in the CIC food intake is fitted to a quadratic equation $y=ax^2+bx+c$, where y is food intake, a is the rate of deceleration, b is the initial speed of eating and c is the amount of food at the start of the meal, which is obviously = 0. This model accounts for 97–99% of the variance of the eating curves and is thus highly accurate (Hubel, Laessle, Lehrke, &

Jass, 2006). The initial eating rate has been regarded as measures of eating drive (Davis & Levine, 1977), the desire to eat (Yeomans, Gray, Mitchell, & True, 1997). The rate of deceleration has been shown to be consistent within subjects from time to time (Hubel et al., 2006; Westerterp-Plantenga, 2000). Three eating patterns have been identified based on the change in eating rate over time: decelerating, linear and accelerating (Barkeling, Rossner, & Sjoberg, 1995; Kissileff & Guss, 2001; Westerterp-Plantenga, 2000). Decelerated eating refers to a significant drop in the speed of eating during the second part of the meal (Westerterp-Plantenga, 2000). Interestingly, Meyer and Pudel (1972) thought of this eating curve as reflecting biological satiation, although they did not provide a biological marker to support their claim. By contrast, a linear eating curve was viewed as reflecting the inability to experience satiation (Kissileff, Thornton & Becker, 1982; Meyer & Pudel, 1972); again, however, direct supporting biological evidence was lacking. The third eating curve, an accelerated speed of eating is not observed in normal subjects, but has been described in e.g., children with the Prader Willi Syndrome (Lindgren et al., 2000) and among individual bulimic patients during binges (Kissileff et al., 1986). This pattern of eating is thus a rather disturbed eating behavior (Elfhag, Barkeling, Carlsson, & Rossner, 2003).

Experimental manipulations have included changes in palatability (Bobroff & Kissileff, 1986), physical state of meal (Kissileff et al., 1980), pharmacological effects (Muurahainen, Kissileff, Lachaussee, & Pi-Sunyer, 1991), body weight, deprivation and gender (Kissileff et al., 1982), factors which may affect the characteristics of the CIC. Obesity (Laessle, Lehrke, & Duckers, 2007) and personality (Elfhag et al., 2003) have also been suggested to affect the shape of the CIC.

The average speed of eating during the meal, i.e., a measure that does not take the shape of the CIC into consideration, has been shown to be consistent within subjects but affected by the hedonic properties of the food, satiety, hunger and food deprivation (Barkeling et al., 1995; Bellisle & Le Magnen, 1981; Laessle, Wurmser, & Pirke, 2000; Spiegel, Kaplan, Tomassini, & Stellar, 1993; Westerterp, Nicolson, Boots, Mordant, & Westerterp, 1988). In these studies, the stability of the eating rate has been viewed as a characteristic of the individual, i.e., as a habitual eating style.

Because eating disorders mainly affect women, this thesis has mainly studied eating behavior in women. On the hypothesis that eating behavior is the cause of the condition of eating disorder patients, the thesis has the following aims.

Aims

1. Review of outcome in anorexia nervosa, theoretical background of available treatments and launch of the hypothesis that eating behavior is a cause of the psychological change in anorexia.
2. Description of eating behavior and the development of satiety, including the effect of experimental change of eating rate on food intake and satiety.
3. Test of the effect of practicing eating at the default decelerated rate on restrained eating, a postulated cognitive controller of eating and the effect of disinhibition.
4. Test of the effect of fasting, the major risk factor for anorexia nervosa, on eating behavior in men and women.
5. Observation of eating behavior in a part of the real world, the school dinner in children in secondary school and the effect of experimental manipulation of eating rate.

Materials and methods

Participants

Paper I Fifty-eight female patients, who were diagnosed with anorexia nervosa and who were treated to remission and remained in remission for 5 years are described. The patients were divided into two groups. Group 1 (n=27, age = 16.3±0.7 years; BMI <14), and group 2 (n=18, age = 17.6±0.6; BMI >15.5) at admission. The other 13 patients had a BMI in between these two groups and were excluded. The patients had been treated before at other treatment sites 2.1±0.3 (group 1) and 1.6±0.3 (group 2) times. They had been ill for 2.4±0.4 (group 1) and 3.2±0.5 (group 2) years.

Paper II Forty-seven women (age = 21.2±1.8 years; BMI = 22.2±1.9 kg/m^2) were recruited from a nearby college campus. They completed a health questionnaire to determine that they were healthy, non-smokers, free from food allergies and had not had an eating disorder or used drugs that affect food intake. Athletes and pregnant and lactating women and four women who did not meet these criteria were excluded. 30 healthy men and women of the same age and body weight were tested to examine the reliability of the method.

Paper III Thirty-four women (age = 21.1±1.6 years; BMI = 22.1±1.7, kg/m^2) were selected as described above. They were selected from a bigger group for eating at a constant rate, i.e., a≈0 in the CIC.

Paper IV Twenty-one women participated in one experiment (age = 17.2±0.9; BMI = 22.2±1.4 kg/m^2) and 13 women (age = 19.6±0.8; BMI = 21.2±1.9 kg/m^2) and 9 men (age = 17.9±1.1; BMI = 21.2±1.8, kg/m^2) participated in another. They were recruited as described above.

Paper V Eighteen girls (age = 13±0.7 years, BMI = 19.7±1.1) and 12 boys (age = 13±4 years, BMI = 20.1±1.5) in secondary school were recruited by an ad. The children were healthy and had no eating disorders symptoms as determined by the Eating Disorders Inventory (EDI).

Foods

The food was familiar to the subjects, rice, sliced chicken and vegetables (Nasigoreng Findus, Bjuv, Sweden; 400 kJ, 4.5 g protein, 18 g fat and 15 g carbohydrate/100 g) and was prepared fresh before each meal; its temperature was 65 °C when served from an oven.

Figure 1. The latest version of Mandometer®.

Mandometer®

Mandometer® (Figure 1) is a development of the method described by Pudel and Meyer (1972) and Kissileff et al. (1980) and records food intake in the same way. Data on food intake and the duration of the meal generated by Mandometer® were fitted to a quadratic equation to yield the CIC.

Curves are displayed on the Mandometer® touch screen to guide patients/participants how much and at what rate to eat during the meal (green curve, Figure 2a). The subjects are able to follow these training curves, because they can see their own eating rate appearing on the screen during the meal (lilac curve, Figure 2b). If the subject deviates by more than 15% from the pre-defined rate, the text: "You eat too fast" or "You eat too slow" appears on the screen (Figure 2c).

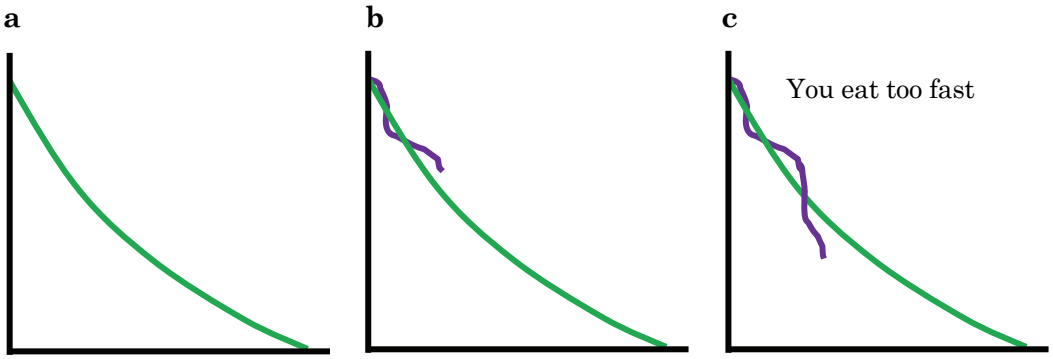

Figure 2. A preprogrammed CIC is displayed on the monitor (a), the subject´s eating rate appears on the monitor (b) and if it deviates from the CIC, a message, "You eat too fast", appears on the screen (c) to allow the subject to adjust her/his speed of eating to the CIC.

Mandometer® also displays a rating scale for the estimation of satiety on the computer screen during the meal. The scale is a revised Borg CR10 Scale (Borg, 1982) with a vertical list composed of labeled categories with ratio properties describing increasing intensities of satiation ("Nothing at all" =0, "Extremely strong = 100 and "Maximal" >100). At regular intervals, subjects are asked to rate their satiations by pointing at the scale on the touch screen (Figure 3).

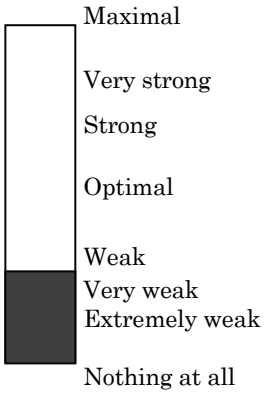

Figure 3. The rating scale used to measure the progression of satiation during the meal.

The cumulative satiety curve was fitted to a two-parameter sigmoid curve: $y=\alpha/(1+e^{-(x-x0)/\beta})$, where α=100, i.e., the maximum of the satiety rating scale, x^0 = time at which satiety has reached the half maximal value, which corresponds to the inflection point of the curve and ß = steepness of the.

As with eating rate, subjects also get feedback for the perception of satiety. Thus, an s-shaped curve, derived from data generated by healthy

volunteers (orange curve, Figure 4), guides the subjects how to perceive satiety during the meal.

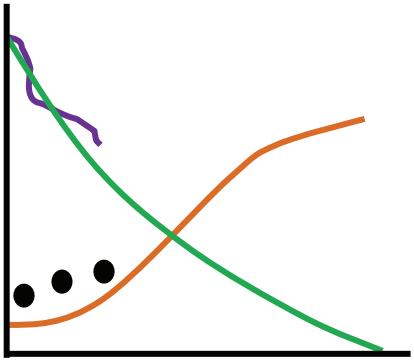

Figure 4. Subjects´ ratings of fullness (Figure 3) are plotted on the Mandometer® screen (black dots) in relation to an s-shaped practice curve (orange curve) just as eating rate (lilac line) emerges on the screen during training in relation to a decelerated practice curve (green line).

Thus, Mandometer® shows simultaneous recording of eating rate and the development of satiety (Figure 4) and allows experimental manipulation of both eating rate and satiety by changing the characteristics of the curves.

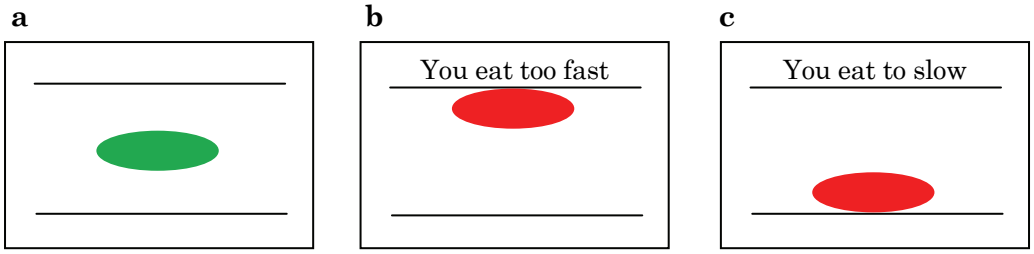

Figure 5. Two 15 mm long lines were displayed on the Mandometer® screen and the subjects were informed that their speed of eating, which appeared as a green oval on the screen (a), should be kept between the lines. If the subjects deviated from the proper speed, the oval turned red and the following message appeared on the screen: "You eat too fast" (b) or "You eat too slow" (c).

A second type of feedback for eating rate was also used. Two lines were displayed on the monitor indicating the upper and lower limit within which the subjects´ eating rate should be maintained during the meal (Figure 5a). These limits were 15% above and below the average value calculated from the CIC that the subject had generated in preliminary testing. If subjects deviate from the preprogrammed CIC, the message "You eat too fast" or "You eat too slow" appeared on the screen (Figure 5b, c). A brief video of the use of Mandometer® is available at www.someguys.se/clients/mandolean/mandometer_popup.html.

Subjective measures

Dutch Eating Behaviors Inventory (DEBQ)

In all studies, except paper I, the subjects filled in the Dutch Eating Behaviors Inventory (DEBQ), as a measure of restrained, emotional, and external eating. The DEBQ, developed by van Strien (1985, 2002) contains 33 questions divided in three subscales; Restrained, Emotional, and External eating. The response ranges from 'never' to 'always' on a 5-point scale. The DEBQ has proved to have good reliability (Cronbach's alphas between 0.80 and 0.95).

Appetite, Mood and Psychopathology

Hunger ratings obtained by use of 100 mm Visual Analogue Scales (VAS) presented on a touch screen, subjects rated their hunger and desire to eat and how much they would eat before the meal. Furthermore, they rated the following aspects of their mood: happy, relaxed, restless and nausea. The vertical line on the VAS was anchored with the words "Not at all" and "Extremely" at each end. In addition, psychopathological symptoms were scored using a self-rating scale, the Comprehensive Psychopathological Rating Scale (Svanborg & Asberg, 1994).

Procedure

Four experiments were conducted in the Mandometer® laboratory and the last study, a combined observational-experimental study, was conducted in a school restaurant. Subjects were scheduled for the experiment, or the test lunch, between 11:00 A.M. and 12:30 P.M. and they were asked to refrain from snacking and drinking (except water) after breakfast, in one experiment they were asked to skip dinner the day before (fasting).

When they first arrived, the subjects were informed about the procedures. Their height and weight were measured and they filled in a health questionnaire. They completed the DEBQ by the end of the experiments when they also were given detailed information about the research. Subjects were tested individually, with food presented on an adjacent table and they were instructed not to read or talk on their cell phone when eating. Nasigoreng was served in all meals and the subjects were instructed that they could eat as much as they wanted. A glass and pitcher of water were left on the table. Subjects completed mood and appetite rating before and after their lunch.

Results

Paper I It took 22±3.3 months for group 1 vs. 10.9±1.4 months for group 2 ($p<0.01$) to go into remission. However, the time course of recovery of the normal pattern of eating behavior and the decrease in psychiatric symptoms occurred in parallel and were maintained during a 5-year follow-up (Figure 6). In parallel, their BMI and increased to normal.

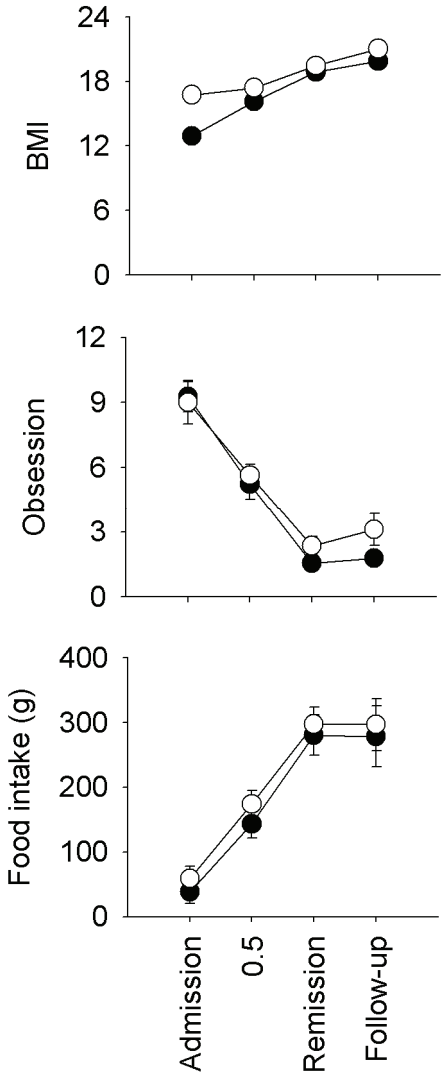

Figure 6. Normalization of BMI, obsession and food intake in anorexic patients treated to remission and followed-up.

Paper II On the basis of a Mandometer® test in the absence of feedback on the computer screen, women could be divided into those with a decelerated CIC, decelerated eaters, and those with a linear CIC, linear eaters. Thus, while decelerated eaters ate at an initially higher speed that linear eaters and their speed of eating decreased during the meal, linear eaters ate at approximately the same speed throughout the meal (Figure 7). There were, however, no differences between the two types of eater in the amount of food consumed and the duration of the meal (paper II).

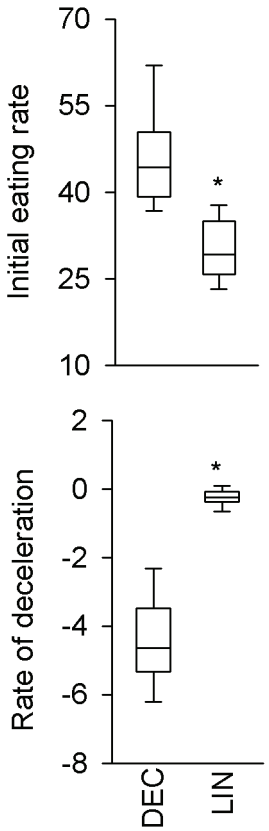

Figure 7. Characteristic of the CIC in decelerated (DEC) and linear (LIN) eaters.

Decelerated eaters responded to experimental challenges in a completely different way compared to linear eaters. For example, while they ate less food when the speed of eating was increased, linear eaters ate more and while they ate about the same amount of food when the speed of eating was experimentally decreased, linear eaters ate less (Figure 8).

Further differences emerged in the other experimental conditions (see paper II), the important point in the context of this summary is that based on the rate of deceleration in the CIC, women could be classified into decelerated and linear eaters, with linear eaters less able than decelerated eaters to monitor their intake when challenged to eat at a rate that deviated from their habitual rate.

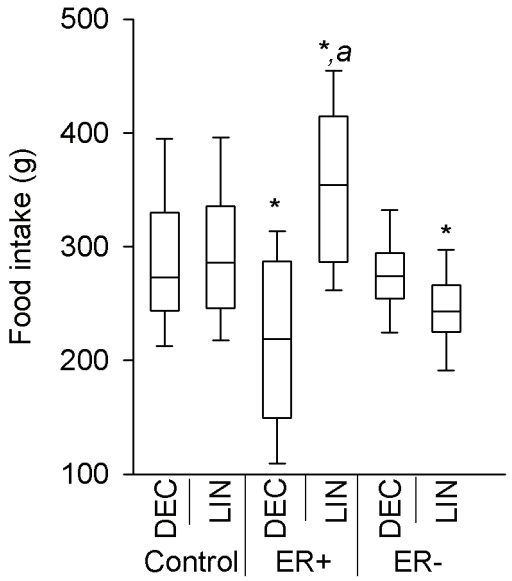

Figure 8. Food intake decelerated (DEC) and linear (LIN) eaters without constraints (Control) and when eating at an increased (ER+), or decreased (ER−) rate.
*Whitin group, [a]between group $p<0.01$.

The rating of satiety during the meal was modelled by the same two parameter sigmoid curve in both decelerated and linear eaters in both basal and experimental Mandometer® tests. We made the interesting observation that when the linear eaters were challenged to eat at a reduced rate, they rated their satiety higher than in the control condition despite eating less food and although they ate more food when eating at a higher rate, they did not increase their rating of satiety during the meal (paper II).

Finally, while linear eaters scored higher on the restraint scale of the DEBQ questionnaire, the rate of deceleration, not the DEBQ restraint score, was related to the amount of food eaten (paper II).

Paper III The finding that linear eaters eat more food when challenged to eat at a higher rate and that they scored higher on the DEBQ restraint scale (paper II) offers a possibility to examine the relationship between eating behavior and the cognitive construct of restrained eating.

A group of women, selected as linear eaters practiced eating at a decelerated rate for eight weeks by adapting to a decelerated curve on the Mandometer® screen (Figure 2). Interestingly, when tested after the training, in the absence of feedback, the women maintained a decelerated pattern of eating (Figure 9). Furthermore, while they overate when challenged to eat at an increased rat before the training, they ate less food in this test of disinhibition after training (Figure 9) and their DEBQ restraint score decreased (paper III).

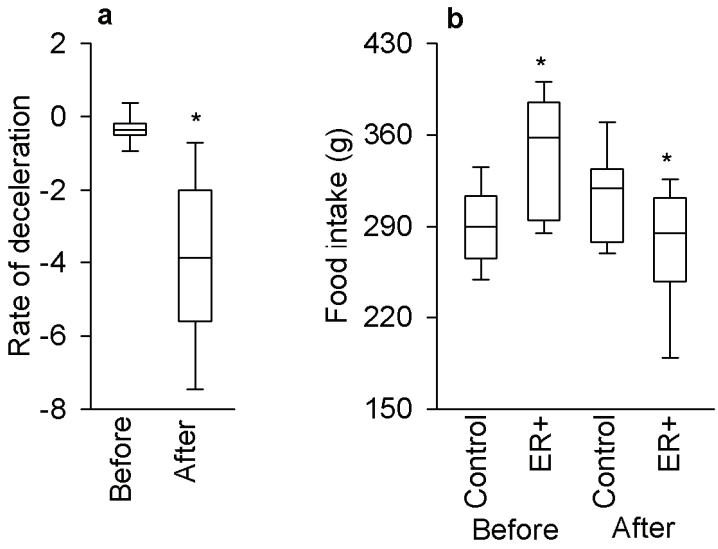

Figure 9. Increased rate of deceleration in the CIC in linear eaters after training to eat at a decelerated rate for eight weeks (a). While the linear eaters ate more food when eating at a higher rate before training, they ate less food in this test after training (b). *p<0.01.

The results reported in paper II suggest that linear eaters are at risk of developing disordered eating behavior and lose control over food intake. The results of paper III suggest, however, that the risk can be reduced by giving linear eaters the opportunity to practice eating at a decelerated rate. Interestingly, such training reduced a measure of the cognitive construct of restrained eating, suggesting that linear eating may be a cause of a cognitive state. This is in line with the basic assumption of the Mandometer® treatment of patients with eating disorders, i.e., that eating behavior is a cause of psychological change in the patients and that eating behavior therefore can be used as an intervention (Bergh et al., 2002). Further research is necessary to test this hypothesis, i.e., whether linear eaters need to practice continuously to maintain a decelerated pattern of eating behavior. In the clinic, once patients have regained a normal pattern of eating, they do not need further assistance from Mandometer®.

Paper IV Dieting is the main risk for anorexia nervosa, which is far more prevalent in women than in men. In a preliminary study we found that whereas women eat less after deprivation of food, men eat more (Södersten et al., 2006). This finding was confirmed in paper IV; we also found that more women than men are linear eaters and that the more the rate of deceleration in the CIC approaches 0 in unrestrained conditions, the less an individual woman will eat after deprivation of food (Figure 10). Men

respond in the opposite way; they eat more food after deprivation and the rate of deceleration of their CIC increases (paper IV).

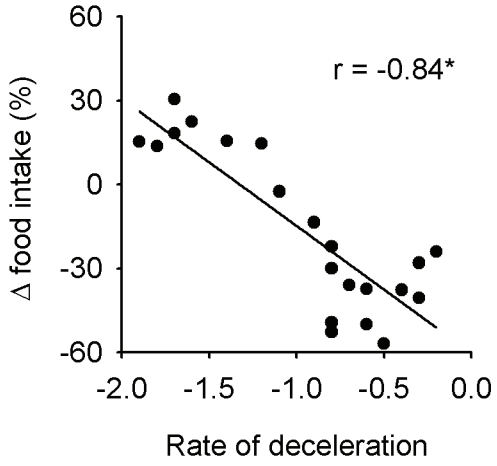

Figure 10. Correlation between the change in food intake (Δ food intake) and the rate of deceleration in the CIC in women who skipped dinner the day before the test. Δ food intake is expressed as percent of intake in the non-deprived test.

Interestingly, the sex difference in the response to fasting was reversed by providing feedback on the Mandometer® screen during the meal (Figure 11).

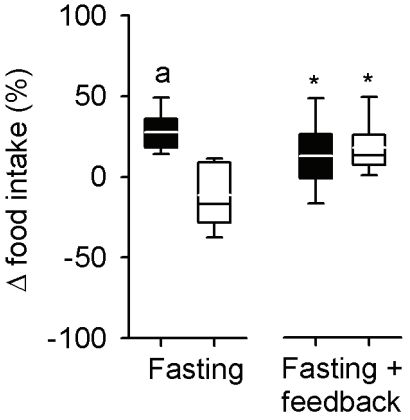

Figure 11. Change in food intake (Δ food intake) after fasting in men (black bars) and women (white bars). Δ food intake is expressed as percent of intake in the non-deprived test. $p<0.01$ *within and [a]between group.

While these results provide further support for our view that linear eating is an eating behavior that puts an individual woman at risk, the results suggest that the risk can be reduced by practicing eating at the proper rate. This supports the use of Mandometer® as a clinical intervention in the management of the eating disorder patients.

The observations made so far in this thesis offer some support for our hypothesis that eating behavior is not "clamped" by biological constraints following after e.g., a period of fasting.

Paper V Children in secondary school have to take their school dinner in a short period of time. This situation may provide a real-life test of the effect of behavioral disinhibition. In a final study we therefore examined how children in secondary school eat their school dinner.

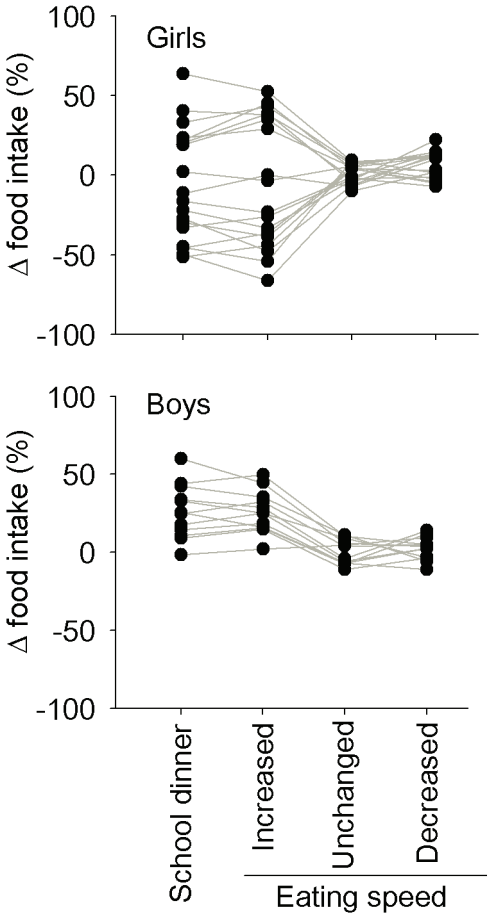

Figure 12. Food intake in 18 girls and 12 boys in secondary school. The change in food intake (Δ food intake) is expressed as percent of intake in a test in a relaxed condition. Eating speed was either Increased, Unchanged or Decreased via feedback from a CIC on the Mandometer® screen. The school dinner was eaten without interference.

We found a marked difference in eating behavior and food intake when the children were allowed to eat in a relaxed condition without constraints compared to when they ate their school dinner. The rate of eating was increased by 50% and only one boy and two girls maintained their intake at the relaxed level when eating the school dinner; about half of the rest of the girls ate more food, the other half ate less food and almost all boys ate more food (Figure 12). These changes were reversed by providing feedback on the Mandometer® screen during the school dinner with a CIC that mimicked the speed of eating in the relaxed condition or a CIC with a reduced eating speed and they were replicated by Mandometer® feedback from a CIC that mimicked the speed of eating of the school dinner (Figure 12).

Apparently, the conditions of the school dinner greatly distort the eating behavior among children in secondary school but the changes are

reversible. However, while food intake between eating in the relaxed condition and the other conditions was highly consistent in individual boys, girls maintained their intake at the relaxed level only when their speed of eating was maintained at their relaxed level or decreased (Figure 13).

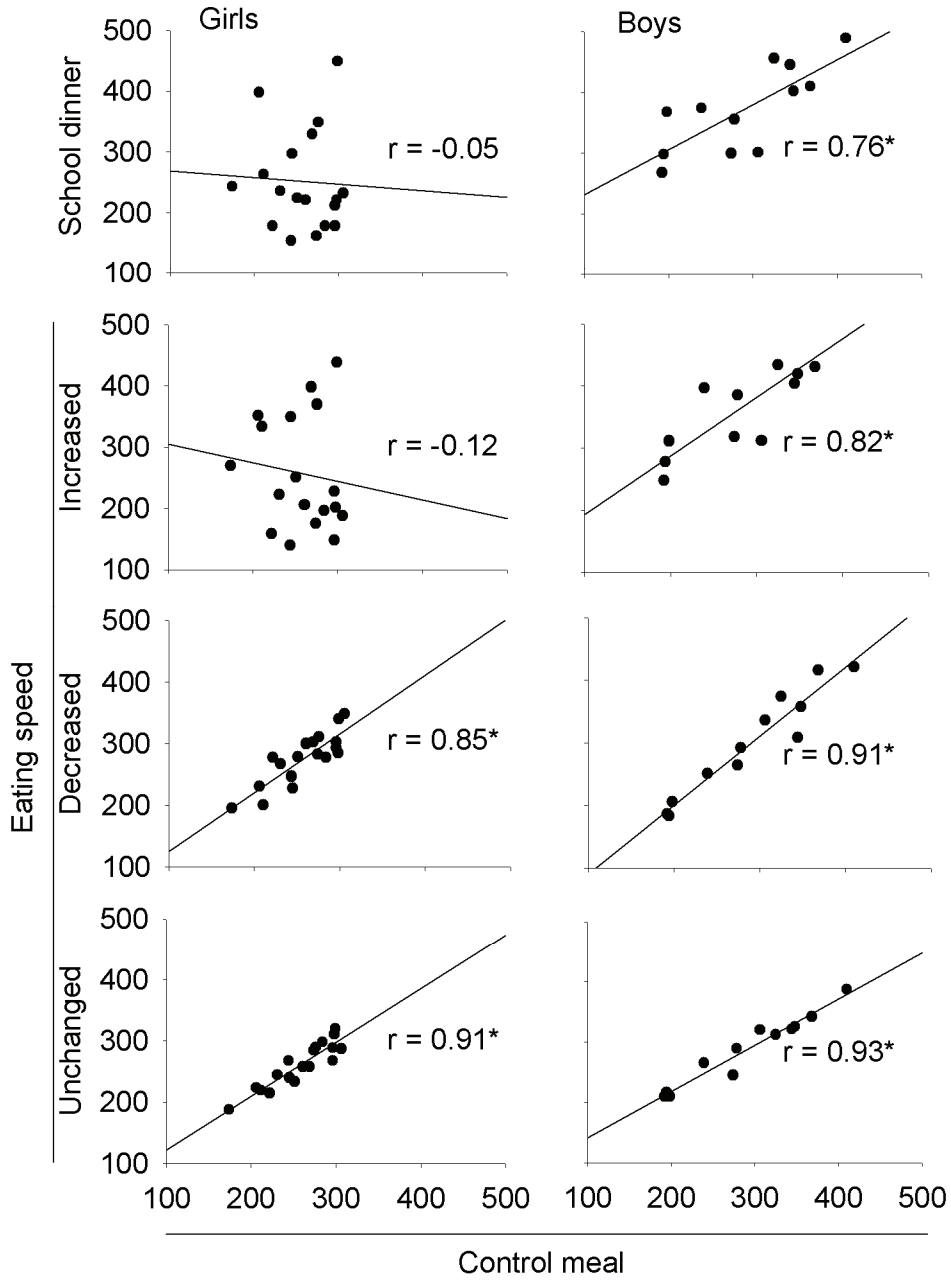

Figure 13. Food intake in relaxed (Control) condition and after experimental maintenance (Unchanged), decrease, or increase of eating speed and during the school dinner in girls and boys. *p<0.01.

Discussion

Theoretical and clinical background

Paper I in this thesis sets the stage for the subsequent experimental work by a reviewing of the theoretical background, outcome and treatment of anorexia nervosa. Because outcome remains poor (Von Holle et al., 2008) the theoretical bases for commonly used treatments is questioned. This appears reasonable; improvement of outcome is the obvious goal of clinical research. The review iterates a previously suggested framework for anorexia nervosa (Bergh & Sodersten, 1996) and launches the hypothesis that eating behavior mediates between the environment and the condition of the patient. We recently updated this point of view and detailed the neurobiological engagement (Södersten et al., 2008), which, therefore, will not be repeated here.

The prototype eating disorder, anorexia nervosa, has a very long history, there is a myriad of colorful descriptions in the non-medical literature (Vanderlinden, Van Dyck, Vandereycken, & Vertommen, 1994). The perhaps best "medical" description of anorexia nervosa was provided by Gull (1874), who noted that patients were hypothermic and hyperactive and therefore targeted his interventions at these symptoms. Gull reported favorable clinical effects but it is unclear precisely how he managed his patients. By contrast, subsequent treatments, including those used at present, have targeted the mental symptoms of the patients and essentially failed; the present hypothesis suggests that the mental symptoms are mediated by the change in eating behavior and that the eating behavior of the patients should therefore be the focus of treatment. We presented data on a group anorexic patients with a very low BMI and another group with a higher, yet low, BMI who were treated from admission to remission and followed up for five years showing that as eating behavior normalized, the mental symptoms dissolved (paper I). The eating behavior and mental symptoms of the patients were similar despite the difference in BMI and, normalization of the mental symptoms occurred in close parallel with the normalization of eating behavior. While the cause-effect relationship between eating behavior and mental symptoms is unclear under these conditions, the results are the basis for the hypothesis that eating behavior is the cause of the mental symptoms. Indirect support for this hypothesis is

derived from the failure to improve outcome by targeting the mental symptoms.

Project, in brief

On the basis of the theoretical starting point and the results reported in paper I, it became important to use a method for the study of eating behavior that allows experimental manipulation of the characteristics of this behavior. It was also desirable to examine if there is a pattern of eating that resembles that of patients with eating disorders, if a change in eating behavior can cause a cognitive change seen in eating disorder patients and if individuals who are exposed to a risk factor for disordered eating, such as fasting, will develop behavioral signs of an eating disorder. Finally, we examined a situation in the real world in which the conditions of eating impose constraints such that the participants, children in secondary school, respond in a way that may put them at risk of developing disordered eating behavior.

The meal: mathematical model and experimental challenges

Eating behavior It has been suggested that the meal is the basic unit for the study of eating behavior (Strubbe & Woods, 2004). The work presented here follows this approach by using a method which simply plots food intake over the duration of the meal, thus producing the cumulative intake curve (CIC). The perhaps most conspicuous characteristic of this curve is the rate at which eating changes over the course of the meal. As first pointed out by Pudel and Meyer (1971), the CIC takes the form of a quadratic curve. Confirmatory evidence was subsequently published (Kissileff et al., 1982). This pattern of eating is stable from test to test (Hubel et al., 2006; Martin et al., 2005; Pudel, 1971; Westerterp-Plantenga, 2000). We replicated these results in paper II but pointed out that a quadratic curve cannot predict intake beyond the meal; a positive quadratic term indicates that intake escalates over time, a term = 0 indicates that eating increases constantly at the same rate and a negative term indicates that intake declines over time. The model, therefore, describes intake within, but not beyond meals. However, the quadratic equation adequately models the meal, the unit of eating behavior (Strubbe & Woods, 2004).

In addition to recording the eating pattern in "baseline meals" Mandometer®, the method used here, also allowed us to manipulate eating conditions by offering feedback on the computer screen. Subjects can be

asked to follow curves of eating which deviate from the baseline CIC that they generate in unrestrained conditions. In paper II, subjects were first found to differ in the rate at which their eating behavior changed over the course of the meal; about a third of the women tested generated decelerated CICs, two third generated linear CICs. This observation is the basis for our introduction of the concepts of "decelerated" and "linear" eaters. These two types of eater also differed in that decelerated eaters eat an initially higher rate than linear eaters. However, there were no differences in the amount of food consumed or in the duration of the meal (paper II).

We found that decelerated and linear eaters differ markedly in their response to manipulation of the meal using feedback on the Mandometer® screen. Thus, while linear eaters ate more food when asked to eat at a higher rate, decelerated eaters did not. Conversely, in contrast to decelerated eaters, who ate about the same amount of food when eating at a reduced rate, linear eaters actually ate less food when challenged to eat at a lower than normal rate. We speculated that decelerated eaters have difficulty eating at a higher rate because of their initially high rate of eating. While linear eaters managed this challenge, perhaps because of their lower initial eating rate, the fact that they ate more food in this condition may reflect an inability to adapt. Their decreased intake when challenged to eat at a lower than normal rate may likewise reflect a reduced ability to adapt. These differences in the response to experimental changes in eating rate between decelerated and linear eaters provided the basis for our suggestion that the decelerated pattern of eating may be the default pattern of eating. Long ago, Skinner (1938) listed a variety of behavior, many of which displayed decelerated CICs over time, including eating behavior, although the mathematical models differed somewhat from the one used here (see paper IV). Observations on the ontogeny of the CIC offer further support for the possibility that a decelerated CIC is the default eating pattern. Thus, it was reported long ago that children generate decelerated CICs at ages 4-6 and that older children and adults display more linear CICs (Jung, 1973). Our finding that 13 year old children generated decelerated CICs is in line with these previous studies (paper V). These observations raise the question why the rate of deceleration decreases with age and also open the possibility that the shape of the CIC might have changed over the years since the studies of Pudel and Meyer (1972) and Jung (1973). Eating behavior may have become more linear over the years.

The differences in the response to experimental changes in the rate of eating between decelerated and linear eaters are the basis for our suggestion that decelerated eaters may be protected from the risk of developing a disordered pattern of eating. They cannot eat overly fast due

to their initially high rate of eating, in fact they experienced nausea when trying to eat quickly (paper II), and while they easily adapted to a lower than normal rate of eating, they did not over-eat, nor under-eat, in this condition. Linear eaters, by contrast, ate more and less when eating at a higher and lower than normal rate and so they appear less able to regulate their intake. The concept of disinhibition has been introduced to denote the failure to maintain food intake and therefore to regulate body weight among people who are at risk of developing disordered eating (van Strien, 1997). Our findings that linear eaters are unable to adjust their intake when challenged to eat at a higher or lower rate suggest that these behavioral tests can replace the cognitive concept of disinhibition. This would appear advantageous as the concept of disinhibition has generated inconsistencies (see discussion in paper III). Hence, eating behavior in response to experimental increases and decreases in eating rate was used as a test of disinhibition in this thesis.

Previous studies have reported an association between increased food intake and inter-meal pauses. Thus, 5 to 60sec long pauses after every 50 g of intake were found to increase food intake (e.g., Yeomans et al., 1997). In the present study, we found that decelerated and linear eaters responded differently to taking pauses within the meal. While linear eaters ate more food when the meal was interrupted, decelerated eaters did not. Environmental changes during the meal, such as interruptions, are well known to affect intake (Wansink, 2004) and this is apparently yet another challenge that makes regulation of intake more difficult for linear eaters. Interestingly, the linear eaters ate more rapidly when they ate food during these interrupted meals; hence their eating behavior in this condition was similar to when their rate of eating was experimentally increased. The suggestion that taking pauses while eating may reduce the intake of food (Brownell, 2000), therefore, was not confirmed by the present study, particularly not among linear eaters. This intervention was originally suggested to slow down the rate of eating, which was suggested long ago to reduce intake (see discussion in Yeomans et al., 1997), but in linear eaters, the opposite effect was obtained and, in the original studies, eating rate was not measured.

Satiety In addition to allowing experimental manipulation of eating rate, Mandometer® makes it possible to measure the development of satiety during the meal as well. While before and after meal ratings of satiety are common (e.g., Westerterp-Plantenga, 2000), results on continuous recording of the feeling of fullness during the meal been reported less often (Yeomans, 2000). We found that satiety emerges during the meal in a similar manner in both decelerated and linear eaters; the same, two parameter sigmoid

model fitted the cumulative satiety curve in both types of eater (paper II). However, some interesting results emerged among the linear eaters. Thus, when compared to their eating behavior in the unrestrained condition, they consumed more food when eating quickly yet they did not experience a higher level of satiety and while they consumed less food when eating slowly they experienced a higher level of satiety (paper II). This is the first indication in the present thesis that linear eaters adopt the eating behavior typical of patients with eating disorders such as Binge Eating Disorder (BED) and anorexia nervosa. A recent direct comparison between the eating behavior of linear eaters challenged to eat at an increased and decreased rate and the eating behavior of BED and anorexic patients confirmed this hypothesis; just as BED patients, linear eaters eat more food yet experience no increase in satiety when eating at an increased rate and, just as anorexic patients, they eat less food yet experience an increased level of satiety when eating at a decreased rate (Ioakimidis, Zandian, Bergh, & Södersten, 2009 in press). It remains, however, to be determined how the satiety estimations generated by Mandometer® can be used to facilitate treatment of eating disorder patients; it seems possible that, like the cognitive characteristics of eating disorder patients, satiety may be an epiphenomenon to eating behavior.

Cognitive control The concept of restrained eating was introduced long ago (Herman & Mack, 1975) and emerged from Schachter´s concepts of internal and external control of eating (Herman & Polivy, 2008; Schachter, 1974). As recently pointed out, the cognitive construct of restrained eating has dominated the analysis of eating behavior and also been thought of as "a set of endurable characteristics" of the individual and as a "cause" of eating (Bryant et al., 2008). This strategy has led to a disassociation between physiology and behavior in which cognitive factors are even thought of as emancipated from physiology; "… the adoption of a cognitively regulated eating style … is necessary if the physiological defense of body weight is to be overcome" (Polivy & Herman, 1985). This development continues (van Strien, Engels, van Staveren, & Herman, 2006; van Strien, Herman, Engels, Larsen, & van Leeuwe, 2007) but is surprising as it appears to be re-introduction of dualism; as we pointed out, cognitive factors are, of course, not emancipated from physiological context (paper III). Also, we questioned the cause-effect relationship as the relationship between eating behavior and cognitive concomitants has not been experimentally determined; there is no a priori reason for cognitive control of eating behavior, the causal relationship may very well be the other way around. In line with the latter possibility, the rate of deceleration, not score on a scale of restrained eating, correlated with food intake (paper II). In

fact, it has been argued that eating behavior occurs mainly in the absence of mental engagement even to such an extent that it appears "mindless" (Wansink, 2006).

The results reported in paper II is the first step in our ambition to restore behaviorism; a good reason for replacement of the cognitive model of eating behavior is the lack of validity of the concept of restrained eating as revealed by variation in outcome measured by available questionnaires (Stice, Fisher, & Lowe, 2004; Williamson et al., 2007), reviewed in paper III) and another, compelling reason is the lack of effect of cognitive treatment of patients with eating disorders (reviewed in paper I).

Linear eaters turned decelerated: behavioral control of cognition

Paper III tested the hypothesis that a change in eating behavior can cause cognitive change, which is perhaps the most important part of the hypothesis which is the basis for Mandometer-treatment (Bergh et al., 2002; Södersten et al., 2008). Women, selected for eating at a constant rate, i.e., linear eaters, practiced eating following a decelerated eating curve displayed on the Mandometer® screen for eight weeks. When tested after the training they maintained a decelerated pattern of eating and, most significantly, they scored lower on the restraint scale of the DEBQ. This observation provides direct support for the hypothesis that a change in eating behavior can cause cognitive change; you are how you eat! Equally interesting, while these linear eaters overate in the behavioral test of disinhibition (eating at an increased rate), which was launched in paper II, they did not overeat in the disinhibition test when converted into decelerated eaters as a result of practicing eating at a decelerated rate. However, these results should be followed up over, the changes in eating behavior and restrained eating may merely be temporary.

Practicing eating with Mandometer® has been used in bringing more than 500 patients into remission in our clinic and is therefore a useful intervention in the management of eating disorders. Once patients have regained a normal pattern of eating, their psychopathological symptoms are also back to normal levels (Bergh et al., 2002; paper I). By contrast, there are no reports in which cognitive training has induced a normal pattern of eating; in one study, outcome among anorexic patients was worse after cognitive therapy than after an alternative therapy (McIntosh et al., 2005) and the only report that cognitive treatment is beneficial in anorexia nervosa merely found a slight reduction in relapse after post-hospitalization treatment, the main effect in that study was a rapid

relapse, in both groups of patients studied (Pike, Walsh, Vitousek, Wilson, & Bauer, 2003).

Interestingly, the diagnosis on which cognitive behavioral treatment is reported to be effective and also best researched and evaluated is obsessive compulsive disorder. However, the behavioral part of the treatment, not the cognitive, causes the main effect (Clark, 2005). Yet, we advise caution in drawing a strict line between the behavioral and cognitive; the "cognitive revolution" in psychology may have overstated the difference between the two approaches (Bargh & Ferguson, 2000). We are not the only ones trying to reinstate behaviorism, cognitive scientists are aware of the possibility of explaining behavior without postulating mental or cognitive mediation. Human behavior is to a large extent "automatic" (Chartrand & Bargh, 1999); even "thinking" has been suggested to occur automatically or perhaps, paradoxically unconsciously (Dijksterhuis, Bos, Nordgren, & van Baaren, 2006). This arrangement may be to our advantage, e.g., when we are faced with a complex, as opposed to simple choice (Dijksterhuis et al., 2006).

Linear eating: the behavioral risk factor for disordered eating revealed by fasting

The main risk factor for anorexia nervosa is a reduction in food intake (Södersten et al., 2008). Hence, we studied the effect on a short period of fasting, skipping dinner, on subsequent eating behavior. In a preliminary experiment women were found to eat less food after such a fast than men (Sodersten, Bergh, & Zandian, 2006). Men ate more food than women in the non-deprived condition and even more food and at a higher average rate after fasting (Sodersten et al., 2006). On the basis of the findings in papers I and II, it was predicted that the rate deceleration in the CIC predicts the reduction in food intake after fasting; as the rate of deceleration approaches 0, the amount of food consumed decreases. This hypothesis was verified and the previously reported sex difference (Sodersten et al., 2006) was replicated. In addition, men responded to fasting by eating at an initially higher rate and with a higher rate of deceleration. While these results extend the results of previous studies, a comprehensive model of how fasting affects food intake lies ahead in time because the details of the CIC in both the non-deprived and deprived condition have not been extensively reported (reviewed in paper IV). More information is obviously important as anorexia nervosa develops over time. However, the present observations that more women than men are linear eaters, that linear eaters eat less after fasting, and that the linearity of eating increases after fasting in

women, but not men, are in line with the marked sex difference in the prevalence of anorexia nervosa. Anorexic women are linear eaters (Ioakimidis et al., 2009 in press) and it appears that this pattern of eating increases already after a brief period of fasting in women.

Importantly, we found that providing feedback on how to eat during the meal reversed the effect of fasting on food intake in both women and men (paper IV). This observation indicates that the biological consequences of fasting, which are different in women and men, do not preclude a normal intake of food in the sexes (reviewed in paper IV). These results are of considerable clinical importance. Firstly, they strengthen our hypothesis that linear eating, which is easily diagnosed using Mandometer®, is a behavioral risk factor for development of disordered eating and secondly, they support the possibility that linear eating can be managed using Mandometer®, which is the perhaps most important intervention of our clinical approach (Bergh et al., 2002).

The sex difference in the effect of a short period of fasting may disappear during prolonged starvation. Thus, an early report on animals suggested that the effect of food deprivation on eating behavior is biphasic; while short term deprivation increased intake and the rate of deceleration, four days of deprivation reduced intake and increased the linearity of eating (Bousfield, 1934). The present results indicate that men, like animals, increase their food intake in the short term, but it is long known that in the long term, men markedly decrease their rate of eating (Keys et al., 1950). However, in that study, food restriction was imposed on the men (Keys et al., 1950) and although starved men and women can continue eating less food when food is made available, starvation can also cause an increase in intake and the rate of eating (Södersten et al., 2008). Further discussion of the effects of fasting on food intake and the rate of deceleration in the CIC must await the collection of more experimental data, which will be difficult for ethical reasons. Studies on anorexic patients, however, clearly show that eating rate and linearity of eating are increased (Ioakimidis et al., 2009 in press), but we don´t know if anorexic men differ from women in this regard.

Eating in the real world may be dangerous: the school dinner is eaten too quickly

Finally, eating outside the laboratory was examined. Eating disorders develop at ages around 13 (Wentz, Gillberg, Anckarsater, Gillberg, & Rastam, 2009) and we examined how children in this age group, i.e., pupils in secondary school, eat their school dinner (paper V). Eating behavior

differed markedly during an unconstrained condition compared to the pattern of eating during the school dinner. The children increased their average speed of eating by about 50% and only two girls and one boy maintained their intake at the relaxed level. This change in eating behavior was prevented by provision of feedback on how to eat using Mandometer®. Also, the change in eating behavior during the school dinner was replicated by increasing the speed of eating experimentally using the same method as used in the other papers in the thesis. Hence, these results using Mandometer® yield the hypothesis that the increase in the speed of eating is the cause of the change in food intake seen in children in secondary school during the school dinner. This interpretation is consistent with the general hypothesis on this thesis that eating behavior can be considered a cause, rather than, as is more often the case, a mere outcome of some biological variation. On the more practical level, the results should encourage reform of the conditions of the school dinner; children in secondary school, and probably at the other levels in the school system, should be provided with enough time to eat their school dinner and the conditions should be relaxed to make the normal pattern of eating possible. The risk is obvious that the children may develop disordered eating unless these conditions are met.

Eating behavior, the brain and the mind

In an incisive essay, Crick (1989) noted that cognitive psychology and linguistics have failed to produce realistic solutions of the problem of the mind because, traditionally, they have paid insufficient attention to the normal function of the brain. While cognitive neuroscience is a step in the right direction, some cognitive scientist apparently still have difficulty, generating cognitive concepts that will be very difficult to relate to brain function (Marshall, 2009). This problem is easy to avoid in the context of the present thesis. Thus, chewing is long known to be anxiolytic (Hollingworth, 1939) and an exceptionally interesting recent paper reported that an inverse benzodiazepine receptor agonist reduces food intake by slowing down the rate of chewing in the rat at a dose below that which causes anxiety (Cottone et al., 2007). These observations open the possibility to explore the neurobiology of the causal relationship between eating behavior and the psychological symptoms of anorexia nervosa suggested in the present thesis, which is one of the future goals of our research group.

Conclusions

1. Outcome in eating disorders remains poor and a new approach is sorely needed. This thesis suggests that by targeting eating behavior, Mandometer® is a useful clinical intervention.

2. By eating at a constant rate, linear eaters are at risk of losing control over food intake. This risk appears when linear eaters are challenged to eat at a high or low speed.

3. By eating at a gradually decreasing rate, decelerated eaters may be protected from the risk of developing disordered eating.

4. Linear eating may be the result of repeated attempts to diet; a brief period of fasting increases the linearity of eating and reduces food intake in women. Men are decelerated eaters and may therefore be protected from the risks of eating disorders.

5. Psychological changes in eating disorder patients dissolve when patients have regained a normal pattern of eating; supporting the hypothesis that eating behavior can cause mental change. This hypothesis receives further support from the finding that the cognitive construct "restrained eating" may be an effect of eating behavior.

6. Eating behavior can be markedly affected by stressful conditions in real life, if children are not allowed sufficient time to eat, they may adopt eating patterns that are similar to those of patients with eating disorders.

7. Changes in eating behavior imposed by external (e.g., the "rush to eat") or internal (e.g., fasting) constraints can be reversed by provision of feedback during the meal, suggesting that eating behavior is flexible rather than "clamped" by such constraint. This is the basis for the use of eating behavior as an intervention in the management of patients who have problems eating.

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