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Effects of smoking cessation and female sex hormones on food intake in postmenopausal women

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EFFECTS OF SMOKING CESSATION AND
FEMALE SEX HORMONES ON
FOOD INTAKE IN POSTMENOPAUSAL WOMEN

A Thesis

Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
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requirements for the degree of
Master of Arts

In

The Department of Psychology

by
Megan Apperson
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ABSTRACT

Following smoking cessation, individuals increase their food intake. Women experience greater postcessation hyperphagia than men, and older women may increase their food intake more than younger women. Some research has suggested that postcessation increases in food intake may be macronutrient specific. However, previous investigations of macronutrient specific changes in food intake following smoking cessation have had significant methodological problems. The current study assessed changes in total food intake and macronutrient selection using the Macronutrient Self-Selection Paradigm (MSSP), a direct, laboratory based measure of food intake that is valid and reliable with respect to macronutrient intake. Fifty-five postmenopausal females completed the MSSP at baseline and within one month of smoking cessation. ANOVAs revealed that following smoking cessation women significantly increased their intake of total kcals, high fat food kcals, and high sugar food kcals. Further analysis indicated that the postcessation hyperphagia was primarily due to an increase in intake of kcals of foods high in both fat and sugar. To investigate the relationship between female sex hormones and postcessation hyperphagia, multiple regression analyses were conducted using estrone sulfate and estradiol to predict changes from baseline to postcessation for total kcals, high fat food kcals, high sugar food kcals, and high fat/high sugar food kcals. Estradiol levels did not enter the regression equation as a significant predictor for any of the dependent variables. Estrone sulfate levels predicted postcessation increases in intake of high sugar food kcals and high fat/high sugar food kcals. However, the relationship was in the opposite direction as hypothesized. To explore this unexpected finding, women who self-selected to use Hormone Replacement Therapy (HRT) and women who did not use...
HRT were compared on measures of weight- and eating-related characteristics. Women who self-selected for HRT had a history of weighing more; had a greater BMI, waist measurement, and hip measurement; had more weight concern, less sense of efficacy over control of food intake, and a more disinhibited eating style. It is argued that these differences between HRT users and non-HRT users may explain the unexpected relationship between estrone sulfate and increases in food intake, although other explanations are also considered.
INTRODUCTION

Although both men and women are susceptible to weight gain following smoking cessation, women gain more weight than men and are more likely to experience major weight gain. In a large study (N=5,887), O’Hara et al. (1996) found that following smoking cessation 19.1% of women and only 7.6% of men experienced major weight gain, defined as greater than 20% of baseline weight. Additional reports indicate that women gain an average of 2.6 kg in the three months following smoking cessation (Hall McGee, Turnstall, Duffy, & Benowitz, 1989), and 5.2 kg by the end of the first year of smoking cessation (O’Hara et al., 1996). Further, postcessation weight gain has been reported to be greater in older women than younger women, with an additional 1.0 kg per-year weight gain predicted with every ten year increase in age (Caan et al., 1996).

Postcessation weight gain must be attributable to a change in the energy balance equation. That is, an increase in energy intake, a decrease in energy expenditure, or a combination of these factors must account for weight gain following smoking cessation. Energy intake and energy expenditure have been assessed in both smoking cessation studies and smoking abstinence studies. Abstinence studies require smokers to temporarily refrain from smoking, as instructed by the experimenter; whereas, participants in smoking cessation studies have expressed a desire to permanently quit smoking and are attempting to do so. As a result of these differences in study criteria, it can be argued that cessation and abstinence studies draw from different populations, and that their response to nicotine removal may be dissimilar. Though this possibility warrants attention, previous smoking abstinence and smoking cessation studies have reported similar effects of nicotine removal on energy expenditure and energy intake. The
similarity of outcomes suggests that, with caution, generalizations can be made across these two research methods.

A postcessation decrease in energy expenditure through reduced physical activity has been refuted by both smoking cessation and abstinence studies. Self-report records of physical activity indicate that an individual’s activity level does not change following smoking cessation (Klesges, Eck, Clark, Meyers, & Hanson, 1990) or during smoking abstinence (Vander Weg, Klesges, Clemens, Meyers, & Pascale, 2001). Direct measures of physical activity, including a motion sensitive ankle measure (Leischow & Stitzer, 1996) and a hip-placed activity monitor (Klesges et al., 1990), have also shown that physical activity does not decrease with smoking cessation, and thus cannot account for postcessation weight gain.

A postcessation decrease in resting energy expenditure could also affect the energy balance equation and thereby contribute to postcessation weight gain. The majority of studies, however, have found that resting metabolic rate does not change, or changes only moderately, follow smoking cessation or smoking abstinence. Vander Weg et al. (2001) found no decrease in participants’ resting metabolic rate during a two-week smoking abstinence using an accurate and reliable measure of metabolism (indirect calorimetry using an open-circuit canopy collection system). Other smoking abstinence studies (Robinson & York, 1986) as well as smoking cessation studies (Perkins, Epstein, & Pastor, 1990) have reported that decreases in resting energy expenditure following nicotine removal, when found, are small and insufficient to account for postcessation weight gain.
Smoking a cigarette increases metabolic activity acutely for 20 to 30 minutes (Perkins, 1992). Removal of this acute effect of smoking a cigarette would result in decreased energy expenditure, and could thereby contribute to postcessation weight gain. Importantly, the acute effects of nicotine may depend crucially on the amount of nicotine inhaled. When nicotine levels are held constant, a modest increase of 6% of baseline energy expenditure lasting 20 minutes after exposure to nicotine has been reported (Perkins et al., 1990b). Perkins et al. (1990b) estimate that this increase would account for approximately 70 additional kcals metabolized per day, translating into a difference of approximately 1 kg in body weight over the course of 3 to 4 months. Given that the average weight gain in a 3-month period is 2.6 kg (Hall et al., 1989), loss of the acute metabolic effects of smoking cannot account for a major portion of postcessation weight gain.

Increased energy intake appears to be the most substantial contributor to postcessation weight gain. An increase in food intake following nicotine removal has been reported across both smoking cessation and smoking abstinence studies. Additionally, women have been found to increase their food intake to a greater extent than men following nicotine removal. Gilbert and Pope (1982) compared men and women in a laboratory environment during one day of smoking abstinence and found that men in their study increased their snack food intake by 50% while women ate 94% more snack foods. Ogden (1994) also reported a sex difference in food intake during smoking abstinence. She compared smokers’ intake of a variety of snack foods made available while smoking or while temporarily abstaining from smoking. When men and women were analyzed together, there was no significant difference in total caloric consumption
during smoking and abstinent sessions. When women were analyzed separately, however, abstaining smokers were found to consume more kcals than were smoking subjects, further suggesting that smoking abstinence differentially impacts the eating behaviors of males and females. Though caution must be taken in extrapolating the outcomes of these abstinence studies to smoking cessation outcomes, these results nonetheless suggest that food intake increases within 24 hours of nicotine removal, and to a greater extent for women than for men.

A prospective study on the effects of smoking cessation found that women’s food intake remained elevated at least three months after smoking cessation. Hall et al. (1989) compared subjects’ precessation and postcessation self-report food records. Both men and women increased their food intake in the first four weeks following cessation. However, twelve weeks after quitting smoking, food intake remained elevated for women while men’s food intake had returned to baseline levels. Further, women’s postcessation food intake predicted weight gain at 26 weeks, while men’s food intake did not.

Further studies have suggested that increases in food intake following smoking cessation may be somewhat greater in women who are postmenopausal. In a sample comprised of both premenopausal and postmenopausal women, Caan et al. (1996) compared self-report food intake records from before and after smoking cessation. During the first month postcessation, women reported an increase in food intake of 163 kcals per day. In another sample comprised of both premenopausal and postmenopausal women, an increase of 227 kcals per day in the 48 days following smoking cessation was reported (Stamford, Matter, Fell & Papanek, 1986). In a study composed exclusively of postmenopausal women, however, greater postcessation increases in food intake were
found. Allen, Brintnell, Hatsukami, and Reich (2004) reported that the postmenopausal women in their study increased their daily caloric consumption by 289 kcals in the first week following nicotine removal, and by 373 kcals during the second week. Though caution is warranted in comparing outcomes across studies, these disparate increases in food intake suggest that postmenopausal women may increase their food intake following smoking cessation to a greater extent than premenopausal women. This hypothesis is supported by the finding that older women gain more weight postcessation than do younger women (Caan et al., 1996).

**Macronutrient Specific Effects of Smoking Cessation**

In addition to measuring the effects of smoking cessation on total caloric intake, it is also important to assess postcessation changes in food selection and specific macronutrient intake. Some foods are more effective at producing satiety and controlling hunger motivation, while other foods contribute to hyperphagia and a positive energy balance. The effects of food on appetite and hunger are determined, in part, by their macronutrient composition. The increase in food intake following smoking cessation may have macronutrient specificity, therefore the relationship between macronutrients and hunger motivation warrants attention.

Both protein and complex carbohydrates have been reported to increase satiety to a greater extent than other macronutrients. Satiety refers to the suppression of food intake and appetite following ingestion of food, and can be assessed by measuring food intake or hunger following a preload. Preloads high in protein have consistently been shown to reduce subsequent consumption (Johnson & Vickers, 1993) or delay onset of the next eating session (Marmonier, Chapelot, & Louis-Sylvestre, 2000) relative to
preloads composed primarily of other macronutrients. In a study assessing the effects of
different macronutrients on satiety, Rolls, Hetherington and Burley (1988) provided
isocaloric preloads with differing macronutrient compositions to subjects, followed by a
self-selection meal. A preload high in complex carbohydrates and a preload high in
protein were associated with significantly less food intake in the subsequent meal than
were preloads primarily composed of other macronutrients, suggesting that these foods
are particularly potent suppressors of appetite and hunger.

In contrast to the satiety inducing effects of complex carbohydrates and protein,
foods high in simple carbohydrates (i.e., simple sugars) appear to increase hunger
motivation and contribute to hyperphagia. Rats given access to a solution high in sugar
ingest more total energy than rats provided with laboratory chow (Kanarek & Marks-
Kaufman, 1979). Human subjects ingest more kcals in a single eating session when
provided with foods high in sugar content than when given foods with less sugar (Green
& Blundell, 1996). Furthermore, individuals following a diet high in sugar consume more
kcals than individuals following a similar diet with complex carbohydrates in place of
sugar (Raben, Macdonald & Astrup, 1997). Together, these studies indicate that sugar
contributes to increased hunger motivation and food intake.

Foods with high fat content have also been associated with increased hunger
motivation and energy intake. When offered foods high in fat, subjects consume more
total kcals than when offered low fat foods, indicating that fat is conducive to
hyperphagia (Green, Wales, Lawton, & Blundell, 2000; Lawton, Burley, Wales, &
Blundell, 1993). Additionally, preference for fat is positively correlated with body
weight (Mela & Sacchetti, 1991), and obese individuals rate high fat solutions as more
enjoyable than do normal weight subjects (Drewnowski, Brunzell, Sande, Iverius & Greenwood, 1985).

The combination of fat and sugar in a food may be particularly conducive to hyperphagia and increased hunger motivation. Rats gain more weight on a diet with foods containing a combination of high levels of fat and sugar than when foods are either high in fat or high in sugar alone (Lucas & Scalafani, 1990). In normal weight human subjects, a combination of fat and sugar in a food is rated preferable to foods high in only fat or sugar (Drewnowski et al., 1985; Drewnowski & Greenwood, 1983). Additionally, foods high in fat and high in sugar may be less effective at producing sensory-specific satiety, a form of negative feedback whereby following consumption, an eaten food is considered less pleasant in comparison to other, uneaten foods. Rolls et al. (1988) compared the effects of foods of various macronutrient compositions on sensory-specific satiety. While consumption of a food high in any specific macronutrient resulted in a reduction of the perceived pleasantness of that food, eating an isocaloric food high in both fat and sugar did not produce a reduction in pleasantness rating of that food. Thus, the negative feedback that contributes to the termination of a feeding session appears to be diminished when the food eaten is high in both fat and sugar.

Self-Report Measures of Macronutrient Intake Postcessation

Self-report measures have been analyzed for changes in macronutrient selection following smoking cessation or abstinence, however, results have been highly inconsistent. Increases in specific macronutrients, to the exclusion of other macronutrients, have been found for total carbohydrate consumption (Allen et al., 2004; Caan et al., 1996;), sugar consumption (Allen et al., 2004; Hall et al., 1989) and fat
consumption (Caan et al., 1996; Hall et al., 1989). Other studies have reported no macronutrient specificity in postcessation food intake (Ogden, 1994). The use of self-report measures is problematic, however, and the inconsistent findings likely reflect self-report measures’ lack of validity. In particular, self-report food intake measures are highly susceptible to underreporting. An investigation comparing self-report food intake to actual intake found an average underreporting of more than 1,000 kcals per day in a sample of obese subjects (Lichtman et al., 1992). Numerous other reports have confirmed the prevalence of underreporting of food intake among normal and overweight women (Samaras, Kelly, & Campbell, 1999; Scagliusi, Polacow, Artioli, Benatti, & Lancha, 2003). Furthermore, there is evidence that among individuals who underreport their food intake, less socially desirable foods, such as foods high in total kcals and fat content, may be underreported to a greater extent than other foods (Samaras et al., 1999; Scagliusi et al., 2003). Self-reports of food intake may therefore be a particularly poor measure of specific macronutrient intake.

**Direct Measures of Macronutrient Selection Postcessation**

Direct, laboratory based measures of macronutrient intake could provide an objective assessment of changes that may occur with smoking cessation. Unfortunately, studies directly measuring food intake have been plagued with methodological problems. A restricted amount of total food provided to participants is one problem in laboratory based food intake studies. In a study by Spring, Wurtman, Gleason, Wurtman, and Kessler (1991), approximately 1,900 kcals per day were provided to the female subjects during smoking cessation. In a similar study in which food intake was not limited by the researchers, normal weight women consumed between 2,013 and 2,265 kcals per day in
the weeks following smoking cessation (Hall et al., 1989), suggesting that the 1,900 kcals provided to overweight and obese women in the study by Spring et al. (1991) may have significantly limited the participants’ total food intake.

In addition to the inadequate amount of total food provided to subjects, the macronutrient variability across foods has been inadequate to determine changes in participants’ macronutrient intake. For example, in a smoking cessation study by Ogden (1994), only one of the four food items available to participants had high protein content. If the participants disliked that one particular food item and did not ingest a significant amount of it, a protein specific effect (i.e., an increase in protein to the exclusion of increases in intake of other macronutrients) could not have been detected.

Insufficient variation in the fat content across foods has been a particularly common problem in studies assessing postcessation changes in macronutrient intake. All foods in Ogden’s study (1994) had a very high fat content, ranging from 44% to 77% kcals from fat. Any increase in total food intake necessarily included an increase in fat intake, therefore negating the possibility of detecting fat-specific changes in appetite. Spring et al. (1991) also did not adequately vary fat content, with most foods containing between 25% and 35% kcals from fat. Again, any fat specific change in appetite following smoking cessation would likely not have been detected given the limited macronutrient variability of the foods provided. In order to determine whether smoking cessation is accompanied by a fat specific effect, the food intake paradigm would need to include a selection of high fat as well as low fat foods. This inattention to foods’ fat content is particularly problematic when considering the unique role of fat in appetite and food intake, as discussed above.
A further problem with past assessments of macronutrient intake is the confounding of complex carbohydrates and simple sugars. In selecting foods to make available to subjects, some researchers (Hatsukami, LaBounty, Hughes, & Laine, 1993; Spring et al., 1991) have not differentiated between simple and complex carbohydrates. Additionally, researchers frequently do not separately analyze complex carbohydrates and simple sugars, and instead analyze a total carbohydrate variable that includes both simple and complex carbohydrates (Cann et al., 1996; Ogden, 1994; Spring et al., 1991). Given the different effects of simple sugars and complex carbohydrates on the control of food intake and appetite, reviewed above, this lack of differentiation is particularly problematic. In one of few smoking cessation studies that included separate analyses of change in complex carbohydrates and sugar, Hall et al. (1989) found that sugar intake increased following smoking cessation while complex carbohydrate intake did not increase. These results suggest that by not distinguishing between simple sugars and complex carbohydrates, the effects of smoking cessation on appetite for and intake of these macronutrients may be overlooked.

Female Sex Hormones and Food Intake Changes with Smoking Cessation

In studying the control of food intake following smoking cessation, it may also be important to consider female sex hormones, as a systematic relationship exists between female sex hormones and the control of food intake and body weight. When estrogen levels are elevated and progesterone levels are low, food intake is reduced in a variety of mammalian species, including rodents, guinea pigs, and monkeys (Czaja & Goy, 1975; Drewett, 1974; Ter Haar, 1972). Human females are also subject to hormonal regulation of food intake. Lower energy intake is reported during the menstrual cycle phase in
which estrogen levels are elevated and progesterone levels are low (i.e., the late follicular and the periovulatory phases), and increased intake is reported when progesterone levels are elevated in opposition to estrogen (i.e., the luteal phase) (Barr, Janelle, & Prior, 1995; Pliner & Fleming, 1983). A review of the literature reported an average increase in energy intake of 10% during the luteal phase of the menstrual cycle (Buffenstein, Poppitt, McDevitt, & Prentice, 1995), with some studies reporting luteal phase increases as great as 504 kcals per day (Dalvit, 1981). Furthermore, in rats it has been shown that ovariectomy, the surgical removal of the ovaries resulting in a state of estrogen deficiency, consistently leads to hyperphagia (Bartness & Waldbillig, 1984; Leshner & Collier, 1973). Supporting the primary role of estrogen deficiency in this response, administration of exogenous estrogen decreases the food intake of ovariectomized animals (Bartness & Waldbillig, 1984; Morin & Fleming, 1978; Wade, 1975).

Rodent studies indicate that the hypophagia accompanying increased estrogen levels has some specificity for reducing fat intake (Geiselman Martin, Vanderweele, & Novin, 1981; Young, Nancy, & Gorski, 1978). Consistent with this effect, human subjects have also reported less fat intake during the late follicular and the periovulatory phases of the menstrual cycle, when estrogen levels are elevated and progesterone levels are low (Barr et al., 1995; Reimer, Debert, House, & Poulin, 2005; Tarasuk & Beaton, 1991). Tarasuk and Beaton (1991) compared intake of fat and other macronutrients ten days prior to menstruation and ten days following menstruation using self-report measures. Participants reported higher intake of fats, but not carbohydrates or proteins, during the luteal phase of the menstrual cycle. Another study, using bio-verified analysis of subjects’ menstrual cycle, found that fat intake increased significantly from the
follicular to the luteal phase of the menstrual cycle (Johnson, Corigan, Lemmon, Bergeron & Crusco, 1994). Estrogen’s effect on food intake therefore appears to be selective for foods high in fat.

The estrogen deficiency that characterizes ovariectomized rats may provide an animal model for the estrogen-deficient state of postmenopausal women. Menopause is characterized by decreased levels of circulating estrogen, and it is this estrogen deficiency that is responsible for the symptoms of menopause (i.e., vasomotor flushes). As the above literature suggests, the decrease in estrogen that occurs during menopause may additionally promote an increase in food intake, and especially fat intake and appetite, thereby contributing to increased body weight. Though decreased estrogen levels characterize menopause, some menopausal women administer exogenous female sex hormones. Most commonly, HRT contains unopposed estrogens or a combination of estrogens and progestin. Women receiving unopposed estrogen therapy might be expected to decrease their food intake, given the similarity of this condition to the late follicular and the periovulatory phases of the menstrual cycle of premenopausal women (i.e. elevated estrogen and low progesterone levels). Consistent with this hypothesis, and consistent with the data from ovariectomized rats, postmenopausal women receiving unopposed estrogen have been found to gain less weight than postmenopausal women receiving placebo (Hassager & Christansen, 1989; PEPI, 1995). However, no known study has considered the food intake of women taking unopposed estrogen therapy.

The combined therapy of estrogen and progesterone can be thought of as pharmacologically mimicking the luteal phase of the menstrual cycle, in which progesterone levels are elevated in opposition to estrogen, and food intake is increased. It
would therefore be hypothesized that postmenopausal women taking combined estrogen/progesterone therapy would have similar food intake levels as premenopausal luteal phase women, and greater food intake than late follicular/periovulatory phase premenopausal women. Additionally, no significant differences would be hypothesized between women treated with combined estrogen/progesterone replacement and those not treated with hormone replacement, as the former have progesterone opposing their estrogen, while the latter have low estrogen (and progesterone) levels. These hypotheses have been supported. Reimer et al. (2005) assessed food intake in the following groups: premenopausal women in their luteal phase; premenopausal women in their late follicular phase; postmenopausal women taking combined estrogen/progesterone replacement; and postmenopausal women not taking hormone replacement. As hypothesized, postmenopausal women taking combined estrogen/progesterone replacement did not significantly differ in total caloric intake from postmenopausal women not taking hormone replacement (2040 kcals/day vs. 2137 kcals/day). Further, both groups of postmenopausal women reported similar food intake as premenopausal women in their luteal phase (2040 kcals/day and 2137 kcals/day vs. 2089 kcals/day). As expected, women in the luteal phase of their menstrual cycle had higher food intake than women in the late follicular phase (2089 kcals/day vs. 1752 kcals/day). Additionally, there was a nonsignificant trend for both groups of postmenopausal women (those using estrogen/progesterone HRT and those not using HRT) to have greater food intake than premenopausal women in the follicular phase of their menstrual cycle (2040 kcals/day and 2137 kcals/day vs. 1752 kcals/day). Overall, these results support the hypophagic effects of estrogen in premenopausal women, as well as the ability of progesterone to...
oppose estrogen’s hypophagic effects in both premenopausal and postmenopausal women.

This overview of the effects of female sex hormones on food intake suggests that different hormone therapies will differentially impact food intake and macronutrient intake. Given that individuals are highly susceptible to hyperphagia during smoking cessation, it can be hypothesized that the levels of female sex hormone of postmenopausal women will be predictive of their change in total energy and macronutrient intake in response to smoking cessation.

Specific Aims

In the present study, the Macronutrient Self-Selection Paradigm (MSSP) will provide a reliable and valid laboratory based measure of total caloric intake and specific macronutrient intake. As discussed above, studies purporting to measure macronutrient intake have been plagued with methodological problems. Importantly, in previous studies the macronutrient content, and especially the fat content, of foods provided to participants has not been systematically and significantly varied (Ogden, 1994; Spring et al., 1991). The measurement of fat intake is further complicated by the finding that an individual’s fat preference is highly food specific (Mela & Sacchetti, 1991). The MSSP overcomes the shortcomings of previous studies by systematically and significantly varying the fat content of foods with their sugar, complex carbohydrates, and protein contents. Additionally, the MSSP provides a wide variety of food items that are common sources of fat in the American diet, thereby minimizing the effect of food-specific fat preferences. Furthermore, the MSSP has been established as a reliable and valid measure of fat intake in both males and females, with strong test-retest reliability, and validity in respect to
long-term macronutrient intake (Geiselman et al., 1998). The MSSP therefore provides a reliable and valid measure of total energy intake as well as intake of fat, sugar, complex carbohydrate, and protein in a single eating session.

The present study will also focus on female sex hormones in postmenopausal women. As previously discussed, female sex hormones are systematically related to food intake. The effects of female sex hormones on appetite and food intake may therefore be particularly prominent when individuals are otherwise prone to hyperphagia, such as during smoking cessation.

**Specific Aims 1)** To compare the total caloric intake and the overall fat and other macronutrient intake of postmenopausal women prior to smoking cessation and during the first month of smoking cessation.

**Specific Aim 1 Hypothesis** It is hypothesized that following smoking cessation, total caloric intake will be greater than before smoking cessation. Additionally, it is hypothesized that intake of kcals of high fat foods, kcals of high sugar foods, and kcals of high fat/high sugar foods will be greater following smoking cessation.

**Specific Aim 2)** To assess the relationship between female sex hormones and postcessation increases in food intake.

**Specific Aim 2 Hypothesis** It is hypothesized that estrogen levels will be negatively related to increases in intake of total kcals, kcals of high fat foods, kcals of high sugar foods, and kcals of high fat/high sugar foods (i.e., higher estrogen levels will be predictive of lesser increases). Progesterone levels will be positively related to increases in intake of total kcals, kcals of high fat foods, kcals of high sugar foods, and kcals of high fat/high sugar foods (i.e., higher progesterone levels will be predictive of greater increases).
METHODS

Subjects

Fifty-five postmenopausal, Caucasian women smokers between the ages of 37 and 66 ($M = 52.05$, $SE = 0.97$) were recruited from the community to participate in a smoking cessation program. Postmenopausal status was defined as having been amenorrheic for at least 12 months, and, if not using HRT, having a serum follicle stimulating hormone (FSH) level $\geq 30$ mIU/ml. Smoking status was defined as self-reporting of greater than 10 cigarettes per day for one year or longer, expired carbon monoxide levels of greater than 10 ppm, and serum cotinine of greater than 25 ng/ml. Women were excluded from the study if they were in a standardized weight-reduction program or taking medication for weight loss; if they had a history or presence of significant psychiatric illness (e.g., eating disorders, psychosis, psychoactive substance abuse, major depression); or if they were unable to complete long-term study commitment, including anticipating moving out of the area prior to completion of the study.

The MSSP

Subjects participating in the MSSP are presented with a large portion of foods varying in macronutrients. The food selection is based on a 2 (Fat factor: High Fat and Low Fat) x 3 (Carbohydrate (CHO) factor: High Simple Sugar, High Complex CHO, and Low CHO/High Protein) x 3 (specific foods within each cell) design (see Table 1). According to this design, three foods are presented for each of the following six cells: High Fat/High Simple Sugar (HF/HS), High Fat/High Complex Carbohydrate (HF/HC), High Fat/Low Carbohydrate/High Protein (HF/LCHO/HP), Low Fat/High Simple Sugar
(LF/HS), Low Fat/High Complex Carbohydrate (LF/HC), and Low Fat/Low Carbohydrate/High Protein (HF/LCHO/HP).

Table 1

Macronutrient Self-Selection Paradigm (MSSP)

<table>
<thead>
<tr>
<th></th>
<th>High Simple Sugar</th>
<th>High Complex CHO</th>
<th>Low CHO/High Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Fat</td>
<td>HF/HS* three foods</td>
<td>HF/HCCHO† three foods</td>
<td>HF/LCHO/HP‡ three foods</td>
</tr>
<tr>
<td>Low Fat</td>
<td>LF/HS§ three foods</td>
<td>LF/HCCHO¶ three foods</td>
<td>LF/LCHO/HP# three foods</td>
</tr>
</tbody>
</table>

* HF/HS: High Fat/High Sugar.
† HF/HCCHO: High Fat/High Complex Carbohydrate.
‡ HF/LCHO/HP: High Fat/Low Complex Carbohydrate/High Protein
§ LF/HS: Low Fat/High Sugar
¶ LF/HCCHO: Low Fat/High Complex Carbohydrate
  # LF/LCHO/HP: Low Fat/Low Complex Carbohydrate/High Protein

The fat content of foods used in the MSSP are varied systematically and significantly with other macronutrients. All food items in the high fat cells have a fat content of ≥45% fat (expressed as a percentage of the total kcals in a food). Foods in the HF/HS cell contain ≥45% fat and ≥30% sugar, foods in the HF/HC cell contained ≥45% fat and ≥30% complex carbohydrates, and foods in the HF/LCHO/HP cell contained ≥45% fat and ≥13% protein (however, most foods in this cell are between 25% and 30% protein). Each food in the low fat cells contain ≤20% fat. Participants receive three test foods from each of the six cells, for a total of 18 food choices. The foods provided to participants are determined on the basis of their hedonic responses to a pretest list of foods conducted prior to the MSSP session. Pretest rating of foods are conducted on a 9-
point Likert scale with the following anchors: 1=dislike extremely; 5= neutral, neither like nor dislike; 9=like extremely.

MSSP Test Procedure

Subjects were instructed to refrain from eating after 2200 hours on the evening before the MSSP and remain unfed through the following afternoon, when the MSSP was conducted. This procedure assured that all subjects had similar nutritional status during the MSSP session. Additionally, subjects were asked not to drink alcohol in the 24 hours prior to the test or to exercise on the morning of the test.

The MSSP was conducted at baseline, following which subjects enrolled in a smoking cessation program. Within one month of smoking cessation, subjects remaining smoke-free completed a second MSSP. Both baseline and postcessation MSSPs were conducted between 1100 and 1400 hours.

Female Sex Hormones

Using blood samples drawn at screening, the female sex hormones estradiol, estrone sulfate, and progesterone were measured in women enrolled in the study. The following clinical chemistry methodologies were used to analyze the female sex hormones: FSH: (Diagnostic Products Corporation, Los Angeles, CA). This assay is performed on the DPC 2000 using an immunoassay with chemiluminescent detection. Interassay coefficient of variation is less than 4.9% with a minimum detectable limit of 1.39 mIU/mL. Ultra-sensitive estradiol: (Diagnostic Systems Laboratories, Webster, TX). This assay was performed using a competitive binding radioimmunoassay. The manufacturer states that the sensitivity of the assay is 2.2 pg/mL with an interassay coefficient of variation less than 12.2%. Estrone Sulfate: (Diagnostic Systems
Laboratories, Webster, TX). This assay is performed using a radioimmunoassay. Interassay coefficient of variation is less than 14.2% with a minimum detectable limit of 0.05 ng/mL. Progesterone - (Diagnostic Products Corporation, Los Angeles, CA). This assay is performed on the DPC 2000 using an immunoassay with chemiluminescence detection. Interassay coefficient of variation is less than 11.9% with a minimum detectable limit of 0.2 ng/mL.

At screening, subjects reported the type of HRT they were using, or reported if they were not using HRT. Subjects were monitored for changes in HRT use across the course of the study. Each woman who was using any HRT regimen was doing so under the supervision of her personal physician.
RESULTS

Analyses of Variance (ANOVA’s) on Total Caloric and Specific Macronutrient Intake in the MSSP

Within-subjects analyses were conducted to assess changes in total caloric intake and specific macronutrient intake from baseline to postcessation. Except as noted, within-subjects analysis of variance (ANOVA) assumptions of independence, normality, and sphericity were observed. When significant interactions were obtained, we performed Bonferroni t-tests to determine the nature of the interaction. The following within-subjects analyses were conducted with kcals intake in the MSSP as the dependent variable.

A one-way ANOVA was conducted with smoking status (baseline and postcessation) as the independent variable to test our hypothesis that women would increase their total caloric intake in the MSSP following smoking cessation. As depicted in Figure 1, a significant effect was obtained, $F(1, 54) = 12.75$, $p = 0.001$, showing that women ingested significantly more total kcals in the MSSP postcessation ($m = 848.1$ kcals) than they had ingested at baseline while they were still smoking ($m = 743.5$ kcals).

To test the hypothesis that women would increase their total caloric intake of the high-fat foods postcessation, we conducted a 2 (baseline and postcessation) X 2 (high fat foods and low fat foods) ANOVA. A significant main effect for smoking status was found, $F(1, 54) = 15.41$, $p = 0.001$, indicating that, for the high fat and the low fat foods combined, the mean caloric intake was greater postcessation ($m = 393.0$ kcals) than at baseline ($m = 341.0$ kcals). A significant main effect for fat was also obtained, $F(1,54) = 111.41$, $p = 0.001$, indicating that, across the two test sessions, the mean caloric intake of high fat foods ($m = 536.7$ kcals) was significantly greater than the mean caloric intake
of low fat foods ($m = 197.3$ kcals). The smoking status X fat interaction was also significant, $F(1, 54) = 11.93, p = 0.001$ (see Figure 2). Post-tests revealed that women’s total caloric intake of high fat foods was significantly greater postcessation ($m = 587.6$ kcals) than it was at baseline while still smoking ($m = 485.7$), $t(54) = 4.11, p = 0.001$; but there was no difference in the total caloric intake of low fat foods from baseline ($m = 196.2$ kcals) to postcessation ($m = 198.4$ kcals), $t(54) = 0.178, p = 0.859$.

A 2 (baseline and postcessation) X 3 (other macronutrient: high sugar, high complex carbohydrate, and high protein foods) ANOVA was conducted to test our hypothesis that women would increase their total caloric intake of high sugar foods from baseline to postcessation. A significant main effect of smoking status was found, $F(1, 54) = 14.54, p = 0.001$, indicating that, across the three levels of the other macronutrient factor, mean caloric intake was greater following smoking cessation ($m = 261.0$ kcals)
than at baseline while still smoking ($m = 226.9$ kcals). The main effect for the other macronutrient factor was not significant, $F(2, 108) = 0.48, p = 0.623$. As depicted in Figure 3, we obtained a significant smoking status X other macronutrient interaction, $F(2, 108) = 7.57, p = 0.001$, but the sphericity assumption was violated. After applying the Geisser-Greenhouse correction, the corrected degrees of freedom were 1.663 and 89.794, and the corrected $p$ value was 0.002. T-tests for simple main effects were then conducted to determine the nature of the interaction. Analyses revealed that women significantly
increased their total caloric intake of high sugar foods postcessation ($m = 299.0$ kcals) in comparison to their intake at baseline while they were still smoking ($m = 210.3$ kcals), $t(54) = 4.09, p=0.001$. Intake of foods high in complex carbohydrates did not differ from baseline ($m = 234.8$ kcals) to postcessation ($m = 229.3$ kcals), $t(54) = 0.38, p = 0.707$, nor did intake of foods high in protein (baseline $m = 235.5$ kcals and postcessation $m = 254.6$ kcals), $t(54) = 1.39, p = 0.169$.

To test our hypothesis that women would selectively increase their total caloric intake of high fat/high sugar foods postcessation, we conducted a 2 x 2 x 3 ANOVA with smoking status (baseline and postcessation), fat (high fat and low fat foods), and other macronutrient (high sugar, high complex carbohydrate, and high protein foods) factors. A significant effect was obtained for smoking status $F(1,54) = 13.82, p = 0.001$, indicating that, across the six cells of the MSSP, the mean caloric intake was significantly

![Figure 3. Total kcals intake of high sugar foods, high complex carbohydrate foods, and high protein foods at baseline and postcessation.](image-url)
greater postcessation \( (m = 130.7 \text{ kcals}) \) than at baseline \( (m = 114.1 \text{ kcals}) \). A significant main effect of fat, \( F(1, 54) = 108.35, p = 0.001 \), showed that, across the smoking and other macronutrient factors, the mean intake of high fat foods \( (m = 178.6 \text{ kcals}) \) was significantly greater than the mean intake of low fat foods \( (m = 66.1 \text{ kcals}) \). Analyses also yielded a significant smoking status X fat interaction, \( F \ (1, 54) = 12.21, p = 0.001 \). Post-tests revealed that, across the three levels of the other macronutrient factor, the mean intake from the high fat foods was significantly greater postcessation \( (m = 195.3 \text{ kcals}) \) than at baseline \( (m = 162.0 \text{ kcals}) \), \( t(54) = 4.04, p = .001 \). There was no difference in the mean intake from the low fat foods across the three levels of the other macronutrient factor \( (\text{baseline} \ m = 66.2 \text{ kcals}; \ \text{postcessation} \ m = 66.0 \text{ kcals}) \), \( t(54) = 0.03, p = .98 \). The smoking X other macronutrient interaction was significant, \( F \ (2, 108) = 7.634, p = 0.001 \); but the sphericity assumption was violated. The Geisser-Greenhouse correction yielded corrected degrees of freedom of 1.653 and 89.277 and a p value of 0.002. Post-tests showed that, across levels of the fat factor, the mean intake from the high sugar foods was significantly greater postcessation \( (m = 149.5 \text{ kcals}) \) than at baseline \( (m = 106.1 \text{ kcals}) \), \( t(54) = 3.95, p = .001 \). The mean intake of the high complex carbohydrate food across levels of the fat factor did not differ from baseline \( (m = 118.3 \text{ kcals}) \) to postcessation \( (m = 113.8 \text{ kcals}) \), \( t(54) = 0.62, p = .54 \), nor did the mean intake of the high protein foods \( (\text{baseline} \ m = 117.7 \text{ kcals}; \ \text{postcessation} \ m = 128.7 \text{ kcals}) \), \( t(54) = 1.66, p = .10 \). We also obtained a smoking status X fat X other macronutrient interaction, \( F(2, 108) = 4.31, p=0.016 \); but the sphericity assumption was again violated. The Geisser-Greenhouse correction adjusted the degrees of freedom to 1.767 and 95.439 and yielded a corrected p value of 0.02. Post-tests revealed that the total caloric intake of high fat/high
sugar foods was significantly increased following smoking cessation ($m = 210.8$ kcals) in comparison to intake of those foods before quitting smoking ($m = 127.7$ kcals), $t(54) = 4.01, p = 0.001$ (see Figure 4). There was a marginally nonsignificant trend for an increased intake of high fat/high protein foods postcessation ($m = 203.5$ kcals) compared to baseline ($m = 179.5$ kcals), $t(54) = 1.92, p = 0.060$. There were no significant differences from baseline to postcessation for intake of hf/hccho, lf/hs, lf/hccho, or lf/hp foods (see Figure 4 and Figure 5).

**Multiple Regression Analyses to Test Serum Levels of Female Sex Hormones as Potential Predictors of Total Caloric and Specific Macronutrient Intake in the MSSP**

Regression analyses were conducted to test serum levels of female sex hormones as potential predictors of increases in total caloric and specific macronutrient intake. Only subjects who were consistent in their use of HRT or no HRT were used in the analyses. Forty-eight women met this criterion and were included, and seven subjects were excluded because their record of taking HRT was unclear. The subjects used in these
analyses included women using unopposed estrogen (n = 23), estrogen plus progestin (n = 8), estrogen and testosterone (n = 3), estrogen, progestin and testosterone (n = 2), and women not using HRT (n = 12).

We proposed to conduct multiple regression analyses using serum levels of estradiol, estrone sulfate, and progesterone as the independent variables to assess the relationship between female sex hormones and changes in food intake from baseline to postcessation. However, we had to eliminate progesterone as an independent variable because the progesterone immunoassay that was conducted on our serum samples had poor sensitivity to exogenous progesterone (medroxyprogesterone). The percent cross reactivity of the present immunoassay to medroxyprogesterone was only 0.029 percent. Endogenous levels of progesterone in postmenopausal women are typically quite low, ranging from ND (not detectable) to 1.0 ng/ml. The assay we used had a calibration range from 0.2 to 40 ng/ml detection of endogenous progesterone. Thus, with a minimum detectable limit of 0.2 ng/ml, more than 80 per cent of our subjects did not
have detectable levels of endogenous progesterone with the use of this assay; i.e., their endogenous progesterone levels were < 0.2 ng/ml.

We, therefore, conducted regression analyses using serum levels of estradiol and estrone sulfate as the independent variables in each of the analyses. Four regression analyses were conducted, using one of the changes in food intake from baseline to postcessation addressed in our specific aims as the dependent variable in each one of the regression analyses. Thus, the dependent variables were postcessation increases in total kcals intake, kcals intake of high fat foods, kcals intake of high sugar foods, and kcals intake of high fat/high sugar foods. The regression-equation criteria for the independent variables were probability of F to enter < .05 and probability of F to remove ≥ .10.

Using postcessation increases in intake of total kcals as the dependent variable, neither estradiol nor estrone sulfate was entered into a predictor equation. Likewise, neither estrogen variable predicted increases from baseline to postcessation in kcals intake of the high fat foods.

However, when postcessation increases in kcals intake of high sugar foods were used as the dependent variable, estrone sulfate was entered as a significant predictor (R = 0.370, R² = 0.137). The ANOVA for this model was F(1, 46) = 7.288, p = 0.010. The standardized β coefficient was 0.370, t(46) = 2.7, p ≤ .01, indicating that higher serum levels of estrone sulfate were predictive of greater increases from baseline to postcessation in kcals intake of high sugar foods. The estradiol variable was not entered into this regression equation.

Estrone sulfate was also a significant predictor of postcessation change in kcals intake of high fat/high sugar foods (R = 0.334, R² = 0.112). The ANOVA for this
regression model was $F(1, 46) = 5.780, p = 0.02$. Estrone sulfate had a standardized $\beta$ coefficient of $0.334, t (46) = 2.404, p < .02$. As was the case with respect to postcessation changes in intake of high sugar food, higher estrone sulfate levels were predictive of greater increases in intake of high fat/high sugar foods postcessation. Estradiol, again, did not enter the equation as a significant predictor of high sugar/high fat foods.

**Comparisons of HRT Users and Non-HRT Users on Weight-Related and Eating-Related Variables**

The above analyses indicated that increased serum levels of estrone sulfate predicted increased intake of high sugar foods and, more specifically, high fat/high sugar foods following smoking cessation. Importantly, in our sample, serum estrone sulfate levels were significantly higher in women who used any HRT ($m = 7.14$ ng/ml, $se = 0.79$) than in women who did not use HRT ($m = 0.713$ ng/ml, $se = 0.13$), $F(1, 46) = 21.65, p < 0.001$. We hypothesized that the relationship between estrone sulfate and postcessation increases in food intake might be explained by baseline differences in eating habits and weight-related variables between women who self-selected to use HRT and women who did not choose to use HRT. Therefore, we conducted ANOVAs comparing women taking any HRT (unopposed estrogen; estrogen and progesterone; estrogen and testosterone; and estrogen, progesterone, and testosterone; $N = 36$) with women not taking HRT ($N = 12$). The dependent variables were weight-related measures and eating habit measures that were assessed at the screening and the baseline visits of the parent study.

HRT users and non-HRT users differed on several measures of body size (see Table 2). The Body Mass Index (BMI) of women using HRT ($m = 26.48, se = 0.88$) was
significantly higher than the BMI of non-HRT users ($m = 23.08$, $se = 1.24$), $F(1,46) = 4.07$, $p = 0.049$. Waist measurements also differed significantly between women who used HRT and women who did not use HRT, $F(1, 46) = 6.03$, $p = 0.018$, with HRT users’ waists measuring larger ($m = 85.58$ cm, $se = 1.88$) than the waists of non-HRT users ($m = 76.03$ cm, $se = 3.71$). Additionally, the hip measurement of HRT users ($m = 103.64$ cm, $se = 1.62$) tended to be larger than the hip measurement of non-HRT users ($m = 97.33$ cm, $se = 2.86$), $F(1, 46) = 3.75$, $p = 0.059$, though this effect was marginally nonsignificant.

Table 2
Differences in Weight- and Eating-Related Variables in Women using HRT or not using HRT

<table>
<thead>
<tr>
<th>Variable</th>
<th>HRT</th>
<th>no HRT</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>26.48 (.88)</td>
<td>23.08 (1.24)</td>
<td>0.049*</td>
</tr>
<tr>
<td>Waist Measure (cm)</td>
<td>85.58 (1.88)</td>
<td>76.03 (3.71)</td>
<td>0.018*</td>
</tr>
<tr>
<td>Hip Measure (cm)</td>
<td>103.64 (1.62)</td>
<td>97.33 (2.86)</td>
<td>0.059</td>
</tr>
<tr>
<td>Lowest Adult Weight (lb)</td>
<td>116.12 (2.27)</td>
<td>103.36 (3.02)</td>
<td>0.014*</td>
</tr>
<tr>
<td>Body Shape Questionnaire</td>
<td>94.12 (5.09)</td>
<td>68.75 (8.40)</td>
<td>0.014*</td>
</tr>
<tr>
<td>Concern about Postcessation Weight Gain</td>
<td>8.11 (1.41)</td>
<td>6.33 (3.45)</td>
<td>0.014*</td>
</tr>
<tr>
<td>Weight Efficacy Lifestyle</td>
<td>110.21 (5.73)</td>
<td>136.75 (10.21)</td>
<td>0.024*</td>
</tr>
<tr>
<td>Eating Inventory - Disinhibition Scale</td>
<td>6.74 (.51)</td>
<td>4.33 (1.18)</td>
<td>0.037*</td>
</tr>
<tr>
<td>Eating Inventory- Restraint Scale</td>
<td>6.58 (.90)</td>
<td>8.63 (.73)</td>
<td>0.137</td>
</tr>
</tbody>
</table>

* Significant at $p \leq 0.05$.

Measures of weight history and concern about body shape and body weight also differed between women using HRT and women not using HRT (see Table 2). The self-
reported lowest adult weight of women on HRT was significantly higher ($m = 116.12$ lbs, $se = 2.27$) than the lowest adult weight of non-HRT users ($m = 103.36$ lbs, $se = 3.02$), $F(1, 42) = 8.751, p = 0.005$. Scores on the Body Shape Questionnaire (Cooper, Taylor, Cooper, & Fairburn, 1987), a measure of concern about body shape, were higher for HRT users ($m = 94.12, se = 5.09$) than for non-HRT users ($m = 68.75, se = 8.40$), $F(1,44) = 6.535, p = 0.014$, indicating that HRT users were more concerned about their body shape. Additionally, when asked to rate their concern about gaining weight as a result of smoking cessation, women who used HRT expressed more weight concern ($m = 8.11, se = 1.41$) than women who did not use HRT ($m = 6.33, se = 3.45$), $F(1, 46) = 6.535, p = 0.014$.

HRT users also differed from nonusers on measures of eating habits (See Table 2). On the Weight Efficacy Lifestyle (WEL) questionnaire (Clark, Abrams, Niaura, Eaton, & Rossi, 1991), women using HRT expressed a lower sense of efficacy over controlling food intake and body weight ($m = 110.21, se = 5.73$) than non-HRT users ($m = 136.75, se = 10.21$), $F(1,44) = 5.43, p = 0.024$. HRT users also differed significantly from women not using HRT on the Disinhibition Scale of the Eating Inventory (Stunkard & Messick, 1985), a measure of an individual’s tendency to lose control over food intake, $F(1,45) = 4.60, p = 0.037$. Women using HRT endorsed a more disinhibited eating style ($m = 6.74, se = 0.51$) than women not using HRT ($m = 4.33, se = 1.18$), $F(1, 45) = 4.60, p = 0.037$. However, HRT users and non-HRT users did not significantly differ on the Dietary Restraint scale of the Eating Inventory, a measure of intention to control body weight by restricting food intake.
DISCUSSION

Smoking Status, Food Intake, and Macronutrient Intake

In the current study, postmenopausal women increased their total caloric intake following smoking cessation. This finding contributes to the established body of literature showing that smoking cessation results in increased food intake (Allen et al., 2004; Caan et al., 1996; Hall et al., 1989; Spring et al., 1991; Vander Weg et al., 2001), and confirms the presence of this effect in postmenopausal women (Allen et al., 2004). Further, the increase in food intake following smoking cessation in the current study was specific to foods high in fat and foods high in sugar. This is congruent with past studies reporting a postcessation increase specific to foods high in sugar (Allen et al., 2004; Perkins, et al. 1990a) or foods high in fat (Hall, et al., 1989). However, it contrasts with other studies that did not find macronutrient specificity for postcessation increases in food intake (Hatsukami et al., 1993; Ogden, 1994). Importantly, these earlier studies relied on self-report measures of food intake, or used direct measures that lack validity with respect to macronutrient intake. The current study is the first to assess changes in macronutrient intake following smoking cessation using a direct measure of macronutrient intake that has shown validity and test-retest reliability, the MSSP. Unlike previously used measures of postcessation changes in food intake, the MSSP also varies macronutrient content systematically, and therefore allows the measurement of intake of specific macronutrient combination. Using the MSSP, the present study found that the intake of high fat/high sugar foods increased significantly following smoking cessation to the exclusion of other macronutrient combinations. Therefore, this study is the first to report that the increased food intake in postmenopausal women following smoking
cessation is primarily due to the increased intake of foods that are high in both fat and sugar. This finding is consistent with research in laboratory rodents, which has shown specific increases in high fat/high sugar foods following cessation of previously chronically administered nicotine (Grunberg, Popp & Winders, 1988).

The specificity of the increase in food intake for high fat/high sugar foods has important implications for the ability of individuals to control food intake, and consequently, weight gain, following smoking cessation. Foods high in simple sugars or high in fat are more hedonically pleasing and less effective at inducing satiety than foods high in other macronutrients (Green & Blundell, 1996; Lucas, Ackroff, & Sclafani, 1998; Green, et al., 2000; Lawton, et al., 1993), and a diet containing foods high in sugar or fat is associated with greater caloric intake and weight gain, or lesser weight loss, than diets lower in fat or sugar (Bray & Popkin, 1998; Raben et al., 1997; Vermunt, Pasman, Schaafsma, & Kardinaal, 2003). Furthermore, when individuals are provided with foods high in both fat and sugar they consume a greater amount of total energy than when foods are high in only fat or only sugar (Green & Blundell, 1996). The current finding, that the increased food intake following smoking cessation is specific to high fat/high sugar foods, suggests that specific attention should be given to techniques to limit the intake of these foods in order to minimize postcessation weight gain.

The physiological mechanisms responsible for increased food intake following smoking cessation are not fully understood. Nicotinic receptors are located throughout the central and peripheral nervous system (Balfour, 1982). Nicotine administration and the discontinuation of chronic nicotine administration alter the activities of many neurotransmitter systems, including those involved in the control of food intake.
(Mathieu-Kia, Kellogg, Butelman, & Kreek, 2002; Miyata, Meguid, Fetissov, Torelli, & Kim, 1999; Rada, Jensen & Hoebel, 2001). The finding of the current study, that postcessation hyperphagia in postmenopausal women is specific to high fat/high sugar foods, suggests that those appetite regulation systems which are known to have specific effects on the intake of high fat and high sugar foods should be considered for their potential role in postcessation hyperphagia. The neurotransmitter serotonin (5-hydroxytryptamine, or 5-HT) is known to have an important role in food intake and has additionally been implicated in the control of intake of high fat foods (Smith, York, & Bray, 1999). Specifically, greater serotonin activity in the hypothalamus is associated with lesser food intake (Leibowitz, Weiss & Shor-Posner, 1988), and increased serotonin activity has been shown to specifically reduce the intake of high fat foods (Smith et al., 1999). In laboratory rodents, nicotine administration into the lateral hypothalamus induces long-lasting increases in serotonin release concurrently with reduced food intake, indicating a role for hypothalamic serotonin activity in nicotine-related hypophagia (Yang, Blaha, Meguid, Oler, & Miyata, 1999). As might be expected, the discontinuation of chronic nicotine administration in laboratory rodents, an animal model of human smoking cessation, results in a reduction of hypothalamic serotonin (Miyata et al., 1999). Decreased hypothalamic serotonin activity is therefore regarded as a potential cause of smoking cessation-related hyperphagia. Rodent and human studies have supported this hypothesis. Levin, Briggs, Christopher and Rose (1993) found that increasing serotonin activity, by administering a serotonin reuptake inhibitor, reduced hyperphagia following cessation of chronic nicotine administration. Spring et al. (1991) found similar results in
humans, with those individuals using serotonin reuptake inhibitors during smoking cessation showing lesser increases in postcessation food intake.

A decrease in dopamine activity following smoking cessation may also contribute to postcessation hyperphagia. Dopamine activity in the hypothalamus is known to play a role in eating behavior, with decreased dopaminergic activity in the lateral hypothalamic area associated with greater food intake (Meguid et al., 2000). Importantly, the dopaminergic control of food intake has shown some specificity for foods high in fat and sugar (Cooper & Al-Naser, 2006). When nicotine administration is discontinued following a period of chronic nicotine treatment, dopamine levels decrease in the lateral hypothalamus, coinciding with increased food intake (Miyata et al., 1999). In support of a role of reduced dopamine activity in postcessation hyperphagia in humans, Lerman et al. (2004) found that individuals with a genetic variation that results in lower neuronal dopaminergic activity showed a greater increase in motivation for food following smoking cessation than individuals who did not have that genetic variation. Additionally, bupropion, a dopamine and noradrenergic reuptake inhibitor, has been found to reduce postcessation food reward (Lerman et al., 2004) and weight gain (Hurt et al., 1997).

Female Sex Hormones, Smoking Cessation and Food Intake

The hypothesized relationship between estrogen levels and food intake was not supported in the current study. Whereas it was hypothesized that greater levels of both estradiol and estrone sulfate would be associated with lesser increases in food intake following smoking cessation, we found that serum estradiol levels did not predict postcession increases in intake of total kcals, high fat food kcals, high sugar food kcals, or high fat/high sugar food kcals. Serum levels of estrone sulfate also did not predict
increases in intake of total kcals or high fat food kcals. Estrone sulfate levels did significantly predict postcessation increases in intake of high sugar food kcals and high fat/high sugar food kcals. However, the relationship was in the opposite direction as hypothesized, with higher estrone sulfate levels predicting greater postcessation increases in intake of high sugar foods and high fat/high sugar foods.

These results appear to be inconsistent with the well-established relationship between estrogen levels and food intake. In cycling women and animals, higher endogenous estrogen levels, when unopposed by progesterone, have been associated with lesser food intake (Buffenstein et al., 1995; Czaja & Goy, 1975; Drewett, 1974). Further, in laboratory animals, reduction of endogenous estrogen levels through ovariectomy results in hyperphagia, while administration of exogenous estrogens to ovariectomized animals decreases food intake (Bartness & Waldbillig, 1984; Czaja & Goy, 1975; Geiselman et al., 1981). Additionally, the current findings appear to be inconsistent with the literature in postmenopausal women, which has shown that women receiving unopposed estrogen, who presumably have higher serum levels of estrogen, have been found to gain less weight than postmenopausal women receiving placebo (Hassager & Christansen, 1989; PEPI, 1995). Due to this unexpected relationship between estrone sulfate and changes in food intake, we investigated possible baseline differences in women using and not using HRT. All of the subjects in our study had self-selected to use HRT or to not use HRT before the commencement of the study. We therefore hypothesized that pre-existing differences between HRT users and non-HRT users might explain the unexpected relationship between estrone sulfate and postcessation hyperphagia as well as the absence of the hypothesized association between estrodial and
increases in food intake. In fact, the two groups of women differed in many weight- and eating-related measures. At baseline, women using HRT weighed significantly more than non-HRT users. Also, the waist and hip measurement of HRT users were larger, and women using HRT had a history of weighing more (i.e., had a higher lowest adult weight) than the non-HRT users. Further, HRT users had significantly more concern about postcessation weight gain, reported less sense of efficacy in their control of food intake, and endorsed a more disinhibited style of eating. These characteristics can be hypothesized to increase HRT users’ vulnerability to postcessation weight gain. Indeed, it has been found that individuals with higher scores on the Disinhibition Scale of the Eating Inventory increased their food intake following smoking abstinence more than individuals with lower Disinhibition Scores (Duffy & Hall, 1988). Further, concern about postcessation weight gain has also been associated with a greater likelihood of postcessation weight gain (Borrelli & Mermelstein, 1998), and women with higher BMIs increase their food intake following two days of smoking abstinence more than women with lower BMIs (Saules, Pomerleau, Snedecor, Brouwer, & Rosenberg, 2004).

Therefore, the pre-existing differences in susceptibility to postcessation weight gain between HRT users and non-HRT users may explain the relationship between estrone sulfate and postcessation increases in food intake found in the current study. However, it should be noted that the current study did not directly address the direction of causality in the relationship between HRT use and the weight- and eating-related characteristics on which HRT users and non-HRT users differed. Thus, it cannot be ruled out that HRT use had a causal effect on these variables. However, in support of the hypothesis that these differences existed prior to HRT treatment, a review of the subjects’ weight history
indicates that the HRT users and non-HRT users’ lowest adult weight typically occurred when they were young adults. This suggests that these individuals may have a history of greater weight- and eating-related problems. Additionally, cognitive variables such as concern about postcessation weight gain and sense of efficacy over food intake seem unlikely to be affected by hormone replacement therapy. Thus, the differences between these two groups of women are most likely due to differences existing prior to HRT selection, rather than being HRT-induced effects.

Differences in psychosocial characteristics between HRT users and non-HRT users have been reported in the literature. Ballinger (1985) found that women who attended menopausal clinics experience more psychosocial stress, depression and anxiety than women who have not attended a clinic for menopause. Additionally, Hardy & Kuh (2002) found that initiation of HRT use was associated with increased psychological symptoms (i.e., anxiety, depression, feelings of panic, irritability), although their data does not address whether HRT usage or psychological symptoms occurred first. Unfortunately, no known studies have assessed differences in weight history or eating-related characteristics between women who self-select to use HRT and women who do not use HRT. While the HRT users in our study had a greater BMI and waist and hip measurements than non-HRT users, a number of studies have reported no difference in the weight or BMI of self-selected HRT users and non-HRT users (Masi, Hawkley, Berry & Cacioppo, 2006; Reubinoff et al., 1995; Reimer et al., 2005; Taylor, MacLennan & Avery, 2006). It is not clear why HRT users in our study have more weight- and eating-related problems. However, unlike the above studies reporting no difference in BMI between HRT users and non-HRT users, our sample is composed exclusively of smokers,
and more specifically smokers attempting to quit smoking. It is therefore of interest as to whether smoking status may moderate the relationship between HRT use and weight- and eating-related variables.

Although the differences in weight- and eating-related characteristics of HRT users and non-HRT users appears to account for the lack of the hypothesized relationship between estrogens and food intake, other possibilities should be considered. It should be noted that few studies have considered the relationship between food intake and female sex hormones in postmenopausal women. In one study that did address this relationship, no association was found between estradiol levels and self-reported food intake in postmenopausal women (Reimer et al., 2005). Additionally, no known study has assessed the effects of unopposed estrogen HRT on food intake in postmenopausal women. Thus, although the hypophagic effects of estrogen are well supported in animals and in premenopausal women, there is currently no direct evidence that these effects are present in postmenopausal women. While it is reasonable to believe that results from animal models would be applicable to postmenopausal women, some features of these studies may limit the extent to which the outcomes transfer to postmenopausal women. In studies on the effect of ovariectomy and estrogen replacement on food intake in laboratory rodents, the animals are often ovariectomized at a young age. The effects of estrogen deficiency on the central nervous system receptors involved in food intake may be markedly different between animals that have been ovariectomized at a young age versus animals that have experienced a gradual loss of estrogen at an older age, as occurs during natural menopause in humans. As a result, the effects of estrogen replacement on food intake may also differ. While some of the women in our study had a surgical
hysterectomy, most of the women had natural menopause and therefore had experienced a gradual loss of estrogen. Thus, the extent to which the animal literature applies to these women is not clear.

A further notable feature of studies assessing the effects of estrogen on food intake in laboratory animals, which may compromise their applicability to the postmenopausal women in the current study, is that the food intake of laboratory rodents is generally studied for only a short period of time following ovariectomy and hormone replacement. In the current study, women were, on average, years past the start of menopause and many had been using HRT for years. Animal studies have not generally assessed food intake beyond the initial days or weeks of ovariectomy and estrogen replacement. It may be that estrogen exerts a more powerful hypophagic effect around the time of initiation of use, and becomes less effective with continued administration.

Conclusions

In conclusion, the postmenopausal women in our study increased their total caloric intake following smoking cessation, and this was primarily due to an increase in intake of high fat/high sugar foods. Future studies will be needed to determine if the increase in high fat/high sugar foods found in the current study applies to men and premenopausal women. While the physiological causes of increased food intake following smoking cessation are not fully understood, the findings of this study suggest that those mechanisms specifically involved in the intake of high fat/high sugar foods should be a focus of attention for future investigation.

Serum levels of estrogen were not predictive of lower increases in food intake, and unexpectedly, higher estrone sulfate levels predicted greater increases in intake of
high sugar and high fat/high sugar foods following smoking cessation. Differences between women who self-selected to use HRT and women who did not use HRT were found in body shape, weight history, and eating characteristics, and it is hypothesized that these baseline differences may account for the unexpected association between estrone sulfate and postcessation hyperphagia. However, other explanations for this effect cannot be ruled out, and further research is needed to address the current gaps in knowledge regarding the effects of female sex hormones on food intake in postmenopausal women.
REFERENCES


VITA

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