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The Role of Low Progesterone and Tension as Triggers of Perimenstrual Chocolate and Sweets Craving: Some Negative Experimental Evidence

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MICHENER, W., P. ROZIN, E. FREEMAN AND L. GALE. *The role of low progesterone and tension as triggers of perimenstrual chocolate and sweets craving: Some negative experimental evidence.* PHYSIOL BEHAV **67**(3) 417–420, 1999.—Approximately half of the 40–50% of North American women who crave chocolate or sweets do so principally in the perimenstrum, the part of the menstrual cycle surrounding the onset of menstruation. We test two hypotheses about the events that trigger these cravings: 1) the premenstrual drop in progesterone levels; or 2) dysphoria or tension in the perimenstruum. Chocolate craving, sweets craving, and other perimenstrual symptoms were rated daily for six menstrual cycles by a sample of women with severe premenstrual syndrome (PMS). Forty-four women satisfied criteria for cyclicity in chocolate craving, and 44 for sweet craving, determined during the first two cycles. Thirty-four subjects satisfied criteria for craving of both chocolate and sweets. After placebo treatments during the third cycle, subjects were randomly assigned, double blind, to administration of placebo, oral micronized progesterone, or alprazolam (a tranquillizer). Treatments were administered from the beginning of the third week to the second day postonset of menstruation during the fourth to sixth months of study. Neither progesterone nor alprazolam decreased chocolate or sweets craving. © 1999 Elsevier Science Inc.

Chocolate and sweet craving Low progesterone Tension Perimenstrual

CHOCOLATE craving occurs in a definite relationship to the menstrual cycle in a substantial minority of women. Using weekly ratings, Tomelleri and Grunewald (24) found that craving for chocolate increased relative to craving for comparable nonchocolate sweets in the week of menses. Cohen, Sherwin, and Fleming (6) found chocolate and chocolate chip cookies the most frequently craved foods before menses, although other sweets were also craved. Rozin, Levine, and Stoess (19) found that 23% of American college women and their mothers reported craving chocolate in the perimenstruum, the days just before and just after the start of menses. The cyclical women chocolate cravers also gave chocolate a higher hedonic rating than men or noncyclical women cravers did.

Craving for unspecified "sweets" is also associated with the perimenstruum (3,17,22,23). Bowen and Grunberg (4) found that subjects consumed more of a sample of sweet foods before menses, but not more of salty or bland foods. The sweet foods included both chocolate and nonchocolate sweets, but no comparisons between the two were made.

It is reasonable to presume that chocolate craving has a physiological basis. Chocolate is a dense source of fat and carbohydrate calories, and contains many known (and perhaps, many unknown) pharmacologically active substances (11). These include caffeine and its related xanthine, theobromine, and the sympathomimetic amines, tyramine and phenylethylamine. These components are activating/arousing substances. In addition, anandamide and two of its analogs, *N*-oleoylethanolamine and *N*-linoleoylethanolamine, have recently been discovered in chocolate (7). These substances could be expected to have a calming/anxiolytic effect if the quantities present are sufficient to produce any noticeable effect.

The claim for a "physiological" basis amounts to two separate claims: (a) some definable set of physiological events/changes causes chocolate craving; and (b) some caloric/pharmacological effect of ingested chocolate satisfies chocolate craving. Although these claims are likely to be empirically linked, they are logically independent.

Michener and Rozin (15) have provided experimental evidence that it is the sensory as opposed to pharmacological

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properties of chocolate that satisfy cravings: the experience of eating chocolate satisfies the craving, whereas the pharmacologically active contents of this same amount of chocolate (taken in capsule form as cocoa powder) has no effect on craving, even 90 min after ingestion, when the activity should have been fully expressed. These authors found that white chocolate, which has all of the calories but neither the pharmacological nor sensory aroma effect, has about half the potency of brown chocolate at reducing craving. This partial effect could be due to some combination of the sensory (textural) experience of white chocolate, and its high caloric load (the same as that of brown chocolate). Most of the subjects in the Michener and Rozin experiment were not perimenstrual cravers, so it is possible that for such cravers, the pharmacological effects of chocolate are important in reducing craving. (No such trend appeared in that experiment, but the number of perimenstrual cravers was too small for an adequate test.) In any event, this experiment has no direct implication for the cause of chocolate craving, because, as we have pointed out, cause and satisfaction do not have to be expressed in the same way. For example, caloric depletion, a clear physiological/systemic event, is reported to cause an enhancement of the pleasure of experiencing a sweet taste (5).

Food cravings are considered to be a symptom of the premenstrual syndrome (1,26). The perimenstruum is a period of particularly low levels of ovarian hormones, estrogen and progesterone. Hence, low progesterone level is a reasonable candidate for causing perimenstrual craving and other perimenstrual symptoms.

Some researchers have suggested that women seek out and consume carbohydrates (25) or sweets (23) to alleviate premenstrual dysphoria. Some have suggested that women self-medicate for any depression with sweets (21) or chocolate (12, 21). On the other hand, perimenstrual chocolate cravings (24) and general food cravings (3) can occur in women who do not suffer any change in mood in the perimenstruum. Clearly, not all perimenstrual food cravings are secondary to mood change. Whether some are, is an open question.

In this study we examine craving for chocolate and nonchocolate sweets in a sample of women with severe premenstrual syndrome (PMS). The women were treated for PMS with progesterone, alprazolam, or placebo. If the normal premenstrual fall in progesterone is critical to perimenstrual chocolate or sweets craving, then exogenous progesterone given in the late luteal phase and early menses should reduce these cravings. Alprazolam reduced premenstrual dysphoria (10). If chocolate and/or sweets craving are secondary to dysphoria, alprazolam should reduce craving as well. Daily ratings of craving for nonchocolate and chocolate sweets were used to evaluate these hypotheses.

MATERIALS AND METHODS

The subjects of this study were women participating in a clinical trial of treatments for premenstrual syndrome (PMS) at the PMS Program at the Hospital of the University of Pennsylvania. All subjects gave written informed consent. The study was approved by the institutional review board of the University of Pennsylvania. The methods used in the clinical trial are described in greater detail elsewhere (10).

Subjects first entered the study by requesting medical treatment for PMS. They were required to be between the ages of 18 and 45, with regular menstrual cycles of 22 to 35 days, have no current major psychiatric diagnosis, and be in general good health. Subjects maintained daily symptom reports for two complete cycles to confirm premenstrual symptoms. If data from both cycles met criteria for PMS, subjects were given one cycle of single-blind placebo. Subjects who continued to meet the PMS criteria after the placebo cycle were randomized to double-blind treatment.

Following the 3-month screening period, 185 subjects were randomly assigned to three months of double-blind treatment with either placebo, oral micronized progesterone, or alprazolam in a flexible dosing schedule. Medication was administered from Day 18 of the cycle to the first day of menses, with a taper on the first 2 menstrual days. The initial daily dose was 1200 mg of progesterone, 1 mg of alprazolam, or four placebo capsules, taken in divided doses, four times per day. After 3 days, the bedtime dose could be increased to two capsules for the remaining 8 days unless precluded by side effects. The dose was tapered by half on the first day of menses and ended on the second menstrual day to preclude withdrawal symptoms such as insomnia, anxiety, and irritability that could occur with alprazolam. In the second treatment cycle, the daily dose started at four or five capsules (if the latter level was reached in the previous cycle) for 3 days and then increased. Dosage increases were allowed to a maximum of 12 capsules per day (three times the initial dose). The mean doses in the third treatment cycle were 1760 mg of progesterone, 1.5 mg of alprazolam, and 6.7 placebo capsules per day (10).

For the analysis of menstrual cycle data, all cycles were standardized to 28 days. Day 28 was set as the day before bleeding, and all days counting backward 17 days (to day 12) were included in the data set. Then the first 11 days in the cycle were included (accounting for 28 days). Thus, for cycles longer than 28 days, the omitted days were between days 11 and 17 before the onset of menses in the next cycle. For cycles shorter than 28 days, the scores on the last available follicular phase day were repeated through Day 11 to produce a 28-day cycle. This method distorts the late follicular phase, but presents an accurate picture of the perimenstruum.

The study subjects rated 17 PMS symptoms daily (with "food craving" as one) according to the scale 0 = not present at all, 1 = minimal: only slightly apparent to you, 2 = moderate: aware of symptom, but does not affect daily activity at all, 3 = a lot: continuously bothered by symptom and/or it interferes with daily activity, 4 = severe: symptom is overwhelming and/or unable to carry out daily activity. In the original study (10), scores were obtained by summing the ratings on Days 23–28 (premenstrual score) and Days 5–10 (postmenstrual score) of each study cycle for the total symptoms and for five symptom dimensions. The symptom dimensions were derived by a previous factor analysis of the Daily Symptom Report (DSR) (26): mood (irritability, mood swings, anxiety, depression, nervous tension, out of control, and crying); mental function (poor coordination, insomnia, confusion, and fatigue); pain (cramps, aches, and headache); physical symptoms (breast tenderness and swelling); and craving foods. The PMS criteria were (a) a total DSR score of at least 70 for Days 23–28, and (b) a DSR score for Days 23–28 at least 50% higher than the score for Days 5–10.

For this particular round of treatment evaluations (testing the effects of progesterone and alprazolam) subjects also made daily ratings of "craving chocolate" and "craving nonchocolate sweets" according to the same 0–4 scale.

Because previous research has shown that chocolate cravings extend into the first few days of menses (14,19,24), the perimenstruum was defined to include the first 2 days of

menses; that is Days 23–28 plus Days 1 and 2 of the "next" cycle (8 days) . Days 7–14 made up the baseline period of comparable length (8 days).

Subjects were considered cyclical chocolate cravers if their chocolate cravings during the perimenstruum were at least twice their baseline cravings, and if their average total chocolate craving score per cycle totaled at least 3. Cyclical nonchocolate sweet craving was defined analogously. Data from the second untreated cycle and the third cycle, in which all subjects were given placebo, were averaged, and used to make these evaluations.

In the present study, the effect of treatment on craving for chocolate and craving for nonchocolate sweets was analyzed by ANOVA. The outcome measure was the decrease in cravings scores in the perimenstruum (Days −6 to +2, where +1 is the first day of menses) in treatment (average of the second and third treatment cycles) compared to screening (average of the second screening cycle and the all-placebo cycle). The last 2 months of treatment are taken to represent treatment effects, because dosages were adjusted upward, if needed, following the first month of treatment. A parallel ANOVA analysis simply compared the level of perimenstrual craving in the last two treatment months, across teatment groups.

Seventy-one subjects provided six cycles of data that did not exceed our criterion for number of missing data points. [This low yield is, in part, due to the fact that chocolate and sweet craving data were not available for all of the 185 subjects in the Freeman et al. (10) study.] Of the 71 subjects, 44 met the criteria for perimenstrual chocolate cravings. The same number met criteria for perimenstrual craving of nonchocolate sweets. The overlap between these two groups was 34.

Our criterion measure for craving in each subject is the mean craving score in the 8-day perimenstrual period, itself averaged over the last 2 months of treatment (months 5 and 6). A second measure, compensating for individual differences in level of baseline craving, is this same score minus the equivalent score for the perimenstrual period in the last two pretreatment months (months 2 and 3). Relevant values are displayed in Table 1.

RESULTS

All groups showed a modest decrease, of about 0.5 rating points per day, from the pretreatment to treatment periods. The cause of this drop (across all conditions) is not known. The degree of decrease was not related to treatment, the decrease being 0.47 for progesterone, 0.35 for alprazolam, and 0.57 (the largest decrease!) for placebo. The ANOVA did not reveal any significant difference in the effects of the three treatments, $F(2, 41) = 0.24$, $p = 0.8$ (all results summarized in Table 1).

Similarly, overall sweet craving was reduced in all groups, to a degree and in a pattern similar to the chocolate craving reduction, with, again, the largest reduction (0.87) in the placebo group. The ANOVA did not show any significant difference among the three reductions, $F(2, 41) = 0.64$, $p = 0.5$.

DISCUSSION

These results establish that there is cyclical variation in craving for chocolate and nonchocolate sweets in some women with PMS. Out of 71 subjects with complete data, 48% experienced cyclical craving for both chocolate and sweets, 14% for chocolate only, and another 14% for nonchocolate sweets only. It is not possible to say whether the rates for sweet and chocolate craving found in this PMS population are higher than general population rates, because there are no studies applying the same criteria to the general population.

The cyclical pattern found here using prospective reports from women with PMS generally confirms the pattern found previously in retrospective data from a sample of all cycling women (19). Like other so-called "premenstrual" symptoms (13) chocolate craving and sweets craving extend into the first few days of menses.

Our reported absence of any differential effect of drug or hormone on chocolate or sweet craving is consistent with the finding that unspecified food cravings were also unaffected by treatment in the original study that provided the data base for this study (10). The original study showed that alprazolam but not progesterone was significantly better than placebo in reducing total symptoms of PMS. Alprazolam was effective at reducing the mood, mental function, and pain factors, while progesterone was effective in reducing physical symptoms (10). Hence, it cannot be argued that our failure to find an effect on craving resulted from ineffective doses. (In addition, of course, the doses were selected to be effective, based on the prior literature and therapeutic practice.)

The overall drop in craving over the 6-month period for all three groups of subjects is striking, and has no obvious explanation. It cannot be a seasonal effect, because subjects were not "in phase," that is, they began the experiment whenever

TABLE 1

EFFECT OF PLACEBO, PROGESTERONE, AND ALPRAZOLAM ON CHOCOLATE AND SWEET CRAVING DURING THE PERIMENSTRUAL PERIOD (DAYS −6 TO −2 OF THE CYCLE) [MEAN CRAVING SCORE/DAY, AVERAGED OVER TWO CYCLES, (SEM)]

Treatment	*n**	Mean Crave/Day Months 5/6	Mean Crave/Day Months 2/3	Mean Difference Months 5/6–1/2
Chocolate				
Placebo	9	0.42 (0.21)	0.99 (0.24)	−0.57
Progesterone	18	0.79 (0.17)	1.26 (0.18)	−0.47
Alprazolam	17	0.62 (0.23)	0.97 (0.18)	−0.35
Sweets				
Placebo	9	0.53 (0.16)	1.41 (0.41)	−0.87
Progesterone	18	0.68 (0.17)	1.21 (0.16)	−0.53
Alprazolam	17	0.77 (0.24)	1.19 (0.19)	−0.42

*Although the *n*s by treatment match precisely between chocolate and sweet cravers, only 34 of the 44 reported subjects are the same individuals for both groups.

they enrolled and passed the screening. In the larger sample in the original study (10), using 17 daily measures (including generalized food craving), there was a general decline in symptoms over the 6-month treatment period. The only factor that did not decline was the pain factor in the placebo group. Food cravings declined significantly ($p < 0.05$) in the alprazolam and progesterone groups, and did not decline significantly in the placebo group ($p < 0.20$), but there was no differential effect when comparing the three groups and controlling for baseline (ANCOVA, $p = 0.47$) (10).

The fact that exogenous progesterone failed to lower chocolate or sweets craving, compared to placebo, suggests that the normal late luteal fall in progesterone may not be critical to the induction of these cravings.

The hypothesis that sweet and/or chocolate craving is secondary to perimenstrual dysphoria is not supported. Alprazolam reduced dysphoria in the original study; that same study reported a reduction in food cravings with alprazolam, but this reduction did not significantly exceed the drop in the placebo group. Alprazolam did not reduce craving for chocolate or nonchocolate sweets compared to placebo, under the conditions of this study. This is consistent with earlier factor analyses suggesting that food craving does not load onto the negative mood factor in PMS (8,9,16,20,26). It does not support the hypothesis that chocolate is craved for a possible antidepressant effect of exogenous phenylethylamine (12), or for a possible anxiolytic effect of exogenous anandamide or its analogs in chocolate.

Another hypothesis ties perimenstrual chocolate craving to antifatigue (14,18) or attentional effects (2,14) of phenylethylamine or other sympathomimetic amines in chocolate. This hypothesis suffers from the defect that perimenstrual women do not crave other sources of sympathomimetic amines, such as cheese and wine [see (14)]. It also does not explain the close association between nonchocolate sweet and chocolate craving. Another possible physiological cause is increased insulin sensitivity in the perimenstruum [see (14), for discussion].

It is possible that dose adjustments or other craving measures could provide evidence for either dysphoric/tension or low progesterone levels, or that these factors contribute to craving only in interaction with other, presently unmeasured factors. We are left with the presumption that perimenstrual triggerings of chocolate and sweet craving have a systemic, physiological component, although our prior data suggest that the satisfaction of chocolate craving may be purely sensory (15).

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