Physiology & Behavior 255 (2022) 113943

Contents lists available at ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/physbeh

Food preferences throughout the menstrual cycle – A computer-assisted neuro-endocrino-psychological investigation

Marie Lefebvre [a,1], Michael P. Hengartner [b,1], Enrico Tronci [c], Toni Mancini [c], Fabian Ille [d], Susanna Röblitz [e], Tillmann Krüger [f], Brigitte Leeners [a,*]

[a] Department of Reproductive Endocrinology, University hospital Zürich, 8910 Zurich, Frauenklinikstr. 10, Switzerland
[b] Department of Applied Psychology, Zurich University for Applied Sciences (ZHAW), Zürich, Switzerland
[c] Department of Computer Science, University of Roma "La Sapienza", Roma, Italy
[d] Center of Competence in Aerospace Biomedical Science & Technology, Lucerne University of Applied Sciences and Arts, Hergiswil, Switzerland
[e] Computational Biology Unit, Department of Informatics, University of Bergen, Bergen, Norway
[f] Department of Psychiatry, Social Psychiatry and Psychotherapy, Medical School Hannover, Hannover, Germany

ARTICLE INFO

Keywords:
Eating behavior
Food preference
Estrogen
Estradiol
Progesterone
Menstrual cycle

ABSTRACT

Background: As eating behavior changes in relation to the menstrual cycle and weight changes with menopausal transition, ovarian hormones appear to be involved in regulating eating behavior. However, observations are contradictory and are difficult to compare, due to methodological problems related to nutritional epidemiology. To better understand the relationship between ovarian steroid hormones and eating behavior, our study evaluates women's responses to visual food cues at different points in the menstrual cycle with their specific serum estrogen/progesterone levels and women's responses in the case of strong estrogen changes in the context of fertility treatments.

Methods: We collected data from 129 women, 44 of whom received in vitro fertilization (IVF) at the Department of Reproductive Endocrinology, University Hospital Zurich. A total of 85 women with natural cycles were recruited at the University Hospital Zurich ($n = 37$) and at the Hannover Medical School ($n = 48$). Our observational study used 4 different measurement time points across the natural cycle and 2 measurement time points in women with supraphysiological estradiol levels during fertility treatments. Using a second cycle, we then tested our results for replication. At these predefined time points, women were shown pictures of 11 categories of food, with 4 items for each category and blood samples for measurement of hormone levels were taken. Food preferences registered at the time of the investigation were indicated on a visual analogue scale (0–100).

Results: We did not find any statistically significant association between women's serum hormone levels and the rating of visually presented food, either during the menstrual cycle or during fertility treatments after controlling for multiple testing (all $p > 0.005$). Ratings for fruits, vegetables, and carbohydrates showed a significant linear decline throughout the first menstrual cycle ($p < 0.01$), which did not replicate in the second cycle ($p > 0.05$). In contrast, the ratings for sweets showed a significant linear decline in both cycles (both $p < 0.01$), with a mean rating of 54.2 and 48.8 in the menstrual phase of the first and second cycle, respectively, to a mean rating of 47.7 and 43.4 in the premenstrual phase of the first and second cycle, respectively. During fertility treatments, no food rating showed a significant change (all $p > 0.05$). Mood such as negative and positive affects did not influence ratings for visual food cues neither throughout the menstrual cycles nor during fertility treatment.

Conclusions: Serum levels of estradiol and progesterone do not correlate with food ratings in women, even when estradiol levels are above the physiological level of a natural menstrual cycle. Since, except for sweets, significant changes in food ratings in a first cycle did not replicate in a second menstrual cycle, significant findings from the literature based on animal or human studies focusing on a single-cycle have to be interpreted with caution.

* Corresponding author at: Department of Reproductive Endocrinology, University Hospital Zürich, Frauenklinikstr. 10, CH 8091 Zürich.
E-mail address: Brigitte.Leeners@usz.ch (B. Leeners).
[1] First and second author have contributed equally to the manuscript.

https://doi.org/10.1016/j.physbeh.2022.113943
Received 9 April 2022; Received in revised form 11 August 2022; Accepted 11 August 2022
Available online 12 August 2022

1. Introduction

According to the latest data from the World Health Organization, obesity is a growing phenomenon worldwide, with women being affected more often than men [31,75]. Gonadal steroid hormones seem to be among the key regulators of energy intake, by influencing signaling pathways of appetite control through different hormone receptors at central as well as peripherical levels [37,47,52,71]. Low estrogen levels are known to contribute to the development of adiposity in women [37, 47].

As early as the 1990s, scientists observed that women's eating behavior varied with the menstrual cycle [9,25]. Dietary intake was found to be higher during the luteal phase than during the follicular phase [1,5,14,16,22,25,30,34,63,71]. In addition, the intake of certain macronutrients, i.e., fat, sweets and proteins has been reported to differ in relation to phases of the menstrual cycle. However, heterogeneous results hamper the understanding of the underlying regulatory mechanisms. For example, women reported that the intake of food and cravings for foods high in fat and/or carbohydrates were higher in the luteal phase than in the follicular phase [5,16,22,24,34,63]. At the same time, other results did not show any differences in food intake in different menstrual cycle phases [9,25,34]. Results on the consumption of sweets are conflicting too, with some findings showing higher cravings for sweets when estrogen concentrations are high [44] and others showing fewer cravings and a lower food intake during these phases [34,47]. Consequently, data on food consumption of sweets, fats, carbohydrates, and unhealthy foods in relation to phases of the menstrual cycle are currently inconsistent.

Current studies on the association between the menstrual cycle and eating behavior are also hampered by serious methodological limitations, that is, the lack of adequate hormonal measurements and small sample sizes [27,51,62]. In fact, hormone measurements were often not taken; conclusions were based on cycle phases only [52,60]. Nutritional epidemiology has been heavily criticized in recent years for problematic methods and weak study designs [3,38,39,61]; indeed, the deficits mentioned are only examples of such methodological problems. To overcome current methodological shortcomings and better understand the role of hormones in human food preferences, we conducted the present study.

Estradiol is produced primarily by the follicles in the ovaries. Estradiol levels vary during the cycle and can increase from less than 200 pmol/l to 800–900 pmol/l during the follicular phase. During fertility treatment, follicular growth is stimulated in a whole group of follicles, which is why the estradiol level at the end of the stimulation phase is about 10 times higher than in a physiological cycle.

As fertility treatment has no influence on other hormone levels, inclusion of women receiving in vitro fertilization (IVF) provides the opportunity for an experimental model of the isolated effect of a high level of natural estradiol level on eating behavior [49,50].

As human eating behavior is the result of many food intake decisions, which in turn are strongly influenced by different internal and external factors including food preferences at the time of the decision [12,32], we investigated women's food preferences. Using data from a large sample of women in a natural menstrual cycle and from women receiving fertility treatment, we evaluated if and how strongly women's preferences to visually presented food cues fluctuated (i) at different stages of the menstrual cycle and (ii) in relation to progesterone and estradiol levels. We evaluated (iii) whether certain foods aroused more interest than others. We compared (iv) results between a first and a second cycle and (v) results between women in the natural cycles and during the stimulation phase of a fertility treatment.

Based on currently available data, we expected that women in phases with high estradiol levels, i.e., in the preovulatory phase and at the end of follicular stimulation, would be more likely to rate healthy foods (e.g. vegetables and fruit) higher than unhealthy foods (e.g. sweets, coke/ lemonade, alcohol, fast food). As the majority of studies investigating fluctuating eating habits focused on chocolate, sweets, proteins, carbohydrate or simply unhealthy/ high-calorie foods, we also expected that foods, and especially unhealthy foods, would be rated higher in the post-ovulatory phases, i.e., when estradiol levels are lower and progesterone levels are higher. As the literature mostly argues for a suppressive effect of estradiol on food intake, we also expected to see lower food preference ratings at the end of the stimulation phase of women receiving fertility treatments.

2. Methods

2.1. Setting and study design

Our data were collected as part of a project investigating the relationship between changes in serum hormone levels and neuropsychological function, mood, stress, and emotions in naturally cycling woman and in women receiving fertility treatment.

Data were collected from 129 healthy women and women with predefined endocrine disorders (polycystic ovary syndrome (PCOS), endometriosis, hyperprolactinemia), 44 of whom were receiving IVF treatment at the Department of Reproductive Endocrinology, University Hospital of Zurich, Switzerland. Eighty-five women for measurements in natural cycles were recruited at the University Hospital of Zurich (n = 37) and at the Hannover Medical School (n = 48). All women with endocrine disorders were recruited in Zurich. The study was conducted as a prospective longitudinal and observational study. To avoid false positives, we tested significant associations in a first cycle for replication in a second cycle.

2.2. Women recruited

The women were recruited through different channels, including advertisements on the university and hospital bulletin boards, personal requests at the time of consultations in the Department of Reproductive Endocrinology, University Hospital Zurich, or recommendations by physicians specialized in gynecological endocrinology, and word-of-mouth recommendations. Study participants received an expense allowance for inconveniences related to study participation. While women whose measurements taken during their menstrual cycle had to come especially for the data collections for the study, in women receiving IVF, data collection was combined with examinations in the context of the IVF treatment.

A control visit at the beginning of the study was carried out for women monitored during their natural menstrual cycle. A medical checkup served to rule out diseases that affect cognition and hormone levels, except for hyperprolactinemia, endometriosis, and PCOS. No woman was perimenopausal. Prolactin, testosterone, follicle stimulating hormone (FSH), luteinizing hormone (LH), progesterone, estradiol, fasting glucose and insulin, thyroid-stimulating hormone (TSH) (as well as anti-Müllerian hormone (AMH) in Zurich) were checked at cycle days 2–5 as baseline characteristics. Women were excluded on the basis of use of oral contraceptives, pregnancy or lactation in the past 6 months, medication, surgery affecting hormones, no regular working hours, important diseases or mental disorders, which might have an impact on test performance, menstrual cycle/ endocrine disorders apart from those related to the endocrine diseases specified above, or insufficient language skills to complete study tasks. In critical cases decision on study participation was discussed and decided by a gynecological endocrinologist/psychotherapist and a neurologist/psychiatrist.

Women receiving IVF underwent the usual investigation for infertility at the Department of Reproductive Endocrinology, University Hospital Zurich. They received a gynecological checkup, a transvaginal ultrasound, as well as hormone measurements to assess hormonal disorders (LH, FSH, estradiol, AMH, testosterone as standard measurements and 17-hydroxyprogesterone, prolactin, and TSH when requested). Uterine hydrosonography, hydro-contrast sonography, or

hysterosalpingography were carried out. Furthermore, each couple was tested for infection with chlamydia, human immunodeficiency virus (HIV), and hepatitis B and C. Language competences, premenstrual syndrome or other medical limitations (for example, psychiatric disorders or medication that could have an impact on cognition) served as exclusion criteria for study participation in naturally cycling women as well as women receiving fertility treatment [49,50].

Socio-epidemiographic information on the 85 naturally menstruating women participating in the first cycle measurements and the 68 women presenting for reevaluation in a second cycle are presented in Table 1.

The 44 women presenting for fertility treatment were aged 36.0 ± 3.4 years (range: 28–44 years). Of these women, 26 received their first treatment and 18 their second treatment. Indications for fertility treatment were idiopathic infertility ($n = 6$), endometriosis ($n = 14$), blocked or removed tubes ($n = 13$), PCOS ($n = 10$), and male infertility alone or in combination with female factors ($n = 34$). None of these women was on a diet or reported pain.

None of the women was either vegetarian or vegan.

2.3. Hormone measurements and assays

A total of 8 hormone measurements were taken in naturally cycling women with a cycle length of 28 ± 4 days. Samples were collected on predefined days, i.e., cycle day 4, 7, 9 or 10, 12, 13, 17, 21, and 28 in a normal 28-day cycle and adjusted to cycle length in case of shorter or longer cycles. In addition to the hormone measurements, ultrasound examinations were performed. The first one was done at the first hormone assessment in the early follicular phase to exclude cysts that might influence the cycle. To evaluate the evolution of the follicle, the second measurement was done on approximately day 11, with adjustment in case of known shorter cycles. The aim of the second ultrasound examination was to plan the pre-ovulatory measurements as accurately as possible. In case of little follicular development, for example, in women with PCOS, supplementary hormone measurements and ultrasound examinations were carried out every 4th – 5th day until follicle maturation or day 30 of the cycle was confirmed.

To confirm the day of ovulation, urine LH tests were conducted (Evial Ovulation Test Midstream, Inophram GmbH, Muri, Switzerland and Clearblue digital Ovulations test, SPD Swiss Precision Diagnostics GmbH, Geneva, Switzerland). Women started the testing 5 days prior to the earliest expected ovulation day or when a 14 mm follicle was seen using ultrasound.

Blood samples for all women were taken at each visit between 7:00 am and 10:00 am. After collection, the samples were sent directly to the laboratory in Zurich, first frozen at −30 °C, and then stored at −80 °C in Hannover. The samples were frozen in Hannover to avoid falsification of results because of different laboratory procedures. All samples were examined by the laboratory in Zurich.

Progesterone evaluations were done with electrochemiluminescence immunoassays (ECLIA), which were put on the Cobas e-602 immunoassay autoanalyzer (Roche Diagnostics GmbH, Penzberg, Germany). The sensitivity of the functional analytical assay for progesterone was 0.48 nmol/L. By evaluating 20 repeat samples over 20 days for quality control, the overall accuracy (inter- and intra-assay) of the assays could be assessed. The overall inaccuracy, indicated as coefficient of variation (CV%), was under 5.1. Estradiol was measured using ECLIA (Elecsys® Estradiol 2), a test established on polyclonal antibodies (Roche Diagnostics GmbH, Penzberg, Germany). Its functional assay sensitivity is 44 pmol/L and the coefficient of variation (CV%) is <7.7%. The ECLIA (Elecsys® Estradiol 3), which has been used since January 15, 2015, was done on a monoclonal antibody (Roche Diagnostics GmbH, Penzberg, Germany), whose functional assay sensitivity is 91.8 pmol/L (25 pg/mL); the CV% is less than 3.36. Typical changes in estradiol and progesterone levels are presented in Fig. 1. [2,15,46].

The analyses were completed at the Institute of Clinical Chemistry of the University Hospital Zurich. The Society for the Promotion of Quality Assurance in Medical Laboratories (INSTAND, Düsseldorf, Germany) and the Reference Institute for Bioanalytics (RfB, Bonn, Germany) conducted external quality controls for all methods of analysis.

While estradiol and progesterone change significantly throughout the menstrual cycle, only estradiol rises sharply throughout the stimulation phase in a fertility treatment, andand other hormone levels remain unchanged. Thus, we deployed a natural and quasi-experimental model to observe the direct association between estradiol and eating behavior.

All neuropsychological tests were realized in a quiet room in the outpatient clinic of each Department. The participants in natural cycles underwent neuropsychological tests and blood sampling at 4 points during the menstrual cycle, i.e., cycle days 2–5 (menstruation), pre-ovulatory, mid-luteal, and pre-menstrual (Fig. 2) and measurements in women receiving fertility treatment at the beginning and the end of the stimulation phase (Fig. 3). The evaluation of food preferences was part of the standardized neuropsychological tests [35,48–50].

The stimulation phase of the fertility treatment was prepared either with a downregulation with daily injections of 0.1 mg Triptorelin (Decapeptyl®) beginning in the midluteal phase of the previous cycle or with 10–30 days of 10 mg Norethisteron (Primolut®) beginning at cycle day 2. For each woman receiving IVF, the hormonal measurements and the neuropsychological tests were conducted at the beginning and at the end of the follicle stimulation phase, with a minimum time interval of 9 days and a maximum of 13 days.

2.4. Measures of reactions to visual food cues

The participants completed the tests in a quiet room on a touchscreen computer, with a trained member of the research team present to verify they had followed the instructions and refrained from eating since the evening prior to the test situation, explain the tests and answer any questions. For each participant, food rating was pretested with 2 examples to make sure the procedure was fully understood. Thereafter, a series of 44 pictures was presented to the subject. For each of the 11 following foods, 4 images extracted from “Adobe” (Supplementary Table 1) had to be rated: fruits, vegetables, carbohydrates, proteins, meat, fat, fast food, dairy products, sweets, alcohol, and soft drinks immediately after each picture appeared. The categories were chosen to include as much as possible of the foods most frequently consumed by women and to also investigate foods consumed unequally by women and men.

The order of the images was mixed so that the 4 images representing any type of food did not appear in a row, this order was kept throughout the test sessions.

After a picture appeared, the women were asked to rate as quickly

Table 1
Socio-epidemiographic characteristics of study participants investigated in their natural menstrual cycle.

	1st cycle $N = 85$	2nd cycle $N = 68$
Age (Mean ± SD)	30.1 ± 5.4 (range: 20–43 years)	29.8 ± 4.9 (range: 20–40 years)
Endocrine pathology		
PCOS (N/%)	16 (18.8%)	13 (19.1%)
Endometriosis (N/%)	13 (15.3%)	11 (16.2%)
Hyperprolaktinemia (N/%)	1 (1.2%)	0
No endocrine pathology (N/%)	56 (65.9%)	45 (66.2%)
BMI (Mean ± SD)	24.9 ± 5.3 (range 17.7 - 45.7)	23.8 ± 4.8 (range 18.7 - 32.3)
Nb of women with obesity (N/%)	12 (14.1%)	9 (13.2%)
University degree (N/%)	27 (31.8%)	23 (33.8%)
Children (N/%)	27 (31.8%)	22 (32.4%)
Married (N/%)	31 (36.5%)	27 (41.6%)

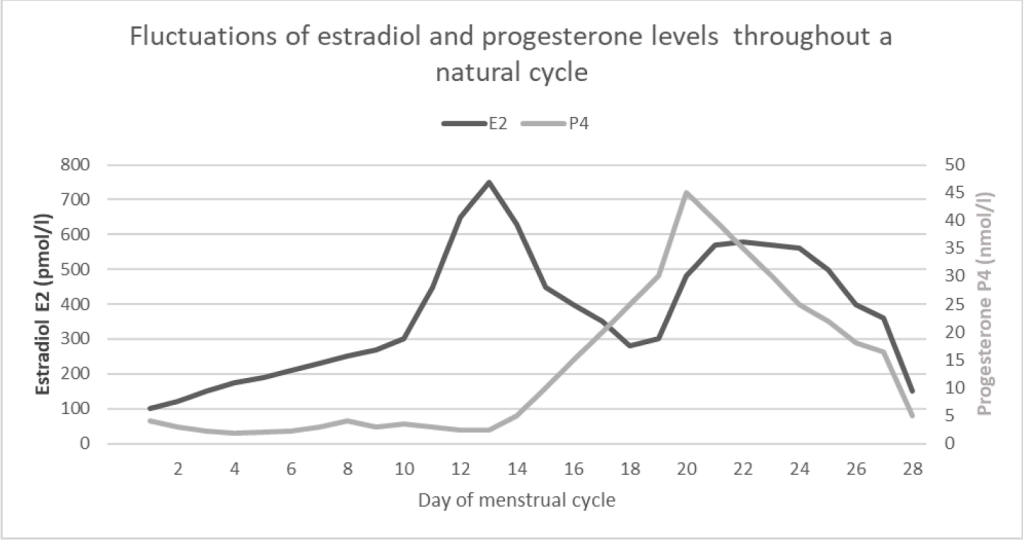

Fig. 1. Fluctuations of estradiol and progesterone levels throughout a natural cycle.

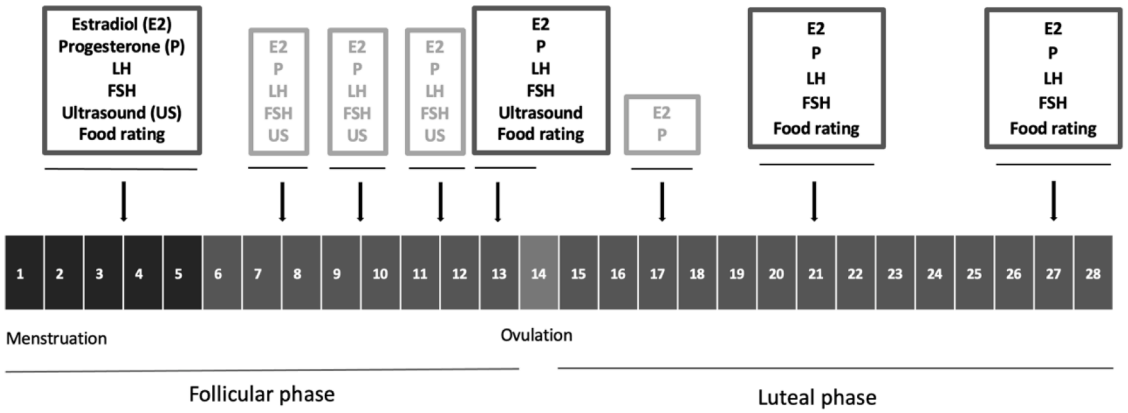

Fig. 2. Measurement points across the menstrual cycle.

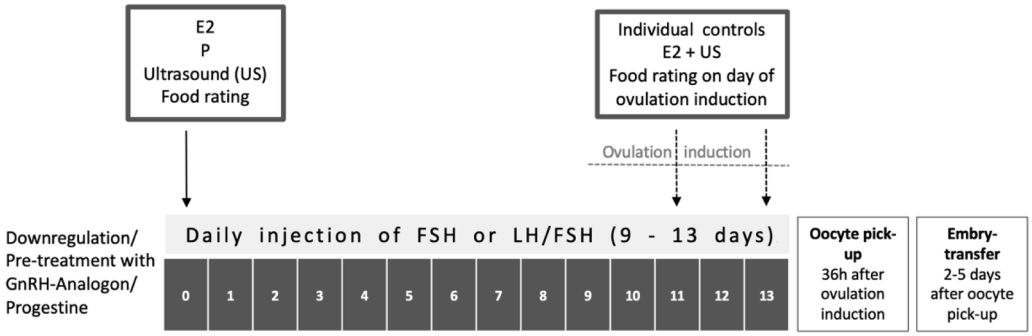

Fig. 3. Measurement points during the stimulation phase of an IVF treatment.

and as precisely as possible on a visual analogue scale (0–100, 0 = not at all, 100 = absolutely) how much they would like to eat or drink the respective food. They were asked to concentrate on rating the food not according to taste but according to what make them feel most like eating or drinking that moment. To start the test, right-handers were asked to place their hand on the right side of the screen and left-handers were asked to place their hand on the left side of the screen. Tests were done in the morning. At both centers, women had not eaten anything since the evening before. Similar pictures appearing in the same order were used in each test session.

2.5. Questionnaire

The emotional state was measured with the Positive and Negative Affect Schedule (PANAS) [72,74]. The scale consists of 20 self-rating items on a five-point Likert scale ranging from 1 "not at all" to 5 "very severe". Both the original scale [72,74] and the German adaptation applied in the present study [45] demonstrated good validity and reliability. In the present study the internal consistency of the negative affect subscale was good (Cronbach's $\alpha = 0.84$; see also [35]. The PANAS was applied at four consecutive time points across the cycle concurrently with the hormone assays and the food rating.

2.6. Statistical analysis

The changes in repeated measurements of food preferences over the menstrual cycle and their associations with serum hormone levels were estimated using generalized estimating equations (GEE). These statistical models were introduced to fit regression analyses that account for within-subject correlation, which is an inherent part of longitudinal studies that rely on repeated outcome measures [77]. GEE pair between- and within- subject effects and are considered to be state of the art for longitudinal data analysis; they are superior to repeated measures (ANOVA) due to their psychometric properties [7,33]. GEE use all available data and impute missing values under the assumption of "missing completely at random" (MCAR). Repeated measures of food ratings scores were entered as the outcome variables and the hormone measures separately as predictor variables. Because the outcome was approximately normally distributed, we fitted all models with normal distribution and the identity link-function. The within-subject covariance was specified with the "unstructured" correlation type to avoid having any constraints on the covariance structure, and a robust sandwich estimator was used to reduce the effects of outliers and influential observations. We entered standardized hormone measures (z-transformed) in all models to ease comparison between estradiol and progesterone. Standardized regression coefficients beta were computed by additionally running a series of models where the outcome variables, i.e., the food ratings, were also z-transformed. According to Cohen's suggestions, effect sizes are considered to be small ($\beta < 0.1$), medium ($\beta \in [0.1; 0.5[$) and large ($\beta \geq 0.5$) [19]. The effect of time (i.e., measurement occasion) was included in all models testing the association between hormone levels and food ratings. No other covariates were included in the models except for the positive and negative affect scales (PANAS) when the potential influence of mood/affectivity was examined. For the analysis of women undergoing fertility treatment, we modelled the interaction between time and estradiol levels, since we were interested in testing whether the steep increase in estradiol levels over time as associated with related changes in food ratings. Due to multiple testing (11 food ratings were regressed on each hormone), we set the level of statistical significance at Bonferroni-corrected $\alpha = 0.005$. All analyses were performed with SPSS 24 for Windows.

Extreme outliers of hormone levels, i.e., values occurring 3 times above the 75th percentile, which were obviously false, were excluded from the statistical analysis. For each hormone measured, this affected 1 or 2 women.

2.6. Ethics

The study was approved by the ethics commissions of Hannover and Zurich (KEK_ZH—Nr 2013–0136) and followed the guidelines of the World Medical Association's Declaration of Helsinki (1964, updated in October 2013). All participants submitted a written informed consent. The study has been registered in clin.trial.gov (NCT02098668).

3. Results

We studied 85 women in their natural cycle and 44 women undergoing fertility treatment. Basic estradiol levels were within the expected range in naturally cycling women and in women receiving IVF, irrespective of the indication for fertility treatment.

Altogether, 4 women had an anovulatory cycle in the first cycle and 3 in the second cycle. As the exclusion of these women did not modify our results, we included them in our investigations. Since an anovulatory cycle also influences hormone levels, and since we wanted to investigate correlations between hormone levels and food ratings, we included these women in the evaluation.

3.1. Ratings of food cues

3.1.1. Ratings across the first and second menstrual cycle in naturally cycling women

The mean values of food ratings during the first and second menstrual cycles are shown in Table 2 and graphically in supplementary Figs. 1 and 2. Ratings were hardly different in both cycles, and at all time points fruits were rated highest, while alcohol received the lowest scores. In general, foods were rated highest in the menstrual phase and lowest in the pre-menstrual phase. Even though we observed a slightly decreasing trend in food ratings throughout each cycle, except for alcohol and coke/lemonade, most foods did not show any significant changes in food rating throughout the cycle. In the first cycle, we observed a significant linear decrease in food ratings over time for fruits, vegetables, carbohydrates, and sweets ($p < 0.01$). In the second cycle, however, this association remained significant only for sweets ($p < 0.01$). The ratings of any other food category found in the first cycle did not replicate in the second cycle. The influence of mood/affectivity was tested by adding the positive and negative affect scales (PANAS) as covariates in the GEE models. Neither positive nor negative affect was related to any food rating (all $p > 0.05$), thus controlling for mood/affectivity did not alter the results for food ratings over time.

3.1.2. Ratings during the stimulation phase of fertility treatment

The mean values of the food ratings at the beginning and at the end of the stimulation phase of IVF treatment are shown in Table 3. Food ratings remained virtually identical over the course of IVF treatment, and no statistically significant change was detected (all $p > 0.05$). As for the women in the natural menstrual cycles, fruits were rated highest, and alcohol was rated lowest at both investigations. PANAS positive affect was significantly associated with fat ($p = 0.026$) and vegetable ratings ($p = 0.015$). PANAS negative affect was significantly associated with dairy products ($p = 0.019$) and coke/lemonade ratings ($p = 0.034$). However, controlling for mood/affectivity did not substantially alter the food ratings over time (no significant change over time).

3.2. Association between food ratings and estradiol/ progesterone levels

3.2.1. Estradiol and progesterone across the first and second menstrual cycle in naturally cycling women

Regression coefficients for the association between food ratings and standardized hormone measurements are presented in Table 4. In both cycles, neither estradiol nor progesterone were associated significantly with food ratings at the corrected 5% significance alpha level (all $p > 0.005$). All effect sizes were negligibly small, with standardized beta coefficients <0.09. Controlling for mood/affectivity (PANAS) did not alter the results for both estradiol and progesterone. Excluding women with an endocrine disorder did not produce any significant association between food ratings and estradiol during the first cycle at corrected 5% significance level alpha except for alcohol ($B = -3.18$, $p = 0.001$), but that result was not replicated in the second cycle ($B = 0.92$, $p = 0.185$). Excluding women with endocrine disorders had no influence on the association between progesterone and food ratings across both cycles (all $p > 0.05$). Detailed results are provided in supplementary Table 1. Finally, excluding overweight women likewise did not alter the results, except for a significant positive association between carbohydrate

Table 2
Ratings of visual food cues across the first and second menstrual cycle in naturally cycling women.

First cycle	Cycle phase			
Visual cues	Menstrual	Pre-ovulatory	Mid-luteal	Pre-menstrual
	Mean (95%-CI)	Mean (95%-CI)	Mean (95%-CI)	Mean (95%-CI)
Fat	53.3	51.6	51.3	51.8
	(49.7 – 56.8)	(48.1 – 55.0)	(48.2 – 54.3)	(48.7 – 54.9)
Fruits #	79.9	77.3	75.4	75.4
	(76.5 – 83.3)	(73.5 – 81.1)	(71.8 – 79.1)	(71.9 – 78.8)
Vegetables #	78.0	73.8	73.0	72.7
	(74.5 – 81.5)	(70.2 – 77.5)	(69.3 – 76.8)	(69.2 – 76.3)
Carbohydrates #	64.9	61.3	60.6	58.1
	(61.2 – 68.7)	(57.8 – 64.7)	(57.3 – 64.0)	(54.6 – 61.7)
Proteins	58.6	58.6	59.6	58.2
	(54.1 – 63.2)	(54.2 – 63.0)	(55.5 – 63.6)	(53.7 – 62.7)
Meat	52.6	50.9	51.7	49.7
	(47.2 – 58.0)	(45.9 – 55.8)	(47.0 – 56.5)	(44.9 – 54.5)
Fast food	47.1	45.2	46.1	42.0
	(42.1 – 52.1)	(40.2 – 50.3)	(41.5 – 50.7)	(37.8 – 46.3)
Dairy products	62.8	61.8	61.9	60.6
	(57.9 – 67.7)	(57.2 – 66.4)	(57.6 – 66.2)	(56.3 – 64.9)
Sweets #	54.2	48.8	49.1	47.7
	(50.1 – 58.2)	(44.5 – 53.0)	(44.9 – 53.2)	(43.7 – 51.8)
Alcohol	30.6	29.1	31.1	31.3
	(26.3 – 34.9)	(25.1 – 33.1)	(26.9 – 35.2)	(27.2 – 35.4)
Coke/ lemonade	37.6	38.0	33.5	38.3
	(31.8 – 43.5)	(32.7 – 43.4)	(28.3 – 38.8)	(32.9 – 43.7)
Estradiol (pmol/l) #	173.4	750.9 (653.8 – 848.1)	570.6 (520.5 – 620.7)	361.0 (307.7 – 414.3)
	(155.5 – 191.3)			
Progesterone (nmol/l) #	1.95	2.43	39.97	16.41
	(1.75 – 2.14)	(2.09 – 2.76)	(34.94 – 44.99)	(12.80 – 20.03)
Second cycle	Cycle phase			
Visual cues	Menstrual	Pre-ovulatory	Mid-luteal	Pre-menstrual
	Mean (95%-CI)	Mean (95%-CI)	Mean (95%-CI)	Mean (95%-CI)
Fat	52.0	52.5	51.2	50.8
	(48.5 – 55.6)	(49.0 – 56.0)	(47.4 – 55.0)	(47.1 – 54.5)
Fruits	74.4	74.1	73.0	72.6
	(69.8 – 78.9)	(70.2 – 78.0)	(68.7 – 77.2)	(68.3 – 76.9)
Vegetables	70.1	69.2	69.4	69.0
	(65.4 – 74.7)	(64.9 – 73.4)	(65.1 – 73.7)	(64.8 – 73.1)
Carbohydrates	58.5	59.0	57.3	57.5
	(54.5 – 62.5)	(55.6 – 62.5)	(53.2 – 61.4)	(53.3 – 61.7)
Proteins	57.2	56.6	58.3	56.9
	(52.5 – 62.0)	(52.0 – 61.3)	(53.6 – 62.9)	(51.6 – 62.2)
Meat	51.2	51.4	51.7	51.6
	(46.0 – 56.3)	(46.2 – 56.6)	(46.7 – 56.7)	(46.6 – 56.7)
Fast food	45.3	44.6	45.0	43.4
	(40.3 – 50.2)	(39.3 – 49.9)	(39.8 – 50.2)	(38.3 – 48.5)
Dairy products	60.3	59.6	59.2	58.2
	(55.4 – 65.2)	(54.6 – 64.6)	(54.2 – 64.2)	(53.1 – 63.2)
Sweets #	48.8	47.7	46.3	43.4
	(44.3 – 53.3)	(43.5 – 52.0)	(41.8 – 50.8)	(39.0 – 47.7)
Alcohol	28.4	28.3	27.7	28.9
	(23.7 – 33.1)	(23.4 – 33.1)	(23.1 – 32.4)	(24.0 – 33.8)
Coke/ lemonade	36.3	35.5	39.2	36.3
	(29.8 – 42.9)	(29.4 – 41.6)	(33.3 – 45.1)	(30.2 – 42.4)
Estradiol (pmol/l) #	187.4	800.5	570.5	306.3
	(166.5 – 208.3)	(675.8 – 925.2)	(509.4 – 631.6)	(247.0 – 365.5)
Progesterone (nmol/l) #	1.88	2.42	41.04	12.22
	(1.65 – 2.10)	(2.09 – 2.75)	(35.28 – 46.79)	(8.75 – 15.69)

Notes.
#: change over time ($p < 0.01$).

ratings and progesterone during the first cycle ($B = 2.80$, $p < 0.001$). All other associations between food ratings and hormone levels did not reach statistical significance at corrected 5% significance level alpha in the second cycle (all $p > 0.005$), including the association between carbohydrate ratings and progesterone ($B = -0.71$, $p = 0.360$). For detailed results, see supplementary Table 2.

Finally, an anonymous reviewer requested that we compute interaction effects between estradiol and progesterone. Although our sample was not sufficiently powered for such an analysis, we complied with this request and found no evidence suggestive of such an interaction effect for any food rating during the first cycle (all $p > 0.1$).

3.2.2. Estradiol serum levels at the beginning and the end of a stimulation phase for IVF

Estradiol levels increased from an average of 54.5 pmol/l (95%-CI: 40.0 – 74.3 pmol/l) at the beginning to 3624.5 pmol/l (95%-CI: 2959.3 – 4439.2) at the end of stimulation. Table 5 shows the regression coefficients to evaluate the association between estradiol and food ratings over the course of the stimulation phase. Although the mean estradiol level rose sharply from the beginning to the end of follicular stimulation, we found no significant association between estradiol level and food ratings at corrected 5% significance level alpha (all $p > 0.005$). Effect sizes were again negligibly small (beta < 0.1), except for vegetables,

Table 3
Food ratings per measurement occasion on women receiving fertility treatment.

Visual cues	Measurement occasion Beginning of stimulation phase	End of stimulation phase
	Mean (95%-CI)	Mean (95%-CI)
Fat	52.5 (48.2 – 56.8)	54.2 (49.7 – 58.6)
Fruits	76.6 (71.5 – 81.6)	75.9 (71.5 – 80.2)
Vegetables	70.4 (65.2 – 75.5)	69.3 (64.9 – 73.8)
Carbohydrates	61.4 (56.1 – 66.7)	61.7 (56.9 – 66.6)
Proteins	59.2 (53.5 – 65.0)	59.9 (54.5 – 65.3)
Meat	52.5 (46.9 – 58.0)	53.1 (47.5 – 58.6)
Fast food	46.3 (39.5 – 53.1)	44.9 (38.3 – 51.5)
Dairy products	63.2 (57.9 – 68.6)	61.2 (55.5 – 66.8)
Sweets	53.9 (48.0 – 59.7)	49.3 (42.7 – 56.0)
Alcohol	24.1 (17.8 – 30.3)	24.2 (17.9 – 30.4)
Coke/ lemonade	30.5 (22.4 – 38.6)	33.7 (26.0 – 41.3)
Estradiol (pmol/l)	54.5 (40.0 – 74.3)	3624.5 (2959.3– 4439.2)

Table 4
Association between food ratings and estradiol/progesterone across the first and second menstrual cycle in naturally cycling women.

First cycle Visual cues	Estradiol		Progesterone	
	B (95%-CI)	P	B (95%-CI)	P
Fat	−0.31 (−1.76 – 1.15)	0.679	1.18 (0.09 – 2.26)	0.033
Fruits	−0.23 (−1.72 – 1.26)	0.760	0.06 (−1.23 – 1.34)	0.930
Vegetables	0.54 (−0.51 – 1.58)	0.317	1.48 (−0.32 – 3.28)	0.106
Carbohydrates	1.21 (−0.17 – 2.58)	0.085	1.27 (0.07 – 2.47)	0.038
Proteins	1.33 (−0.19 – 2.85)	0.087	0.04 (−1.27 – 1.34)	0.957
Meat	−1.36 (−3.18 – 0.47)	0.146	1.44 (−0.58 – 3.46)	0.161
Fast Food	0.10 (−1.94 – 2.14)	0.925	0.23 (−1.76 – 2.21)	0.825
Dairy products	0.45 (−1.11 – 2.00)	0.573	0.70 (−0.67 – 2.08)	0.315
Sweets	0.46 (−0.99 – 1.90)	0.534	−0.43 (−1.86 – 1.00)	0.553
Alcohol	−0.97 (−2.16 – 0.21)	0.108	0.09 (−1.09 – 1.28)	0.876
Coke/ Lemonade	−0.14 (−1.68 – 1.41)	0.864	0.94 (−0.66 – 2.53)	0.249
Second cycle Visual cues				
	B (95%-CI)	P	B (95%-CI)	P
Fat	−0.72 (−2.05 – 0.61)	0.287	−1.14 (−2.73 – 0.45)	0.160
Fruits	−0.11 (−1.07 – 0.86)	0.825	−1.06 (−2.50 – 0.38)	0.148
Vegetables	0.32 (−0.67 – 1.31)	0.526	0.91 (−0.27 – 2.09)	0.132
Carbohydrates	−0.69 (−2.05 – 0.66)	0.317	−0.97 (−2.42 – 0.48)	0.189
Proteins	0.60 (−1.27 – 2.46)	0.531	0.15 (−1.28 – 1.58)	0.840
Meat	−0.58 (−1.84 – 0.67)	0.364	0.42 (−1.40 – 2.24)	0.653
Fast Food	−1.64 (−3.60 – 0.31)	0.099	0.86 (−1.14 – 2.86)	0.398
Dairy products	0.73 (−1.03 – 2.48)	0.419	−0.56 (−1.77 – 0.66)	0.371
Sweets	−1.32 (−2.57 - −0.07)	0.039	−0.93 (−2.45 – 0.60)	0.236
Alcohol	0.98 (−0.31 – 2.27)	0.136	0.82 (−0.81 – 2.44)	0.323
Coke/ Lemonade	0.86 (−0.37 – 2.09)	0.171	−0.02 (−2.01 – 1.97)	0.984

Notes.
Corrected significance level alpha=0.005.

carbohydrates, and meat, where small but non-significant effects were detected (betas = −0.16, −0.24, and −0.17, respectively). Controlling for mood/affectivity (PANAS) did not alter the results substantially, that is, all associations remained statistically not significant.

Table 5
Association between food ratings and estradiol increase during fertility treatment.

	Association with estradiol increase	
Visual cues		
	B (95%-CI)	P
Fat	0.84 (−2.23 – 3.90)	0.593
Fruits	−1.01 (−3.07 – 1.06)	0.339
Vegetables	−2.83 (−6.25 – 0.58)	0.104
Carbohydrates	−4.27 (−7.31 - −1.23)	0.006
Proteins	−0.81 (−4.80 – 3.18)	0.691
Meat	−3.29 (−7.53 – 0.95)	0.128
Fast food	−1.54 (−6.10 – 3.02)	0.508
Dairy products	−0.88 (−5.35 – 3.59)	0.700
Sweets	1.40 (−4.48 – 7.28)	0.640
Alcohol	−1.12 (−5.81 – 3.58)	0.641
Coke/ lemonade	−2.70 (−9.47 – 4.07)	0.435

Note.
Corrected significance level alpha=0.005.

4. Discussion

Investigating a large sample of women at 4 different time points in a natural menstrual cycle as well as women receiving fertility treatment at the beginning and at the end of the stimulation phase, we observed a significant decrease in food ratings for fruits, vegetables, carbohydrates, and sweets across a first cycle, but no changes in relation to the beginning and the end of an IVF stimulation phase. However, except for sweets, these results could not be confirmed in a second cycle. Our data show no association between estradiol or progesterone levels and response to visual food cues over two consecutive menstrual cycles or in association with supraphysiological estradiol levels related to fertility treatment. The decline in preferences for sweets over the menstrual cycle thus does not appear to be associated with hormone levels. Mood/ affectivity is not associated with results.

Our results are at odds with findings supporting a correlation between ovarian steroid hormones and food preferences or cravings [13,18,25,60,68,69,73], but they are consistent with food cravings in 35 women before and after seeing food items and in relation to the cycle phase assessed by urinary LH [56]. No significant variation in cravings for foods rich in fats and sugars could also be demonstrated between the follicular phase and the late luteal phase during a single cycle. Cravings for chocolate, which we classify as a sweet food, also showed no significant variation across the cycle [78]. Our results further agree with an evaluation of self-reported food cravings in 4 measurements per cycle and up to 2 cycles [34]. Although results can not directly be compared because food cravings may differ from ratings of visual food cues, these findings support lack of an association between hormone levels and food preferences. As food ratings do not necessarily turn into actual food intake our results are not in contrast to the numerous findings supporting an association between hormones and food intake.

As we investigated a high number of participants, compared their reactions to food cues with physiological and supra-physiological hormone values up to 4 times in 1 cycle and used a second cycle to validate our results from a first cycle our methodological approach allows very reliable data to understand the role of ovarian hormones on women's food preferences.

Apart from the one study agreeing with our results [34], all other studies failed to replicate their results in a second cycle. Our findings of fewer associations in a second compared to a first cycle supports that a replication of results is mandatory to validate the findings from a first cycle. Presumably, many studies have obtained significant correlations because of false positives, which have not been tested for replication. As overall food ratings were relatively high in the first cycle, regression to the mean might have caused a false-positive relationship, which could be excluded by our measurements in a second cycle [8,67]. A psychological learning effect as well as order effects may be other explanations

for discrepancies.

In contrast to our findings, 4 studies reported increased food cravings for sweets, carbohydrates, and fat in the luteal phase, but these measurements were evaluated in only 1 cycle and no hormonal measurements were taken to determine cycle phase or to confirm ovulation [13,18,60,68]. Because of the large inter-individual variations in cycle length and hormonal values, it is problematic to assert a link between hormones and eating behavior in women without having measured hormone values. Another explanation for the differences in findings may be an interaction effect between estradiol and progesterone [5,41], taking the limited sample size into account, this seems not to be the case in our findings. taki

Statements on the association between estradiol and eating habits are partly derived from different species of animals, in particular mice and rats ([5,6,17,21,26,40,58,64,76]). However, the hormonal cycle in different animal species is markedly different from that of women, and unlike primates, mice and rats have an ovarian cycle that cannot be used as a human model [6]. Furthermore, food ratings based on visual cues and cravings cannot be measured in animals [65].

Desire for a particular food and eating behavior is regulated by a variety of factors [12,65]. On the one hand personal factors, such as general food preferences, emotions, mood, cognition, satiety, hunger, and personality may define ratings of a specific food [32]. On the other hand, external factors i.e., socio-cultural background, social rules on eating behavior, experiences with certain foods or with comments made by parents, but also external stimuli, such as how the food is presented and how it smells have a significant impact on food preferences ([[12], 32,43,66,78]). Therefore, we used the same visual food cues in each test situation, standardized prandial state and investigated mood/affectivity as a confounding factor. As our focus was the association between hormones and food preferences, we estimated that although there might have been individual differences, general habits and preferences should be stable throughout the study period and therefore not interfere with findings. However, eating habits may have modified results for certain types of food (e.g. when asking whether a woman would like to drink alcohol in the morning, she may have answered according to her drinking habits in the afternoon or evening), which would explain the discrepancies with the results of other studies.

Negative affects seem to initiate food intake and eating may reduce the intensity of negative feelings [53,54]. Changes in mood, have been reported to be linked to the menstrual cycle and are further modulated by internal and external factors as well as life situations such as a fertility treatment [20,23,28,35]. However, our results showed no correlation between mood/affect and food ratings in relation to hormone levels, either in women with natural cycles or in fertility treatments.

Although endometriosis may induce pain, none of the women diagnosed with endometriosis experienced relevant pain, which might influence food ratings. While women were not explicitely asked about endometriosis-related pain, they reported general well-being prior to the test situation. To adjust for any relevant impact, we included mood and affect in our analysis. Also, the exclusion of women with endocrine disorders did not alter our results.

Different results may also result from the way food stimuli were presented. In line with our approach, 2 studies presented pictures [4, 30]. Several studies analyzing food preferences and cravings exposed women to real food [56], which may explain differences in findings. Other studies measured food cravings according to women's self-reporting from home [34,78], so that food stimuli correspond to everyday life, but were not standardized. While we investigated reactions to 11 groups of foods, others limited their investigation to 2 groups, for example, high-energy and low-caloric foods with several types of food in each category [4,30]. As the food items presented in our study focused on the type but not the quantity of the food presented, ratings might have been influenced by differences in the quantities shown. Experiments differed greatly in their measurements of reactions to food stimuli. In one study women had to indicate the intensity of their desire to eat a certain food at a certain time in their cycle [56]. Other studies measured the number of food cravings at a certain time without necessarily measuring the intensity of desire for that food, while further studies investigated the amount or type of food eaten [9,13,14,16,22,29, 34]. Two fMRI studies on humans which measured activation of brain regions in reaction to visual food cues observed greater reactions to visual food cues during the luteal phase [4], but both study samples were small and only one study assessed serum estradiol and progesterone levels and across two cycles, as in our study [4].

The desire to eat a food, or the activation of certain brain regions do not necessarily translate into actual food intake; this was shown by several studies that measured both aspects of eating behavior [9,34,56]. Our results can therefore not make a direct statement about eating behavior in terms of food intake, but about food preferences related to hormonal changes. As preferences felt during the morning do not necessarily result in specific food intake during the day, we cannot also not draw any conclusions on the final intake of healthy or unhealthy food, especially as healthiness strongly depends on quantity.

The time of the day of the investigation will likely influence food preference ratings. While our study used tests in the morning, other studies started their tests in the late morning and finished in the afternoon [4,13,56]. Some tested women in the afternoon [30] or assigned times throughout the day in a randomised manner [60].

Obesity is known to be associated with dietary changes related to cyclic hormonal changes [22,36,55], but exclusion of overweight women did not alter results on food ratings in our study.

4.1. Strength and limitations

While most studies had 10–20 participants, our sample is far larger. However, an even larger group would allow to compensate for substantial differences in hormone levels at certain phases of the cycle and allow analysis of interactions between estradiol and progesterone [35].

Our study is one of only a few studies to measure estrogen and progesterone hormone values instead of drawing conclusions based on cycle phases [13,14,29], body temperature [9,29], hormonal measurement in saliva [42], or LH values [30,34]. Another strength of our study is the serial hormone measurements, at up to 4 predefined time points during the natural cycle, as well as 2 measurements during the stimulation phase of a fertility treatment. This combination allowed us to evaluate responses as a function of hormone levels, i.e., we have a quasi-experimental condition to stringently study the influence of estradiol. Measurements throughout 2 cycles allowed us to minimize the risk of incidental findings and to increase the reliability of the results. However, to avoid effects of regression to the mean as well as psychological learning, a balanced design where women are assessed randomly at different cycle phases would have been beneficial. We showed a total of 11 food categories, whereas many other studies compared only 2 categories, and we presented different types of food. Other studies used caloric content as a categorization criterion. While pictures of fruit, vegetables, and sweets are likely to be able to induce food cravings, preferences for other foods, fat for example, are likely to be more difficult to measure by visual cues. Furthermore, our categorization does not allow us to interpret our results according to the healthiness of the food.

Since we measured hormone levels in serum, we can draw conclusions only about systemic hormone effects and not about local hormone effects, for example, in the brain. Furthermore, in this study, we compared objective hormone levels with subjective estimations of food preferences. As all our hormone and food-rating measurements were taken between 7:30 am and 10:00 am, we can rule out inter-individual time-of-day variations that might confound our results. Since the activation of the feeling of hunger in the brain depends not only on the energy content of the food but also on the satiety status [10,57,70], standardization of the prandial state excluded this confounder. In contrast, women were not asked about actual satiety, their last meal,

general food preferences, morning eating habits, whether they usually ate breakfast and were hungry at the time of the investigation or their sleep quality before the testing. All these factors, as well as room temperature, lighting, noise, cultural differences along with attention, social desirability, aiming for healthy eating when preparing for pregnancy, all of which contribute to the complex regulation of eating behavior, have not been standardized and may therefore likely have influenced findings [11,12,32,59]).

5. Conclusion

Our study showed no reliable associations between rising estradiol levels during fertility treatment and fluctuating estradiol and progesterone levels during physiological menstrual cycles on the one hand and responses to visual food cues on the other hand. No link could also be shown in association with different affects. Our results indicate that available findings on the association between ovarian hormones and food ratings should be interpreted critically, significant associations between female steroid hormones and responses to food cues may for example be based on false-positive results due to small sample sizes or lack of replication of results from a first cycle. Future studies on eating behavior should consider the complex interplay between different factors involved in its regulation and investigate to what extent food preferences translate into actual food intake.

CRediT authorship contribution statement

Marie Lefebvre: Conceptualization, Writing – original draft. **Michael P. Hengartner:** Conceptualization, Data curation, Formal analysis, Writing – review & editing. **Enrico Tronci:** Methodology, Project administration, Funding acquisition, Resources, Writing – review & editing. **Toni Mancini:** Conceptualization, Methodology, Writing – review & editing. **Fabian Ille:** Conceptualization, Methodology, Writing – review & editing. **Susanna Röblitz:** Methodology, Funding acquisition, Writing – review & editing. **Tillmann Krüger:** Conceptualization, Methodology, Funding acquisition, Resources, Writing – review & editing. **Brigitte Leeners:** Conceptualization, Funding acquisition, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft.

Declaration of Competing Interest

The authors declare no potential conflict of interest.

Acknowledgments

The evaluation of the hormonal parameters was supported by a FP-7 European Commission grant (PAEON 600773) and by the Bangerter-Rhyner Foundation. The sponsors had no further role in the experimental design, the collection, analysis, and interpretation of data, the writing of this report, or the decision to submit this paper for publication. We thank all study participants and acknowledge their time-consuming participation in our study.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.physbeh.2022.113943.

References

[1] M. Alonso-Alonso, F. Ziemke, F. Magkos, F.A. Barrios, M. Brinkoetter, I. Boyd, C. S. Mantzoros, Brain responses to food images during the early and late follicular phase of the menstrual cycle in healthy young women: relation to fasting and feeding, Am. J. Clin. Nutr. 94 (2) (2011) 377–384, https://doi.org/10.3945/ajcn.110.010736.

[2] M.E. Alliende, Mean versus individual hormonal profiles in the menstrual cycle, Fertil. Steril. 78 (1) (2002) 90–95, https://doi.org/10.1016/s0015-0282(02)03167-9.

[3] E. Archer, G. Pavela, C.J. Lavie, The Inadmissibility of what we eat in America and NHANES dietary data in nutrition and obesity research and the scientific formulation of national dietary guidelines, Mayo Clin. Proc. 90 (7) (2015) 911–926, https://doi.org/10.1016/j.mayocp.2015.04.009.

[4] Y. Arnoni-Bauer, A. Bick, N. Raz, T. Imbar, S. Amos, O. Agmon, R. Weiss, Is it me or my hormones? Neuroendocrine activation profiles to visual food stimuli across the menstrual cycle, J. Clin. Endocrinol. Metab. 102 (9) (2017) 3406–3414, https://doi.org/10.1210/jc.2016-3921.

[5] L. Asarian, N. Geary, Modulation of appetite by gonadal steroid hormones, Philos. Trans. R. Soc. Lond. B Biol. Sci. 361 (1471) (2006) 1251–1263, https://doi.org/10.1098/rstb.2006.1860.

[6] L. Asarian, N. Geary, Sex differences in the physiology of eating, Am. J. Physiol. Regul. Integr. Comp. Physiol. 305 (11) (2013) R1215–R1267, https://doi.org/10.1152/ajpregu.00446.2012.

[7] G.A. Ballinger, Using generalized estimating equations for longitudinal data analysis, Organ Res. Methods 7 (2) (2004) 127–150, https://doi.org/10.1177/1094428104263672.

[8] A.G. Barnett, J.C. van der Pols, A.J. Dobson, Regression to the mean: what it is and how to deal with it, Int. J. Epidemiol. 34 (1) (2005) 215–220, https://doi.org/10.1093/ije/dyh299.

[9] S.I. Barr, K.C. Janelle, J.C. Prior, Energy intakes are higher during the luteal phase of ovulatory menstrual cycles, Am. J. Clin. Nutr. 61 (1) (1995) 39–43, https://doi.org/10.1093/ajcn/61.1.39.

[10] J.D. Beaver, A.D. Lawrence, J. van Ditzhuijzen, M.H. Davis, A. Woods, A.J. Calder, Individual differences in reward drive predict neural responses to images of food, J. Neurosci. 26 (19) (2006) 5160–5166, https://doi.org/10.1523/jneurosci.0350-06.2006.

[11] G.B. Bissonette, M.R. Roesch, Neurophysiology of reward-guided behavior: correlates related to predictions, value, motivation, errors, attention, and action, Curr. Top. Behav. Neurosci. 27 (2016) 199–230, https://doi.org/10.1007/7854_2015_382.

[12] R.G. Boswell, H. Kober, Food cue reactivity and craving predict eating and weight gain: a meta-analytic review, Obes. Rev. 17 (2) (2016) 159–177, https://doi.org/10.1111/obr.12354.

[13] D.J. Bowen, N.E. Grunberg, Variations in food preference and consumption across the menstrual cycle, Physiol. Behav. 47 (2) (1990) 287–291, https://doi.org/10.1016/0031-9384(90)90144-s.

[14] I.M. Brennan, K.L. Feltrin, N.S. Nair, T. Hausken, T.J. Little, D. Gentilcore, C. Feinle-Bisset, Effects of the phases of the menstrual cycle on gastric emptying, glycemia, plasma GLP-1 and insulin, and energy intake in healthy lean women, Am. J. Physiol. Gastrointest. Liver Physiol. 297 (3) (2009) G602–G610, https://doi.org/10.1152/ajpgi.00051.2009.

[15] F.J. Broekmans, M.R. Soules, B.C. Fauser, Ovarian aging: mechanisms and clinical consequences, Endocr. Rev. 30 (5) (2009) 465–493, https://doi.org/10.1210/er.2009-0006.

[16] M. Bryant, K.P. Truesdale, L. Dye, Modest changes in dietary intake across the menstrual cycle: implications for food intake research, Br. J. Nutr. 96 (5) (2006) 888–894, https://doi.org/10.1017/bjn20061931.

[17] P.C. Butera, D.M. Wojcik, S.J. Clough, Effects of estradiol on food intake and meal patterns for diets that differ in flavor and fat content, Physiol. Behav. 99 (1) (2010) 142–145, https://doi.org/10.1016/j.physbeh.2009.10.009.

[18] I.T. Cohen, B.B. Sherwin, A.S. Fleming, Food cravings, mood, and the menstrual cycle, Horm. Behav. 21 (4) (1987) 457–470, https://doi.org/10.1016/0018-506x(87)90004-3.

[19] J. Cohen, Statistical Power Analysis For the Behavioral Sciences, Routledge, 2013.

[20] A. Collins, P. Eneroth, B.M. Landgren, Psychoneuroendocrine stress responses and mood as related to the menstrual cycle, Psychosom. Med. 47 (6) (1985) 512–527, https://doi.org/10.1097/00006842-198511000-00002.

[21] A. Contini, F. Sanna, P. Maccioni, G. Colombo, A. Argiolas, Comparison between male and female rats in a model of self-administration of a chocolate-flavored beverage: behavioral and neurochemical studies, Behav. Brain Res. 344 (2018) 28–41, https://doi.org/10.1016/j.bbr.2018.02.004.

[22] G.B. Cross, J. Marley, H. Miles, K. Willson, Changes in nutrient intake during the menstrual cycle of overweight women with premenstrual syndrome, Br. J. Nutr. 85 (4) (2001) 475–482, https://doi.org/10.1079/bjn2000283.

[23] D.M. Davydov, D. Shapiro, I.B. Goldstein, A. Chicz-DeMet, Moods in everyday situations: effects of menstrual cycle, work, and stress hormones, J. Psychosom. Res. 58 (4) (2005) 343–349, https://doi.org/10.1016/j.jpsychores.2004.11.003.

[24] L. Davidsen, B. Vistisen, A. Astrup, Impact of the menstrual cycle on determinants of energy balance: a putative role in weight loss attempts, Int. J. Obes. (Lond.) 31 (12) (2007) 1777–1785, https://doi.org/10.1038/sj.ijo.0803699.

[25] L. Dye, J.E. Blundell, Menstrual cycle and appetite control: implications for weight regulation, Hum. Reprod. 12 (6) (1997) 1142–1151, https://doi.org/10.1093/humrep/12.6.1142.

[26] L.A. Eckel, Estradiol: a rhythmic, inhibitory, indirect control of meal size, Physiol. Behav. 82 (1) (2004) 35–41, https://doi.org/10.1016/j.physbeh.2004.04.023.

[27] C. Edler, S.F. Lipson, P.K. Keel, Ovarian hormones and binge eating in bulimia nervosa, Psychol. Med. 37 (1) (2007) 131–141, https://doi.org/10.1017/s0033291706008956.

[28] M.A. Farage, T.W. Osborn, A.B. MacLean, Cognitive, sensory, and emotional changes associated with the menstrual cycle: a review, Arch. Gynecol. Obstet. 278 (4) (2008) 299–307, https://doi.org/10.1007/s00404-008-0708-2.

[29] A.K. Fong, M.J. Kretsch, Changes in dietary intake, urinary nitrogen, and urinary volume across the menstrual cycle, Am. J. Clin. Nutr. 57 (1) (1993) 43–46, https://doi.org/10.1093/ajcn/57.1.43.
[30] T.C. Frank, G.L. Kim, A. Krzemien, D.A. Van Vugt, Effect of menstrual cycle phase on corticolimbic brain activation by visual food cues, Brain Res. 1363 (2010) 81–92, https://doi.org/10.1016/j.brainres.2010.09.071.
[31] F. Garawi, K. Devries, N. Thorogood, R. Uauy, Global differences between women and men in the prevalence of obesity: is there an association with gender inequality? Eur. J. Clin. Nutr. 68 (10) (2014) 1101–1106, https://doi.org/10.1038/ejcn.2014.86.
[32] M.D. Gellman, L. LaCaille, Eating behavior, Encyclopedia of Behavioral Medicine711–712 https://doi.org/10.1007/978-3-030-39903-0_1613 (2020) 2020.
[33] R.D. Gibbons, D. Hedeker, S. DuToit, Advances in analysis of longitudinal data, Annu. Rev. Clin. Psychol. 6 (6) (2010) 79–107, https://doi.org/10.1146/annurev.clinpsy.032408.153550.
[34] A.M. Gorczyca, L.A. Sjaarda, E.M. Mitchell, N.J. Perkins, K.C. Schliep, J. Wactawski-Wende, S.L. Mumford, Changes in macronutrient, micronutrient, and food group intakes throughout the menstrual cycle in healthy, premenopausal women, Eur. J. Nutr. 55 (3) (2016) 1181–1188, https://doi.org/10.1007/s00394-015-0931-0.
[35] M.P. Hengartner, T.H.C. Kruger, K. Geraedts, E. Tronci, T. Mancini, F. Ille, B. Leeners, Negative affect is unrelated to fluctuations in hormone levels across the menstrual cycle: evidence from a multisite observational study across two successive cycles, J. Psychosom. Res. 99 (2017) 21–27, https://doi.org/10.1016/j.jpsychores.2017.05.018.
[36] L.S. Heuberger, S. Gobbi, S.C. Weber, G. Graf, P.N. Tobler, L. Asarian, N. Geary, M. Roth, B. Leeners, Is it worth it? Obesity affects snack food across the menstrual cycle, Front. Neurosci. 16 (2022), 800976, https://doi.org/10.3389/fnins.2022.800976.
[37] A.L. Hirschberg, Sex hormones, appetite and eating behaviour in women, Maturitas 71 (3) (2012) 248–256, https://doi.org/10.1016/j.maturitas.2011.12.016.
[38] J.P.A. Ioannidis, The challenge of reforming nutritional epidemiologic research, JAMA 320 (10) (2018) 969–970, https://doi.org/10.1001/jama.2018.11025.
[39] J.P.A. Ioannidis, Unreformed nutritional epidemiology: a lamp post in the dark forest, Eur. J. Epidemiol. 34 (4) (2019) 327–331, https://doi.org/10.1007/s10654-019-00487-5.
[40] K.L. Klump, K.M. Culbert, C.L. Sisk, Sex differences in binge eating: gonadal hormone effects across development, Annu. Rev. Clin. Psychol. 13 (2017) 183–207, https://doi.org/10.1146/annurev-clinpsy-032816-045309.
[41] K.L. Klump, P.K. Keel, S.E. Racine, S.A. Burt, M. Neale, C.L. Sisk, J.Y. Hu, The interactive effects of estrogen and progesterone on changes in emotional eating across the menstrual cycle, J. Abnorm. Psychol. 122 (1) (2013) 131–137, https://doi.org/10.1037/a0029524.
[42] K.L. Klump, S.E. Racine, B. Hildebrandt, S.A. Burt, M. Neale, C.L. Sisk, P.K. Keel, Ovarian hormone influences on dysregulated eating: a comparison of associations in women with versus without binge episodes, Clin. Psychol. Sci. 2 (4) (2014) 545–559, https://doi.org/10.1177/2167702614521794.
[43] M.L. Kringelbach, J. O'Doherty, E.T. Rolls, C. Andrews, Activation of the human orbitofrontal cortex to a liquid food stimulus is correlated with its subjective pleasantness, Cereb. Cortex 13 (10) (2003) 1064–1071, https://doi.org/10.1093/cercor/13.10.1064.
[44] S. Krishnan, R.R. Tryon, W.F. Horn, L. Welch, N.L. Keim, Estradiol, SHBG and leptin interplay with food craving and intake across the menstrual cycle, Physiol. Behav. 165 (2016) 304–312, https://doi.org/10.1016/j.physbeh.2016.08.010.
[45] H. Krohne, B. Egloff, C. Kohlmann, A. Tausch, Investigations with a German version of the positive and negative affect schedule (PANAS), Diagnostica 42 (2) (1996) 139–156.
[46] A. La Marca, G. Stabile, A.C. Artenisio, A Volpe, Serum anti-Mullerian hormone throughout the human menstrual cycle, Hum. Reprod. 21 (12) (2006) 3103–3107, 10.1093/h Ovarian Aging: Mechanisms and Clinical Consequences umrep/del291 10.1002/(sici)1097-4695(19980905)36:3<357::aid-neu5>3.0.co;2-v.
[47] B. Leeners, N. Geary, P.N. Tobler, L. Asarian, Ovarian hormones and obesity, Hum. Reprod. Update 23 (3) (2017) 300–321, https://doi.org/10.1093/humupd/dmw045.
[48] B. Leeners, T.H.C. Kruger, K. Geraedts, E. Tronci, T. Mancini, F. Ille, M. P. Hengartner, Lack of associations between female hormone levels and visuospatial working memory, divided attention and cognitive bias across two consecutive menstrual cycles, Front. Behav. Neurosci. 11 (2017) 120, https://doi.org/10.3389/fnbeh.2017.00120.
[49] B. Leeners, T. Krüger, K. Geraedts, E. Tronci, T. Mancini, F. Ille, M.P. Hengartner, Cognitive function in association with high estradiol levels resulting from fertility treatment, Horm. Behav. 130 (2021), 104951, https://doi.org/10.1016/j.yhbeh.2021.104951.
[50] B. Leeners, T.H.C. Krüger, K. Geraedts, E. Tronci, T. Mancini, M. Egli, F. Ille, Associations between natural physiological and supraphysiological estradiol levels and stress perception, Front. Psychol. 10 (2019) 1296, https://doi.org/10.3389/fpsyg.2019.01296.
[51] N.A. Lester, P.K. Keel, S.F. Lipson, Symptom fluctuation in bulimia nervosa: relation to menstrual-cycle phase and cortisol levels, Psychol. Med. 33 (1) (2003) 51–60, https://doi.org/10.1017/s0033291702006815.
[52] R. Ma, M.E. Mikhail, K.M. Culbert, A.W. Johnson, C.L. Sisk, K.L. Klump, Ovarian hormones and reward processes in palatable food intake and binge eating, Physiology (Bethesda). 35 (1) (2020) 69–78, https://doi.org/10.1152/physiol.00013.2019.
[53] M. Macht, How emotions affect eating: a five-way model, Appetite 50 (1) (2008) 1–11, https://doi.org/10.1016/j.appet.2007.07.002.
[54] M. Macht, G. Simons, Emotional Eating, in: I. Nyklíček, A. Vingerhoets, M. Zeelenberg (Eds.), Emotion Regulation and Well-Being, Springer, New York, 2011, pp. 281–295, https://doi.org/10.1007/978-1-4419-6953-8_17.
[55] J. McNeil, É. Doucet, Possible factors for altered energy balance across the menstrual cycle: a closer look at the severity of PMS, reward driven behaviors and leptin variations, Eur. J. Obstet. Gynecol. Reprod. Biol. 163 (1) (2012) 5–10, https://doi.org/10.1016/j.ejogrb.2012.03.008.
[56] M.A. McVay, A.L. Copeland, H.S. Newman, P.J. Geiselman, Food cravings and food cue responding across the menstrual cycle in a non-eating disordered sample, Appetite 59 (2) (2012) 591–600, https://doi.org/10.1016/j.appet.2012.07.011.
[57] S. Mehta, S.J. Melhorn, A. Smeraglio, V. Tyagi, T. Grabowski, M.W. Schwartz, E. A. Schur, Regional brain response to visual food cues is a marker of satiety that predicts food choice, Am. J. Clin. Nutr. 96 (5) (2012) 989–999, https://doi.org/10.3945/ajcn.112.042341.
[58] M.V. Micioni Di Bonaventura, T.A. Lutz, A. Romano, M. Pucci, N. Geary, L. Asarian, C. Cifani, Estrogenic suppression of binge-like eating elicited by cyclic food restriction and frustrative-nonreward stress in female rats, Int. J. Eat. Disord. 50 (6) (2017) 624–635, https://doi.org/10.1002/eat.22687.
[59] N.C. Orloff, J.M. Hormes, Pickles and ice cream! Food cravings in pregnancy: hypotheses, preliminary evidence, and directions for future research, Front. Psychol. 5 (2014) 1076, https://doi.org/10.3389/fpsyg.2014.01076.
[60] M.N. Parker, M. Tanofsky-Kraff, R.D. Crosby, M.E. Byrne, S. LeMay-Russell, T. N. Swanson, J.A. Yanovski, Food cravings and loss-of-control eating in youth: associations with gonadal hormone concentrations, Int. J. Eat. Disord. 54 (8) (2021) 1426–1437, https://doi.org/10.1002/eat.23530.
[61] K.E. Peace, J. Yin, H. Rochani, S. Pandeya, S. Young, A serious flaw in nutrition epidemiology: a meta-analysis study, Int. J. Biostat. 14 (2) (2018), https://doi.org/10.1515/ijb-2018-0079.
[62] S.E. Racine, K.M. Culbert, P.K. Keel, C.L. Sisk, S.A. Burt, K.L. Klump, Differential associations between ovarian hormones and disordered eating symptoms across the menstrual cycle in women, Int. J. Eat. Disord. 45 (3) (2012) 333–344, https://doi.org/10.1002/eat.20941.
[63] S.C. Reed, F.R. Levin, S.M. Evans, Changes in mood, cognitive performance and appetite in the late luteal and follicular phases of the menstrual cycle in women with and without PMDD (premenstrual dysphoric disorder), Horm. Behav. 54 (1) (2008) 185–193, https://doi.org/10.1016/j.yhbeh.2008.02.018.
[64] J.E. Richard, L. López-Ferreras, R.H. Anderberg, K. Olandersson, K.P. Skibicka, Estradiol is a critical regulator of food-reward behavior, Psychoneuroendocrinology 78 (2017) 193–202, https://doi.org/10.1016/j.psyneuen.2017.01.014.
[65] B.C. Rodríguez-Martín, A. Meule, Food craving: new contributions on its assessment, moderators, and consequences, Front. Psychol. 6 (2015) 21, https://doi.org/10.3389/fpsyg.2015.00021.
[66] E.T. Rolls, F. Grabenhorst, The orbitofrontal cortex and beyond: from affect to decision-making, Prog. Neurobiol. 86 (3) (2008) 216–244, https://doi.org/10.1016/j.pneurobio.2008.09.001.
[67] S. Senn, Francis Galton and regression to the mean, Significance 8 (3) (2011) 124–126, https://doi.org/10.1111/j.1740-9713.2011.00509.x.
[68] L.B. Souza, K.A. Martins, M.M. Cordeiro, Y.S. Rodrigues, B.P.M. Rafacho, R. A. Bomfim, Do food intake and food cravings change during the menstrual cycle of young women? Rev. Bras. Ginecol. Obstet. 40 (11) (2018) 686–692, https://doi.org/10.1055/s-0038-1675831.
[69] R. Tomelleri, K.K. Grunewald, Menstrual cycle and food cravings in young college women, J. Am. Diet. Assoc. 87 (3) (1987) 311–315.
[70] L.N. van der Laan, D.T. de Ridder, M.A. Viergever, P.A. Smeets, The first taste is always with the eyes: a meta-analysis on the neural correlates of processing visual food cues, Neuroimage 55 (1) (2011) 296–303, https://doi.org/10.1016/j.neuroimage.2010.11.055.
[71] D.A. Van Vugt, Brain imaging studies of appetite in the context of obesity and the menstrual cycle, Hum. Reprod. Update 16 (3) (2010) 276–292, https://doi.org/10.1093/humupd/dmp051.
[72] D. Watson, L.A. Clark, A. Tellegen, Development and validation of brief measures of positive and negative affect: the PANAS scales, J. Pers. Soc. Psychol. 54 (6) (1988) 1063–1070, https://doi.org/10.1037//0022-3514.54.6.1063.
[73] H.P. Weingarten, D. Elston, Food cravings in a college population, Appetite 17 (3) (1991) 167–175, https://doi.org/10.1016/0195-6663(91)90019-o.
[74] T.A. Widiger, D.B. Samuel, Diagnostic categories or dimensions? A question for the diagnostic and statistical manual of mental disorders–fifth edition, J. Abnorm. Psychol. 114 (4) (2005) 494–504, https://doi.org/10.1037/0021-843x.114.4.494.
[75] World Health Organization, Obesity and Overweight, 2021. https://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight.
[76] K.E. Yoest, J.A. Cummings, J.B. Becker, Estradiol, dopamine and motivation, Cent. Nerv. Syst. Agents Med. Chem. 14 (2) (2014) 83–89, https://doi.org/10.2174/1871524914666141226103135.
[77] S.L. Zeger, K.Y. Liang, P.S. Albert, Models for longitudinal data: a generalized estimating equation approach, Biometrics 44 (4) (1988) 1049–1060.
[78] D.A. Zellner, A. Garriga-Trillo, S. Centeno, E. Wadsworth, Chocolate craving and the menstrual cycle, Appetite 42 (1) (2004) 119–121, https://doi.org/10.1016/j.appet.2003.11.004.