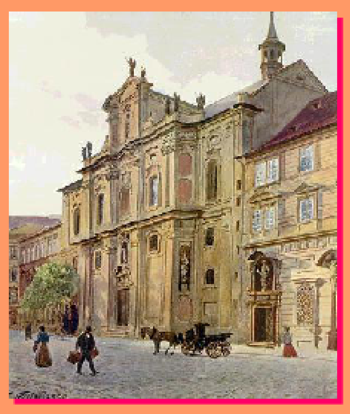
Influence of Food on Daily Profiles of Steroids



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Introduction

A large amount of information has been accumulated on the time structure of the endocrine system. Circadian rhythms of physiological actions including metabolism and behaviour are generated by central and peripheral circadian oscillators, which are tuned up by periodic environmental or physiological stimuli. A master circadian pacemaker in the hypothalamic suprachiasmatic nucleus (SCN) is directly controlled by daily changes of light-dark cycles, and coordinates the timing of other oscillators by direct and indirect neuronal, hormonal and behavioural signals. The daily rhythm of food intake creates stimuli that calibrate most peripheral and central oscillators. Some of these could be involved in the daily rhythm of food anticipatory activity (Patton and Mistlberger 2013).
The highly coordinated output of the hypothalamic biological clock not only governs the daily rhythm in sleep/wake (or feeding/fasting) behaviour but also has direct control over many aspects of hormone release. In fact, a significant proportion of our current understanding of the circadian clock has its roots in studies of the intimate connections between the hypothalamic clock and multiple endocrine axes (Kalsbeeg and Fliers 2013).
Until now, most attention was paid to the main hormones such as melatonin (Vaněček 1998, Trivedi a Kumar 2014), cortisol (Dickmeis 2009, Son et al. 2011, Chung et al. 2011), testosterone (Karatsoreos et al. 2007), estradiol (Christian and Moenter 2010), the neurohormones oxytocin and vasopressin (Forsling 2000) and enterohormones or hormones related to food intake (Konturek et al. 2011). Only rare reports have dealt with other steroid hormones. Some data were published on dehydroepiandrosterone (Stárka et al. 2015) and its hydroxymetabolites, no data could we find for allopregnanolone or pregnenolone. However, in many situations, particularly for neuroactive metabolites, these steroids can extensively modulate many brain functions like mood or behaviour.

Objectives

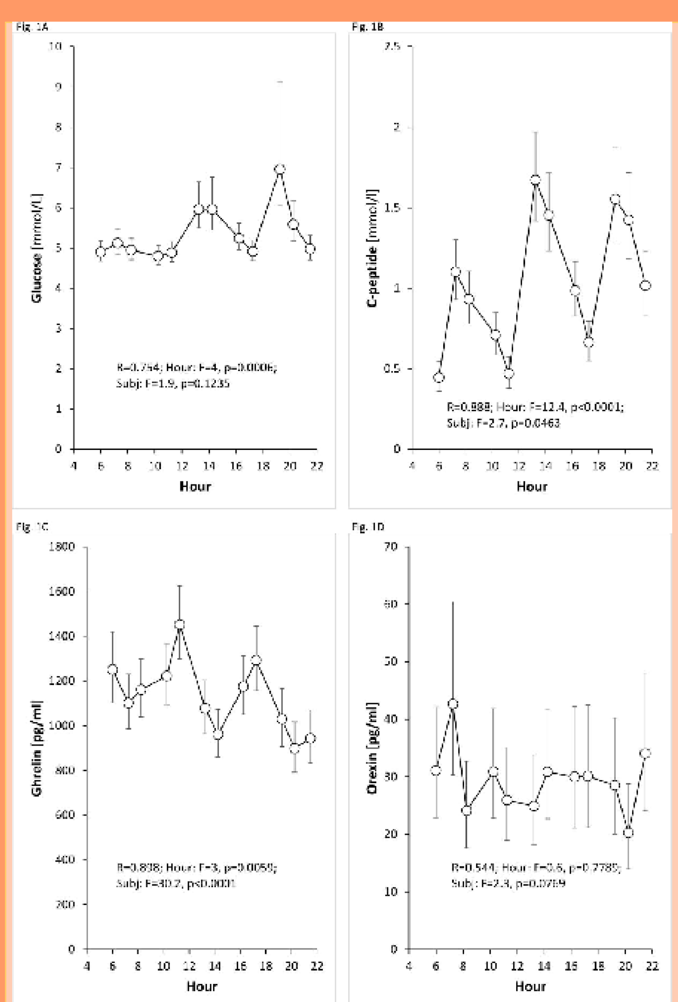
Whereas the daily profiles of the main steroid hormones are well known, minor differences in the course of their levels related to defined and standardised food intake were studied rarely.

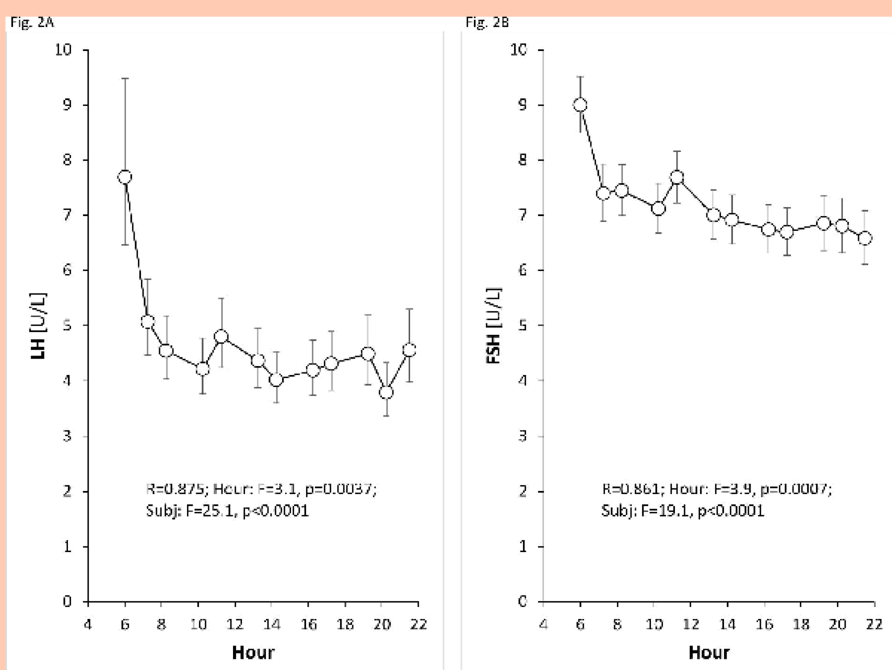
Aim of the study:
Describe the effects of food intake, which could change the basal course of the daily hormone profiles.

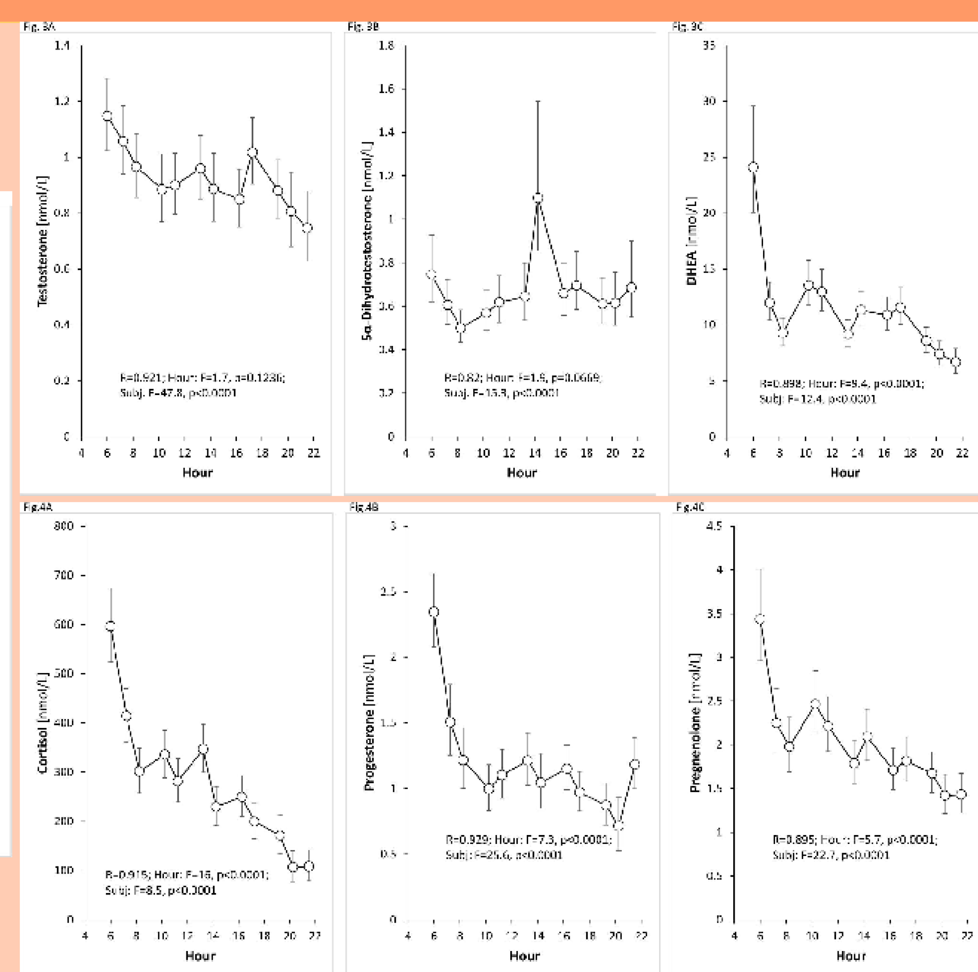
Methods

Eight women (mean age 29.48±2.99 years, mean BMI 21.3±1.3kg/m2) in follicular phase of menstrual cycle were examined. The levels of C-peptide, glucose, LH, FSH, SHBG, orexin A, ghrelin, cortisol, testosterone, dihydrotestosterone, progesterone, pregnenolone, estrone and estradiol were studied during a daily regimen (16 hours) that included standardized food intake.
The first blood withdrawal was at 6 a.m. (30 minutes after awaking) after overnight fasting. The next withdrawals were always one and two hours after eating according to the following schedule (7:15, 8:15, 10:15, 11:15 a.m.; 1:15, 2:15, 4:15, 5:15, 7:15, 8:15 p.m.). The last blood withdrawal was 30 minutes before sleep, at 9:30 p.m. Breakfast (2 slice of bread, ham, cheese and tea) was served at 6:15, a snack (yogurt) at 9:15, lunch (beef broth soup, turkey, potato dumplings, and sauerkraut) at 12:15, an afternoon snack (apple) at 15:15, and dinner (tomato, 2 slices of bread, ham and cheese) at 18:15.
The study protocol has been approved by Local Ethical Committee. A written informed consent was obtained from all participants.

Results







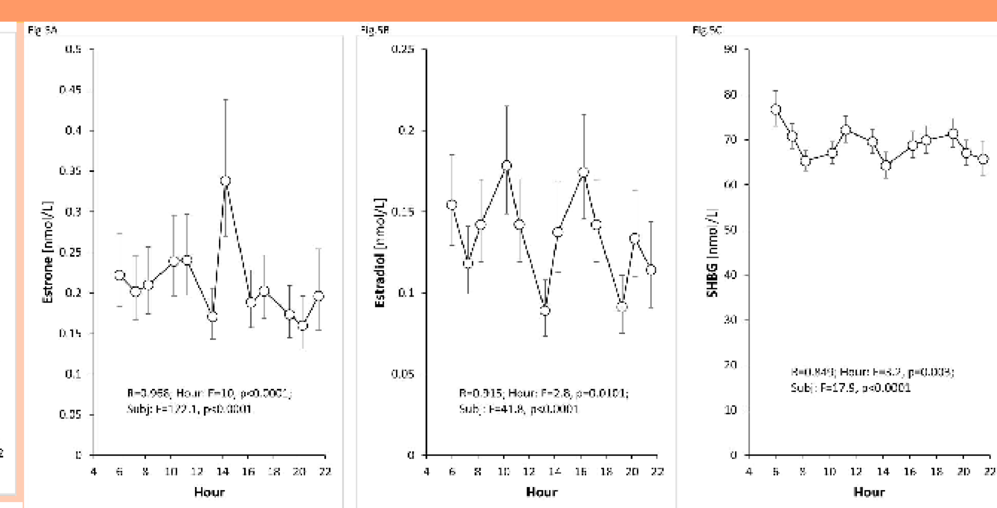


Table 1: Statistical characteristic of diurnal profiles of steroid hormones and other hormones/substances using repeated measures ANOVA with the factors Hour and Subject
H-F = Hour factor showing the differences between time periods
S-F = Subject factor showing the differences between individual subjects
p = significance

substance	hour		subject	
	H-F	p	S-F	p
ghrelin	3	0.0059	30.2	<0.0001
orexin	0.6	0.7789	2.3	0.0769
glucose	4	0.0006	1.9	0.1235
C-peptide	12.4	<0.0001	2.7	0.0463
LH	3.1	0.0037	25.1	<0.0001
FSH	3.9	0.0007	19.1	<0.0001
SHBG	3.2	0.003	17.9	<0.0001
cortisol	16	<0.0001	8.5	<0.0001
progesterone	7.3	<0.0001	25.6	<0.0001
pregnenolone	5.7	<0.0001	22.7	<0.0001
testosterone	1.7	0.1236	47.8	<0.0001
DHT	1.9	0.0669	15.3	<0.0001
DHEA	11.42	<0.0001	12.4	<0.0001
estrone	10	<0.0001	122.1	<0.0001
estradiol	2.8	0.0101	41.5	<0.0001

The majority of the hormones showed significant differences of their levels during the day between hours and especially between subjects (Table 1). Non-significant differences between hours were only found for orexin, testosterone, and dihydrotestosterone (Table 1, H-F), and non-significant differences between subjects (Table 1, S-F) were only found for orexin, glucose and C-peptide.
A significant increase of glucose and C-peptide was observed 1 and 2 hours following the main meals lunch and dinner (P = 0,001, Figs 1 A,B; means and 95% confidence intervals are given in all figures). The most striking marker of food intake was the increase of C-peptide (Fig. 1B), which was significant after breakfast, lunch and dinner.
Ghrelin levels had a significant minimum after lunch and dinner (Fig.1C), whereas the differences in orexin levels over the course of the day were insignificant (Fig.1D, Table 1). LH and FSH (Fig.2A,B) showed a continuous decrease during the day, with no significant additional decrease after main meals. Androgen levels (testosterone Fig. 3A, dihydrotestosterone Fig. 3B) did not show significant relationships to food intake, with the exception of an increase in dihydrotestosterone 2 hours after lunch. Dehydroepiandrosterone (Fig. 3C) significantly decreased 1 and 2 hours after lunch and breakfast respectively.SHBG (Fig. 5C) showed a small decrease after meals.
All three C21 steroids (cortisol Fig. 4A, progesterone Fig. 4B and pregnenolone Fig. 4C) showed a significant decrease one hour after awakening a then a continuous decrease during the day. Cortisolemia decreased continuously throughout the day, and an additional significant decrease of cortisol related to food intake was only observed 2 hours after lunch (Fig. 4A).
Estrogens (estrone Fig. 5A and estradiol Fig. 5B) did not show any striking trend in daily profiles; estradiol decreased significantly after lunch and dinner.

Conclusions

In our study the known nycthemeral rhythm of LH, FSH, cortisol, dehydroepiandrosterone, progesterone and pregnenolone and decrease of ghrelin after food intake were confirmed, but significant changes after meals were also newly observed for the levels of cortisol, dehydroepiandrosterone, estradiol and SHBG. These effects were seen only after the main meals lunch and dinner. After breakfast, these effects are probably masked by the huge changes in the nycthemeral rhythm, and after snacks (yogurt and apples) the effects of food intake were either too small or the time period between eating the meal and the blood withdrawal was too long. It follows that for analytical determination of above mentioned hormones not only the time of blood withdrawals but also food consumption has an important influence upon the resulting values.

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