Mathematical Model for the Diurnal Rhythm of Leptin in Healthy Young Women

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Abstract- New parameters can be introduced to expand families of distributions for added flexibility or to construct covariate models. Introduction of scale parameter usually leads to the accelerated life model, and taking powers of the survival function introduces a parameter that leads to the proportional hazard model of Morgenstern gumbel bivariate distribution was applied to find the diurnal rhythm of leptin depends on energy, or carbohydrate, availability, not intake, and exercise has no suppressive effect on the diurnal rhythm of leptin beyond the impact of its energy cost on energy availability.

Index Terms- Luteinizing hormone; pulsatility parameter, survival functions

I. INTRODUCTION

The independent effects of energy availability and exercise stress on the 24-h mean and amplitude of the diurnal rhythm of leptin.Before their participation,volunteers received a detailed oral and written description of the screening process and experimental protocol,which was approved by the Institutional of university.All volunteers signed an informed consent document. The daily exercise treatment consisted of a series of supervised 30min bouts of walking on a treadmill at 70% of each individual's aerobic capacity, with 10-min rest intervals between bouts until each subject had expended 30 kcal. After the baseline days ,dietary energy intake was controlled by feeding subjects measured amounts of the liquid dietary product, Ensure. Subjects were permitted to drink water ad libitum, but nothing else. Compliance with the energy availability treatments was checked each morning by monitoring urinary acetoacetate levels with Multistix dip sticks. For each subject, 24-h mean leptin concentration was calculated, and leptin time series were expressed both as absolute concentrations and as relative concentrations normalized to the 24-h mean for each subject.

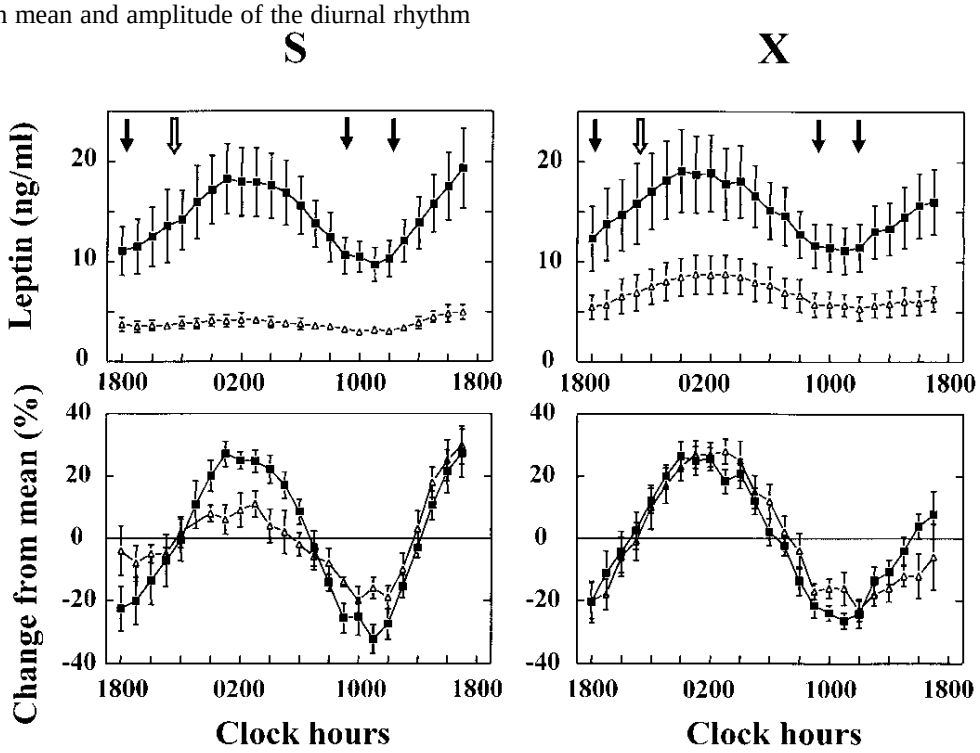


Fig.The 24-h group mean leptin rhythms at the end of 4 days of abalanced (j) and low (n). *Left*: sedentary treatment group (S, *n* =5 7). *Right*: exercising treatment group (X, *n*= 5 9). In S, but not inX, low energy availability blunted the amplitude of the diurnal leptin rhythm as a percentage of the 24-h mean.Values are means 6 SE. Meal times were at 1800, 0900, 1200 (solid arrows),and 2100 (B only, open arrows).

The resulting two time series for each subject were analyzed by cosinor rhythmometry with the assumption of a period of 24 h. All leptin parameters were calculated from the raw leptin data and not from the fitted cosinor curve. The acrophase and nadir were defined as the maximum and minimum leptin concentrations, respectively. Amplitude was defined as one half of the difference between the acrophase and the nadir.

Figure shows the leptin profiles measured during the 24-h frequent blood sampling period. The profiles are presented separately as concentrations and as percentage changes from each individual's 24-h mean. Profiles for balanced and low energy availability treatments are plotted together for comparison. Table presents summary statistics for the profiles shown in Fig.

Table *Leptin parameters after balanced energy availability treatments and effects of low energy availability*

		Sedentary (S)		Exercise (X)	
	Units	Balanced	L effect	Balanced	L effect
Leptin concentrations					
24-h Mean	ng/ml	14.3 ± 1.8	−10.5 ± 1.6‡	15.0 ± 1.8	−8.2 ± 1.4‡
	%		−72 ± 3%‡		−53 ± 3%*‡
At acrophase	ng/ml	18.7 ± 2.3	−14.4 ± 2.0‡	19.6 ± 2.3	−10.8 ± 1.9‡
At nadir	ng/ml	9.5 ± 1.1	−6.5 ± 1.0‡	8.9 ± 2.3	−5.1 ± 0.8‡
Amplitude	ng/ml	4.6 ± 0.7	−3.9 ± 0.6‡	4.6 ± 0.6	−2.8 ± 0.6†
	%		−85 ± 3‡		−58 ± 6*‡
% Change from 24-h mean					
At acrophase	%	30 ± 2	−17 ± 3†	31 ± 2	0 ± 4*
At nadir	%	−34 ± 3	13 ± 5†	−31 ± 2	8 ± 2†
Amplitude	%	32 ± 2	−15 ± 4†	31 ± 2	−4 ± 3*

All values are means ± SE. Effects of low energy availability by exercise expenditure less than effects by dietary restriction: * $P < 0.05$. Effects of low energy availability (L effects = low energy availability values − balanced energy availability values): † $P < 0.01$, ‡ $P < 0.001$.

Comparing exercising women (X) to sedentary women (S) at the same energy availabilities revealed that exercise stress had no suppressive effect on either the 24-h mean (P >0.2) or the amplitude (P > 0.3) of the diurnal leptin rhythm. As mentioned above, however, the unexpectedly excessive rises in leptin during the afternoon of the 2nd day of sampling were smaller in the exercising than in the sedentary women.

Comparing women receiving low energy availability treatments with themselves when they received balanced energy availability treatments revealed that low energy availability strongly suppressed both the 24-h mean and amplitude of the diurnal rhythm of leptin . Low energy availability blunted the amplitude of the leptin rhythm by 10% in all seven sedentary women, and cosinor rhythm analysis was unable to detect a significant rhythm in two of the women . By contrast, the rhythm was maintained in all nine of the exercising women during the low energy availability treatment , and the amplitude was blunted by 10% in only two. Thus there was an interaction between energy availability and exercise stress on both the 24-h mean and amplitude of the diurnal leptin rhythm . This interaction was due to the greater suppression of both the 24-h mean and amplitude of leptin in the sedentary women by low energy availability.

The diurnal rhythm of leptin displayed by the women in this experiment after the balanced energy availability treatments in figure was similar to the rhythms observed in other groups who consumed their diets as oral meals .As in some other experiments however, leptin levels were much higher at the end of the 24-h frequent blood sampling period than at the beginning because of an excessive rise in leptin during the afternoon of the 2nd day of our 24-h frequent blood sampling period in figure probably as an artifact of our feeding schedule. Throughout the treatment period, we controlled energy availability on a 24-h clock from 0800 to 0800, but the frequent blood sampling period was scheduled from 1700 to 1700. During the frequent blood sampling, we administered the balance of the first day's food between 1700 and midnight, in keeping with the feeding schedule during the treatment period, but we administered the entire next day's food between 0900 and 1200, causing an unusually strong drive for leptin secretion in the afternoon. Exercise stress had no suppressive effect on either the 24-h mean or amplitude of the diurnal rhythm of leptin.

II. MATHAMATICAL MODEL

New parameters can be introduced to expand families of distributions for added flexibility or to construct covariate models. Introduction to scale parameter usually leads to the accelerated life model, and taking powers of the survival function introduces a parameter that leads to the proportional hazard model. Marshall and Olkin (1997) introduced a method of obtaining an extended family of distributions including one more parameter. For a random variable with a distribution function F(x) and survival function $\overline{F}(x)$,we can obtain a new family of distribution functions called univariate Marshall-Olkin family having cumulative distribution G(x) given by

$$G(x) = \frac{F(x)}{\alpha + (1-\alpha)F(x)}; -\infty < x < \infty; 0 < \alpha < \infty$$

Then the corresponding survival function is

$$\overline{G}(x) = \frac{\alpha \overline{F}(x)}{1-(1-\alpha)\overline{F}(x)}; -\infty < x < \infty; 0 < \alpha < \infty$$

This new family involves an additional parameter α. In bivariate case if (X,Y)be a random vector with joint survival function $\overline{F}$ (*x*,*y*),then

$$G(x,y) = \frac{F(x,y)}{\alpha+(1-\alpha)F(x,y)};-\infty<x<\infty;-\infty<y<\infty;0<\alpha<\infty.$$

Constitute Marshall –Olkin bivariate family of distributions. The new parameter α results in added flexibility of distributions and influence the reliability properties.

Consider the brvariate exponential distribution of Gumbe(1960) with joint cumulative distribution function.

$$F(x_1,x_2)=1-e^{-x_1}-e^{-x_2}+e^{-\left(x_1^m+x_2^m\right)^{\frac{1}{m}}},x_1,x_2>0,m\geq 1$$

The survival function of the Morgenstern Gumbel bivariate distribution can be obtained as

$$\overline{F}(x_1,x_2)=e^{-\left(x_1^m+x_2^m\right)^{\frac{1}{m}}}$$

Consider the survival function $\overline{F}$. The new family of survival functions is constructed using Marshall-Olkin method by taking

$$\overline{G}(x;\alpha)=\frac{\alpha\overline{F}(x)}{1-(1-\alpha)\overline{F}(x)};0<\alpha<\infty$$

When α =1, we get

$\overline{G} = \overline{F}$

Marshall – Olkin Gumbel bivariate exponential distribution can be written as

$$\overline{G}(x_1;x_2)=\frac{\alpha\overline{F}(x_1,x_2)}{1-(1-\alpha)\overline{F}(x_1,x_2)};\alpha>0,x_1>0,x_2>0$$

$$=\frac{\alpha e^{-\left(x_1^m+x_2^m\right)^{\frac{1}{m}}}}{1-(1-\alpha)e^{-\left(x_1^m+x_2^m\right)^{\frac{1}{m}}}}$$

When α =1, it easily follows that $\overline{G} = \overline{F}$

From these we get

$$\overline{G}_{X_1}(x_1)=\frac{\alpha e^{-x_1}}{1-(1-\alpha)e^{-x_1}};\alpha>0,x_1>0$$

And

$$\overline{G}_{X_2}(x_2)=\frac{\alpha e^{-x_2}}{1-(1-\alpha)e^{-x_2}};\alpha>0,x_2>0$$

There are univariate Marshall-Olkin exponential distributions

Theorem 7.2.1 Let N be a geometric random variable with $p(N=n)=pq^{n-1}$,

N=1,2….,0<p<1,q=1-p

Consider a sequence $\{(X_i,Y_i),\ i\geq 1\}$ of *i. i.*d random variables with common survival function $\overline{F}$ (*x*,*y*), N and (X_i,Y_i),are independent for all $i\geq 1$. Let $U_N=\min_{1\leq i\leq N} X_i$ and $V_N=\min_{1\leq i\leq N} Y_i$. Then the random vector (U_N,V_N) is distributed as Marshall – Olkin Gumbel Exponential(MOGE (*m*,*p*))if and only if (X_i,Y_i),has the Gumbel bivariate distribution with parameter m.

Proof. Let $\overline{S}$ (*x*,*y*), be the survival function of (U_N,V_N) . By definition

$$\overline{S}(x,y) = P(U_N>x, V_N>y)$$

$$=\sum_{i=1}^{n}\left(\overline{F}(x,y)\right)^n pq^{n-1}$$

$$=\frac{p\overline{F}(x,y)}{1-(1-p)\overline{F}(x,y)}$$

$$=\frac{pe^{-(x^m+y^m)^{\frac{1}{m}}}}{1-(1-p)e^{-(x^m+y^m)^{\frac{1}{m}}}}$$

$\rightarrow$ MOBGE(*m*,*p*)

Conversely let(U_N,V_N) has MOGE(*m*,*p*)distribution. Then solving the equation was get.

$$\frac{p\overline{F}(x,y)}{1-(1-p)\overline{F}(x,y)} = \frac{pe^{-(x^m+y^m)^{\frac{1}{m}}}}{1-(1-p)e^{-(x^m+y^m)^{\frac{1}{m}}}}$$

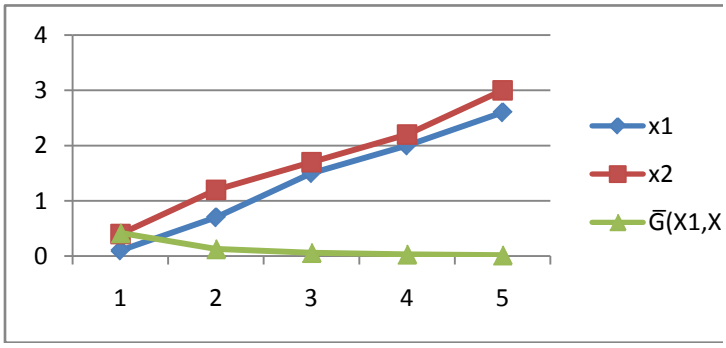
Then we get,

$$\overline{F}(x,y) = e^{-\left(x^m + y^m\right)^{\frac{1}{m}}}$$

Which is the survival function of the Morgenstern Gumbel exponential distribution with parameter m.

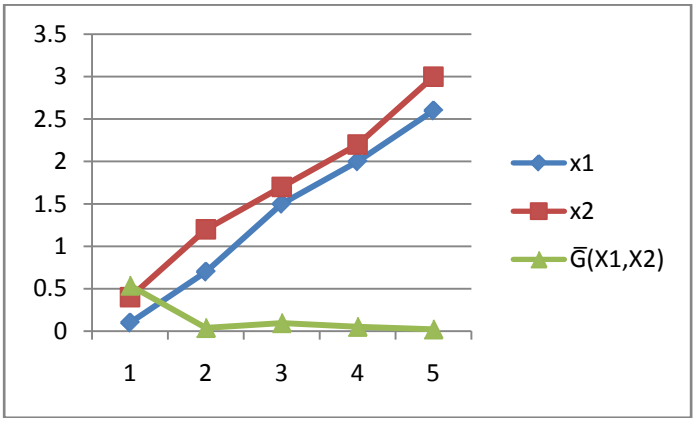
Leptin level in sedentary treatment group

X_1	X_2	$\bar{G}(X_1,X_2)$
0.1	0.4	0.418469
0.7	1.2	0.129825
1.5	1.7	0.061828
2	2.2	0.033297
2.6	3	0.017632



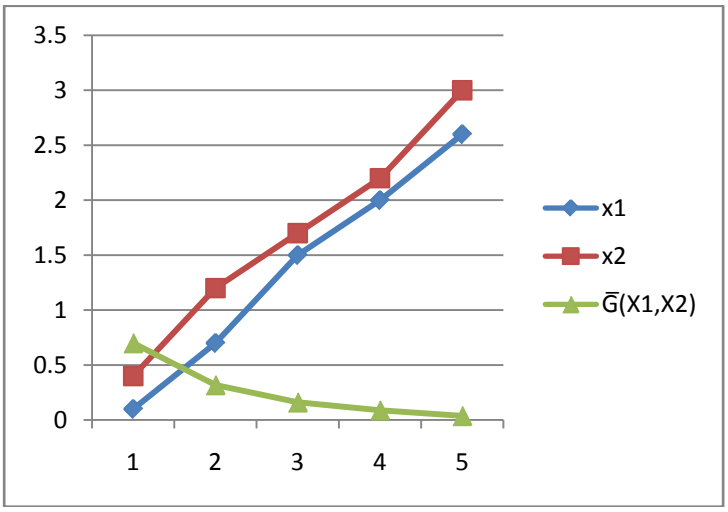
Leptin level in exercising treatment group

X_1	X_2	$\bar{G}(X_1,X_2)$
0.1	0.4	0.538496
0.7	1.2	0.039567
1.5	1.7	0.097089
2	2.2	0.053288
2.6	3	0.022881



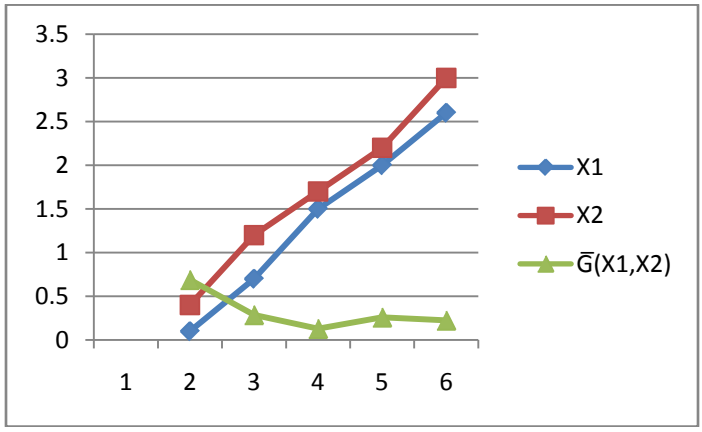
Mean for leptin in sedentary treatment group

X_1	X_2	$\bar{G}(X_1,X_2)$
0.1	0.4	0.700207
0.7	1.2	0.318379
1.5	1.7	0.161762
2	2.2	0.089550
2.6	3	0.038154



Mean for leptin in exercising treatment group

X_1	X_2	$\bar{G}(X_1,X_2)$
0.1	0.4	0.689103
0.7	1.2	0.286986
1.5	1.7	0.129572
2	2.2	0.259413
2.6	3	0.223891



III. CONCLUSION

The survival function of the M.G bivariate distribution was applied in diurnal rhythm of leptin depends on energy, or carbohydrate, availability, not intake, and exercise has no suppressive effect on the diurnal rhythm of leptin beyond the impact of its energy cost on energy availability and also found cumulative distribution function of leptin hormone.

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