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MENSTRUAL CYCLE AND ENDURANCE TRAINING IN OVULATORY WOMEN

by

Aaron. Mansur R. Mogadam

B.B.A, Tehran University, 1980

THESIS SUBMITTED IN PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE OF
MASTER OF SCIENCE
in the Department
of
Mathematics & Statistics

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ABSTRACT

This project consists of analysis and model fitting for a data set including menstrual cycle, hormonal, morphometric, fitness, and endurance training variables. The objective was to determine whether intense endurance training in sedentary ovulatory women is associated with hormonal and menstrual cycle changes. The forward selection procedure was employed to investigate the existence of an association. Confidence regions for the regression surfaces are also provided.

DEDICATION

To my parents, for their unfailing love & support!

" The teacher who walks in the shadow of the temple,
among his followers, gives not of his wisdom but rather
of his faith and his lovingness.

If he is indeed wise he does not bid you enter the
house of his wisdom, but rather leads you to the
threshold of your own mind."

The Prophet.

BY

Kahlil Gibran

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I would also like to thank Dr. Jerilynn C. Prior and Miss Yvette Vigna for helping me to understand the medical and the biological aspects of this project.

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CHAPTER 1

THE PROBLEM

1.1 Introduction

With increasing numbers of women becoming involved in intense sports, questions are being asked about the effects of this activity on the reproductive function and pregnancy.

The normal menstrual cycle seems straightforward enough: vaginal bleeding for a few days each month. In reality, though, the "period" is a very precisely regulated and complex sequence of carefully timed events. More than seven hormones act in the brain, to prepare the female for the fertilization of an ovum. (Ref. 1, 2, and 3).

There are, however, phases of life when reproduction may be decreased or temporarily stopped. Energies are sometimes needed for even more basic functions, such as when intense labour is required to respond to a natural disaster. Anthropologists, for example, have documented the work and birth spacing of the Kung San women of Kalahari Desert in Africa. These women use no birth control, yet they have their children three to five years apart. The women are food gatherers, walking twenty to thirty kilometers a day carrying heavy loads; it appears that the energy required by these women in food gathering decreases their fertility.

After settling in villages, a fact which offers a change in agricultural food supplies and a more sedentary life style, the Kalahari women give birth every eighteen months to two years, (Ref. 1 page 36).

1.2 Biological Interpretation

Changes in the menstrual cycle associated with natural disasters, psychological stress, and physical activity are probably caused by alterations in the hormone-directing part of the brain, the hypothalamus. The hypothalamus produces the gonadotrophin releasing hormone (GnRH) which stimulates the pituitary gland to produce and release the luteinizing hormone (LH) and follicle-stimulating hormone (FSH). These two pituitary hormones promote production of the ovarian steroids estrogen and progesterone. (Ref. 5).

The normal menstrual cycle is twenty-one to thirty-six days in length, counting from the first day of flow up to the last day before the next flow. An egg is released (ovulation) at midcycle. The number of days of flow is from two to five days.

The normal menstrual cycle can be divided into two parts. The first part of the cycle, the follicular phase, begins on the first day of flow and ends at ovulation, this phase is usually fourteen to eighteen days. (Ref. 1 page

36).

The largest increase in estrogen is observed during the latter part of the follicular phase, just prior to ovulation. The high estrogen signal is received by the hypothalamus and pituitary gland and leads to sudden pituitary release of LH and (Ref. 1 page 36) FSH. This large LH surge preceded by a smaller FSH surge, triggers ovulation.

The second half of the cycle, referred to as the luteal phase, is ten to sixteen days in duration. The luteal phase begins after ovulation and lasts until the next flow starts. It is the declining production of estrogen and progesterone that causes menstruation at the end of the luteal phase. (Ref. 1 page 37).

Pituitary gonadotropins are regulated from below as well as from above. LH and FSH release are under feedback control by the major gonadal steroids, estrogen, and progesterone. Estrogen, when at low levels, has a negative feedback effect and increases the synthesis and storage of FSH and LH. It does not appear to alter LH secretion but inhibits FSH secretion. During the middle of the cycle when the hormonal explosion takes place, estrogen maintains a high level which stimulates a sustained pulse of FSH and LH. Estrogen feedback has become positive rather than negative. Progesterone also controls LH and FSH secretion. Progesterone administration in normal and hypogonadal women pretested with estrogen is necessary for midcycle surge of normal intensity and duration (Ref. 4 page 68).

1.3 Scientific Belief

Many factors besides exercise are hypothesised to be cause of menstrual cycle changes. These factors include weight loss in young women (Ref. 12), psychological stress, seasonal light cycle (Ref. 13), previous reproductive history, and physical illness (Ref. 5). These factors cause alterations in the production of the hypothalamic, pituitary and ovarian hormones leading to menstrual cycle variation.

Biologically it is expected that an increase in the intensity of exercising decreases percentage body fat (with or without weight loss). Weight or fat loss and intense exercise decrease pituitary (LH) and ovarian (estrogen and progesterone) hormones; it is this change in pituitary and ovarian hormones that causes menstrual cycle variation.

Other very good medical research looking at the menstrual cycle changes with exercise has been confined to descriptive statistics (see Bullen Ref. 15). The forward selection procedure used here would enable more astute physiological assessment of the complex changes documented only categorically.

CHAPTER 2

THE DATA

Dr. Jerilynn C. Prior, Assistant Professor in the Department of Medicine at the University of British Columbia (U.B.C.), presented data which dealt with menstrual cycle disorders from strenuous exercise in previously inactive women.

Subjects were found through notices on bulletin boards on fitness centres, hospitals, universities, community centres, newspapers, etc. It was required that the subjects be between the ages of 20-40, healthy, sane, ovulatory, have had no significant change in weight for over six months, have had no synthetic hormone use for six months, and have had no regular aerobic exercise for six months. Based on these elements twelve women were chosen among those who were interviewed. After the selection procedure the subjects were observed during a nonexercise (control) phase. This phase consisted of two ovulatory menstrual cycles. All of the testing was in the midluteal phase (days 18-21) as identified through basal temperature records.

After the initial control phase, the subjects started on a carefully graded running exercise program while keeping records of their exercise (time, distance), their basal

A gradual increase in running either in distance or intensity is called a graded running exercise program.

pulse and weekly weight.

The phases of the study were:

i) Time A:

Control or pre-exercise phase, consisting of two months.

ii) Time B:

Early exercise or after six weeks of exercise.

iii) Time C:

Late exercise or after six months of exercise.

At the end of each of these three time periods A, B, and C specific hormonal and temperature tests were performed to document percent body fat, fitness, hormonal and temperature responses. Eight sets of variables (Morphometric, Fitness, Menstrual Cycle, Temperature Testing, Stress, Hormone-Baseline, Naloxone, GnRH, Hematology) were measured at each of the three times. Morphometric, fitness, running, and hormone variables were suspected to be associated with changes in menstrual cycle variables.

A short summary of these variables and their biological definitions is as follows.

		<u>Short Name</u>
Set A)	Morphometric Variables:	
1.	Dry weight - weight of a subject in shorts and T-shirt; determined by standing on a balance beam scale.	DW
2.	Sum of skinfolds - measurements of the thickness of a double layer of skin and underlying adipose (fat) tissue, but not muscle. The skinfold is raised by pinching the skin between the thumb and index finger. The assessment of subcutaneous fat is measured at specific skinfold sites using calipers. Measurements from each of the skinfold sites are added together to obtain Sum of Skinfolds (Ref.(6)).	SS

3. Percent Body Fat

%BF

- sum of skinfold thickness is fed into a formula to estimate body density (BD). Percent fat was computed from body density according to the formula of Brozek (Ref.(7)).

$$\% \text{ Fat} = ((4.570/\text{BD}) - 4.141) \times 100$$

4. Underwater weight

UWW

- weight of a subject submerged in a tank of water after expelling air out of her lungs.

5. Percent Body Fat

UW%BF

- a person with more bone and muscle mass for the same total body weight will weigh more in the water, have a higher body density and a lower percentage body fat than a person with less muscle mass.

Set B) Fitness Variable:

6 Trimps - a measure of general fitness, involving respiratory efficiency and pulse rate. Therefore it is expected that intense exercise increases trimps.

TRPS

Set C) Menstrual Cycle and Running variables:

1. Cycle Length - total number of cycle days starting with the first day of flow and ending the day before the next period. begins. Normal cycle length is 25-32 days. CYCL

2. Follicular Length FOLL
- the follicular phase extends from the first day of flow until the time of ovulation. A normal follicular length is 10-20 days.

3. Luteal Phase LUTL
- the luteal phase extends from ovulation until the start of the next menstrual flow. The normal luteal length is 10-16 days long. The luteal phase is characterized by higher temperatures than those recorded during the follicular phase. This thermal shift is caused by the action of progesterone, a gonadal hormone produced by the ovary if ovulation has occurred. If ovulation does not take place there will be no progesterone production, and no increase in temperature.

4. Flow Length FLWL
 - a normal flow length is 3-5 days.
5. Mean Temperature MEANTP
 - an arithmetic mean of all daily temperatures for a given cycle.
6. Miles per Cycle MIL/CY
 - all the miles run during a given menstrual cycle are simply added together and recorded as miles/cycle.
7. Miles per cycle day MIL/CD
 - cycle length is divided into miles/cycle to give an average of the miles run for each cycle day.
8. Miles per run MIL/RN
 - number of days run in a cycle are divided into the miles run during that cycle to give an average run length.
8. Miles per week MIL/W
 - self-explanatory
9. Number of days run per cycle NDRUN/CY
 - self-explanatory.

Set D) Hormones:

- (Chemical substances produced by endocrine glands (special cells), which travel in the bloodstream to a target organ where their effect is produced.)

1. Testosterone TEST
- produced by the ovary and adrenal gland in women.
2. Estrogen ESTR
- produced by the ovary and fat cells of the body.
3. Progesterone PROG
- produced by the ovary following ovulation.
4. FSH FSH
- follicle stimulating hormone produced by the pituitary gland.
5. LH LH
- luteinizing hormone produced by the pituitary gland.
6. TSH TSH
- thyroid stimulating hormone produced by the pituitary gland.

7.

T3

T3

- active thyroid hormone made by the thyroid gland.

8.

Prolactin

PROL

- produced by the pituitary gland.

From the twelve women who started the program only seven completed all three phases of the program (those who dropped out did not differ from those who continued). A small number of observations missing from these seven women were estimated using description and missing data, PAM, from BMDP Statistical Software.²

A portion of the raw data is shown in the following page in table 1.

2.1 The Goal of the Analysis

The objective is to find whether changes in the CYCL, FOLL, LUTL, and FLWL from A to B, and, from A to C, are associated with the hormonal changes. Hormonal changes are believed to be directed from intense exercise training and or through morphometric factors such as lower percentage

²PAM replaces invalid values using means, regression on the variable most highly correlated with the missing variable, regression on a highly correlated set of variables, or regression on all available variables. Regression method on a selected set of variables was used for this data. (for more see section 12.2 of Ref.(8)).

Table 1: A Subset of the Raw Data

-----TIME A-----								
Subject	DW	SS	ZBF	UW	UWZBF	TRPS	CYCL	FOLL
1	61.4	54.70	29.4	1.90	21.30	0	30.5	17.5
2	68.8	43.10	25.5	1.65	25.30	0	29.5	19.0
3	66.0	51.20	27.2	1.15	29.90	0	28.0	17.0
4	45.1	23.50	16.3	1.95	14.75	0	30.0	15.0
5	65.6	40.55	23.9	1.85	25.70	0	30.5	15.5
6	51.8	29.40	21.5	1.75	22.10	0	26.0	14.0
7	53.2	40.80	25.2	1.25	25.90	0	28.0	16.5

LUTL	FLWL	MEANTP	MIL/CY	MIL/CD	MIL/RN	MIL/W	NDRUN/CY
1	13.0	4.57	36.8	0	0	0	0
2	10.5	4.57	36.5	0	0	0	0
3	11.0	3.50	36.5	0	0	0	0
4	15.0	4.00	36.6	0	0	0	0
5	15.0	5.00	36.5	0	0	0	0
6	12.0	5.00	36.7	0	0	0	0
7	11.5	5.00	36.6	0	0	0	0

TEST	ESTR	PROG	FSH	LH	TSH	T3	PROL
1	29	65	14	7	15	0.9	108
2	42	129	14	5	21	1.3	106
3	31	210	16	4	15	0.7	117
4	73	214	9	4	6	1.4	103
5	73	78	5	12	30	1.4	92
6	32	103	10	10	49	1.0	42
7	51	126	12	5	16	1.0	110

-----TIME B-----							
Subject	DW	SS	ZBF	UW	UWZBF	TRPS	CYCL
1	60.5	50.1	28.3	2.10	19.6	15.00	26.5
2	70.1	42.0	25.1	1.70	24.5	22.50	25.0
3	85.5	58.7	27.1	1.15	29.7	36.50	32.0
4	46.1	25.0	17.1	2.00	14.7	22.00	26.5
5	67.1	41.3	24.1	2.05	23.2	20.00	30.5
6	60.9	27.1	20.7	1.75	21.6	20.30	26.0
7	54.5	42.1	25.1	1.25	25.3	17.85	29.0

FOLL	LUTL	FLWL	MEANTP	MIL/CY	MIL/CD	MIL/RN
1	14.0	12.5	5.00	36.60	20.75	0.55
2	19.5	8.5	5.20	36.50	32.60	1.20
3	22.0	10.0	4.00	36.55	47.00	1.60
4	17.0	11.5	4.00	36.50	33.50	1.10
5	15.0	14.5	4.04	36.50	36.00	1.20
6	11.5	14.5	3.50	36.70	43.00	1.65
7	17.5	6.5	5.00	36.60	21.20	0.07

MIL/W	NDRUN/CY	TEST	ESTR	PROG	FSH	LH	TSH
1	6.30	10.0	42	79	18	8	0.7
2	7.70	15.0	21	112	18	13	2.1
3	15.60	9.0	57	204	10	10	0.8
4	8.00	14.0	49	157	7	4	1.0
5	9.08	12.5	43	139	8	7	0.8
6	11.39	17.5	27	175	15	8	1.0
7	6.60	9.5	42	102	11	6	0.8

T3	PROL
1	100
2	98
3	102
4	96
5	93
6	91
7	49

-----TIME C-----							
Subject	DW	SS	ZBF	UW	UWZBF	TRPS	CYCL
1	58.2	47.4	27.6	2.00	18.3	23.0	25.5
2	66.6	46.3	27.3	1.60	24.9	43.5	28.0
3	64.2	46.2	25.6	1.22	27.0	32.0	28.0
4	51.1	31.9	20.9	1.75	20.0	20.0	28.0
5	66.6	42.0	24.7	1.80	24.9	31.0	28.0
6	62.3	28.4	24.0	1.73	22.6	39.5	26.0
7	53.8	40.3	25.6	0.90	27.7	32.4	23.0

FOLL	LUTL	FLWL	MEANTP	MIL/CY	MIL/CD	MIL/RN
1	13.50	12.00	5.00	36.60	20.20	0.75
2	15.00	5.00	4.23	36.60	57.00	2.00
3	17.00	11.00	3.39	36.65	39.87	2.20
4	20.17	10.25	3.00	36.50	60.00	2.10
5	19.50	8.50	4.18	36.40	36.70	1.35
6	13.50	12.50	4.00	36.65	51.15	1.95
7	13.50	9.50	5.00	36.55	23.55	0.06

MIL/W	NDRUN/CY	TEST	ESTR	PROG	FSH	LH	TSH
1	6.25	7.0	63	76	12	2	0.75
2	15.25	10.0	28	163	18	7	1.30
3	12.80	8.5	24	61	4	6	0.60
4	15.00	22.0	53	52	2	4	0.90
5	11.62	9.0	46	199	12	5	0.60
6	15.65	11.0	38	189	9	8	0.95
7	7.70	5.5	15	128	5	7	0.80

T3	PROL
1	93
2	114
3	117
4	65
5	87
6	84
7	111

body fat.

CHAPTER 3

REGRESSION ANALYSIS

3.1 Model Fitting

Linear regression models were employed to investigate any association between the changes in the menstrual cycle and hormonal and other variables. The regression analysis of the changes is divided into two sections (phase A to B, and A to C). In each section the changes in morphometric and fitness variables with regard to running variables, the changes in hormones with respect to running, morphometric, and fitness variables, and at last the changes in menstrual cycle variables, are studied. The following gives a general idea of what was done for all of these sections. A more detailed explanation including graphs and tables, is given in the corresponding sections.

T-tests on averages have been employed to test whether averages of morphometric, fitness, hormonal, and menstrual cycle variables have changed over the given time spans. That is to test:

$$H_0: \mu_i - \mu_j = 0$$

vs.

It is of scientific interest to compare the result of early exercise (time B), and late exercise (time C), with control or pre-exercise phase (time A). The analysis for time B to C was not addressed because there were too few subjects for the variations to show any patterns.

$$H_1: \mu_i - \mu_j \neq 0$$

where μ_i and μ_j are theoretical population² averages at different time levels. The results are shown in Appendix A and are discussed in the corresponding sections.

A source file on MINI]AB was used to produce scatter plots of Δ CYCL, Δ FOLL, Δ LUTL, Δ FLWL (Δ before a variable stands for change), hormonal changes, morphometric variables, and fitness variable over each of the two time spans, against values of candidate independent variables during the given time spans, to get a visual appraisal of any trends or associations. A few of these plots are shown in the following sections. (In the figures CH before a variable stands for change).

Studying such plots in general may suggest whether or not the response variable is associated with the explanatory variable and if so in what sort of way (linear, quadratic, and so on).

The forward selection procedure was employed for further investigation. The following steps were followed:

Step 1: The first variable to enter the model is that variable that is most highly correlated with the dependent variable and then a simple linear regression is fitted:

$$Y_i = \beta_0 + \beta_1 x_i + e_i$$

²For more discussion on the population terminology, see Statistical Critique.

where the dependent variable Y_i is the value of the change in a morphometric, fitness, hormonal, or menstrual cycle variable over the given time span in the i th subject, β_0 and β_1 are theoretical population parameters, x_i is the value of the independent variable in the i th subject and ϵ_i s are modeled as independent³ error terms having a normal distribution with mean 0 and variance σ^2 where i ranges from 1 to 7.

β_0 and β_1 are unknown, so that suitable estimates b_0 and b_1 will be sought to produce 'fitted' values:

$$\hat{Y}_i = b_0 + b_1 x_i$$

which gives a fitting error

$$e_i = Y_i - \hat{Y}_i$$

known as a residual, the discrepancy between observation i and the corresponding outcome fitted by the model. The estimates b_0 and b_1 are found by the method of least squares. A brief discussion of the method of least squares and its properties is given in Appendix B.

A source file consisting of MIDAS and MINITAB commands was written to run simple regressions of the dependent variables (i.e., changes in physiological variables) over each of the two time spans.

Here tests concerning β_1 are of interest, particularly of the form:

³For the discussion of random sampling see Statistical Critique, section 3.4.

$$H_0: \beta_1 = 0$$

vs.

$$H_1: \beta_1 \neq 0$$

The reason for interest in testing whether $\beta_1 = 0$ is that $\beta_1 = 0$ implies that there is no association between the dependent variable and the corresponding independent variable.

T statistics were used to do the above test. A table of the regressions with the lowest p-values is given in each section. If the T statistic for the independent variable with the highest correlation is not significant it can be concluded for this data that none of the independent variables is useful as a single predictor. At this step simple regressions of Δ morphometric and Δ fitness on running variables, Δ hormones on running, Δ morphometric, and Δ fitness, Δ menstrual cycle on Δ morphometric, Δ fitness, running, and Δ hormone variables were studied separately.

Step 2: First order models with two independent variables were fitted:

$$Y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \epsilon_i$$

where Y_i is the change in the dependent variable over the given time span for the i th individual, and x_{i1} and x_{i2} are the values of the two independent variables.

To test whether there is an association between the dependent variable and the set of X variables, that is, to test

$$H_0: \beta_1 = \beta_2 = 0$$

vs.

H_1 : not both equal 0,

F-test statistics were used. The test statistic denoted by F is distributed as $F(2, n-3)$ when H_0 holds.

The improvement (partial) F statistic associated with each remaining variable based on a regression equation containing that variable and the variable initially selected was calculated, to test whether the second variable contributes significantly to the model given the first variable is already in the model. It should be noted that the improvement test was done twice:

- (1) second variable given first in the model.
- (2) first variable given second in the model. (Ref. 10 page 227).

In this way multiple regressions of Δ hormones on Δ fitness and running, and also Δ menstrual on Δ fitness, running and Δ hormones variables were considered.

Departures from the model were studied by residual plots. If the model is reasonable the residuals should be structureless; in particular, they should be unrelated to any other variable including the fitted and the response variable. Therefore plots of residuals versus the fitted values were studied.

A combined source file on MIDAS and MINITAB was written to perform all of the above analyses. The stepwise regression procedures available on statistical packages were avoided. There are several reasons for this. (a) Since the procedures automatically "snoop" through many models the model selected may fit the data "too well". That is, the procedures can look at many variables and select ones which, by pure chance, give a good fit. (b) Automatic procedures cannot take into account special knowledge that the analyst may have about his data. (for more see page 79 of the MINITAB manual).

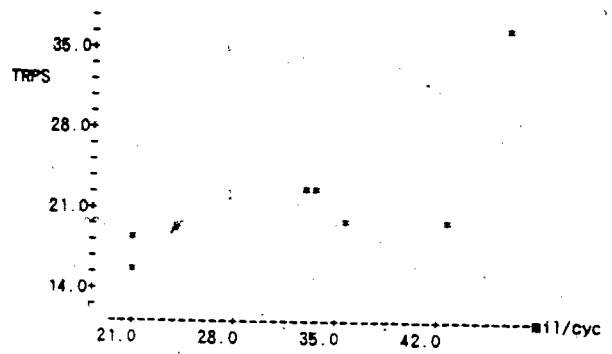
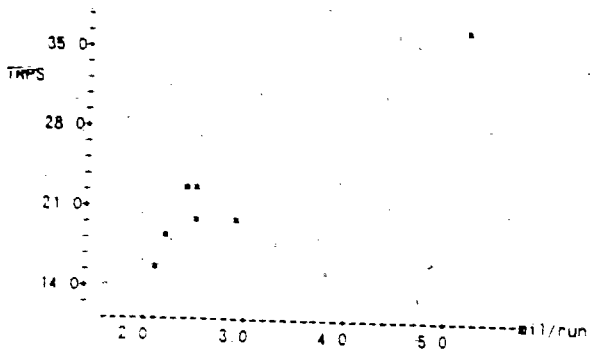
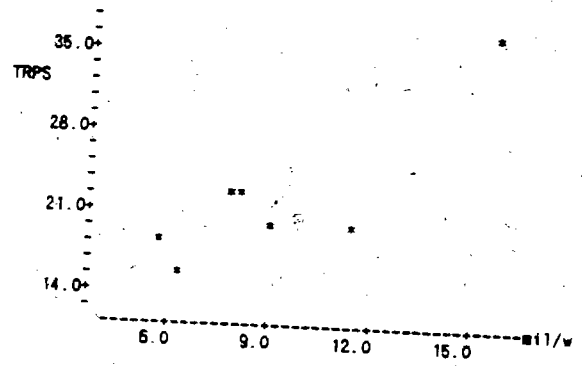
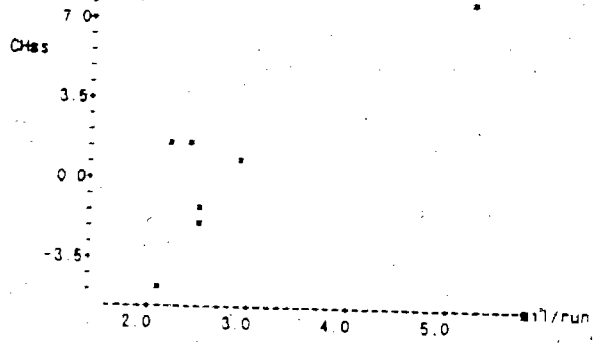
3.2 Regression Analysis from Phase A to B

3.2.1 *Morphometric and fitness parameters*

Biologically it is expected that the change in morphometric and fitness variables is associated with the running variables. Based on this belief scatter plots of (ΔDW , ΔSS ,) vs. (MIL/CY, MIL/CD,) were studied carefully; a few of these plots are shown in Figure 3.2a.

The purpose of these plots is to inspect whether or not the explanatory variable is associated with the response variable (ΔDW , ΔSS , $\Delta \%BF$, ΔUWW , $\Delta UW \%BF$, TRPS), and if so, then in what sort of way (linear, quadratic, and so on). It seems that linear association would be an adequate assumption for many of these plots, in view of the small

Figure 3.2a: Δ Morphometric and Fitness variables vs. Running



sample size. For some of these plots (TRPS vs. MIL/CY) some positive association have been detected, and there seems to be no need to employ a model more sophisticated than first-order regression with constant variance (homoscedasticity).⁴ Some of the plots on Page 21 would not look significant if a single point were removed (i.e subject 3).⁵

T-tests on averages to detect changes over phase A to B (without any independent variable) in DW, SS, %BF, ..., were performed and no significant changes was observed, except for TRPS. The results are shown in Table 1 of Appendix A.

For further analysis, linear regression was employed to investigate whether the data reveals any association between the morphometric variables and fitness variable change and running variables. Each dependent variable (Δ DW, Δ SS, Δ %BF, Δ UWW, Δ UW%BF, TRPS) was regressed on the running variables (MIL/CY, ML/CD, MIL/RN, MIL/W, NDRUN/CY) one variable at a time. To test whether the dependent variable is significantly associated with the corresponding independent variable, the t-test for slope was utilised.

The following table contains significant regressions and their significance levels.

⁴Homoscedastic scatter diagrams have oval-shaped residual plots. (i.e. regression estimates off by the same amounts all along regression line.

⁵for more see section 3.4

<u>Dependent</u>	<u>Explanatory</u>	<u>P-value</u>
ΔSS	MIL/RUN	0.010
TRPS	MIL/CY	0.040
"	MIL/RN	0.000
"	MIL/W	0.005

It seems that there is a strong association between the change in SS from phase A to B and MIL/RUN, and also the increase in TRPS (which is a measure of exercise intensity) is highly associated with MIL/CY, MIL/RN, and MIL/W.

3.2.2 Hormones

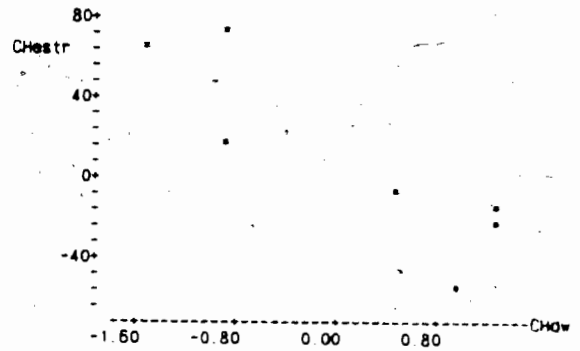
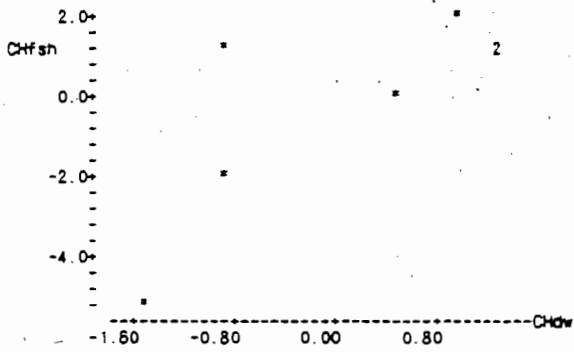
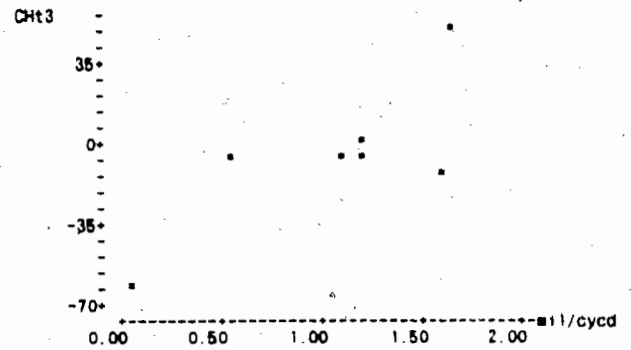
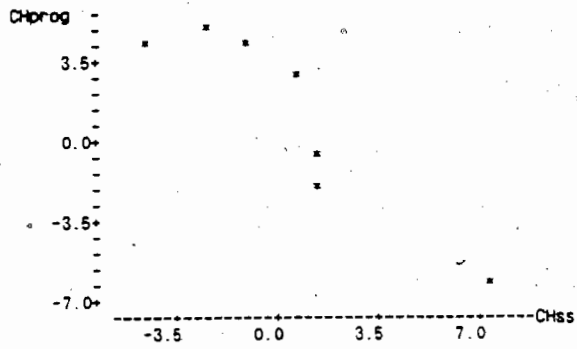
Biologically it is believed that hormonal changes are associated with the changes in morphometric variables, fitness variable and running.

To determine whether the data reveals any association, scatter plots of hormone changes ($\Delta ESTR$, $\Delta PROG$,) vs. running and the change in morphometric and fitness variables, were studied.

Figure 3.2b displays these plots. Studying the scatter plots reveals that there is a strong negative linear association between $\Delta ESTR$ and ΔDW , and also between $\Delta PROG$ and ΔSS . It is hard to detect any strong association between running variables and hormones at this stage of analysis.

T test on averages to detect changes over phase A to B in $ESTR$, $PROG$, ..., indicate no significance changes; the

Figure 3.2b: Hormone Changes vs. Running



result is shown in Table 1 of Appendix A.

For further investigation, simple regressions of Δ PROG, Δ ESTR, Δ FSH, Δ LH, and Δ T3 on running variables, and change in morphometric and fitness variables, were examined. Significant regressions and their significance levels are illustrated in the following table.

Dependent	Explanatory	P-value
Δ ESTR	Δ DW	0.013
Δ PROG	Δ SS	0.005
Δ FSH	Δ DW	0.040
Δ T3	MIL/CD	0.040

It can be concluded that Δ ESTR and Δ FSH are significantly associated with Δ DW and Δ PROG is strongly associated with Δ SS, etc. No significant regression was found for Δ LH.

Next, regressions with two independent variables were considered, where Δ PROG, Δ ESTR, ... are the dependent variables and Δ DW, Δ SS, ..., TRPS, and MIL/CY, MIL/CD, ... are the independent variables. Each dependent variable is regressed on two independent variables, one from the morphometric variables (including TRPS), and the other one from ruunig variables. One object is to test whether the corresponding dependent variable is significantly explained by the two independent variables in the model, that is testing:

$$H_0: \beta_1 = \beta_2 = 0$$

vs.

$$H_1: \text{Either } \beta_1 \text{ or } \beta_2 \neq 0.$$

The test statistic for the analysis of variance approach is denoted F. It compares MSR (Mean Square Regression) and MSE (Mean Square Error) in the following fashion:

$$F = \text{MSR} / \text{MSE}$$

Under the null hypothesis F, has the F(2,4) distribution. If

the null hypothesis is rejected a t-ratio is used to test whether the slope against one independent variable is significantly different than zero given that the other independent variable is already in the model.

The following table summarizes all of those regressions among those described which showed a significance level of 0.05 or smaller. In some cases (ΔLH , and ΔFSH), where no significant regression was found, the regression with the lowest significance level is shown.

Dependent	Explanatory	P-level	RSQ	Signif F
Δ ESTR:	Δ DW	0.02	81.8%	0.045
	MIL/CY	0.46		
Δ PROG:	Δ SS	0.005	88.7%	0.010
	MIL/CY	0.19		
Δ PROG:	TRPS	0.01	82.8%	0.030
	MIL/CD	0.06		
Δ PROG:	Δ %BF	0.05	81.7%	0.033
	MIL/RUN	0.032		
Δ FSH	Δ DW	0.19	66.5%	0.110
	MIL/CY	0.03		
Δ LH:	Δ %BF	0.15	54.8%	0.200
	MIL/CY	0.32		
Δ T3:	Δ SS	0.009	93.6%	0.004
	MIL/CD	0.002		
Δ T3:	TRPS	0.008	93.9%	0.003
	MIL/CD	0.001		

It seems that Δ ESTR is significantly associated with Δ DW, and MIL/CY is insignificant when Δ DW is already in the model. And also the change in PROG seems to be highly

associated with the change in %BF and MIL/RUN. There is no significant association in ΔLH with fitness and running variables. $\Delta T3$ is associated with ΔSS and MIL/CD.

3.2.3 Menstrual Cycle

It is known a priori that the change in the menstrual cycle variables is associated with the running variables indirectly through the intermediary effect of the change in hormones, fitness and morphometric variables. With this in mind, scatter plots of $\Delta CYCL$, $\Delta FOLL$, $\Delta LUTL$, and $\Delta FLWL$ vs $\Delta ESTR$, $\Delta PROG$, ..., ΔDW , ΔSS , ..., and MIL/CYC, MIL/CYD, ..., were studied carefully. Some of these plots are shown in figures 3.2c through 3.2g.

Careful study of these plots reveal that there is a strong non-zero monotone association between $\Delta CYCL$ and TRPS, $\Delta CYCL$ and ΔSS , and also between $\Delta FOLL$ and TRPS, $\Delta FOLL$ and ΔSS , $\Delta FOLL$ and $\Delta PROG$, and also $\Delta FOLL$ and $\Delta ESTR$. This linear pattern can also be seen between $\Delta LUTL$ and $\Delta \%BF$, and also $\Delta LUTL$ and $\Delta ESTR$. For the rest of the scatter plots there seems to be no strong suggestion of any trend. Many of these plots seem to depend strongly on the influence of just one individual (individual 3).⁶

A simple t-test (without any independent variable) of the hypothesis of $\Delta=0$ vs $\Delta \neq 0$ shows significance. This does not necessarily suggest $\Delta=0$; it could also be attributed to

⁶for more see section 3.4

Figure 3.2c: Scatter Plots of $\Delta CYCL$

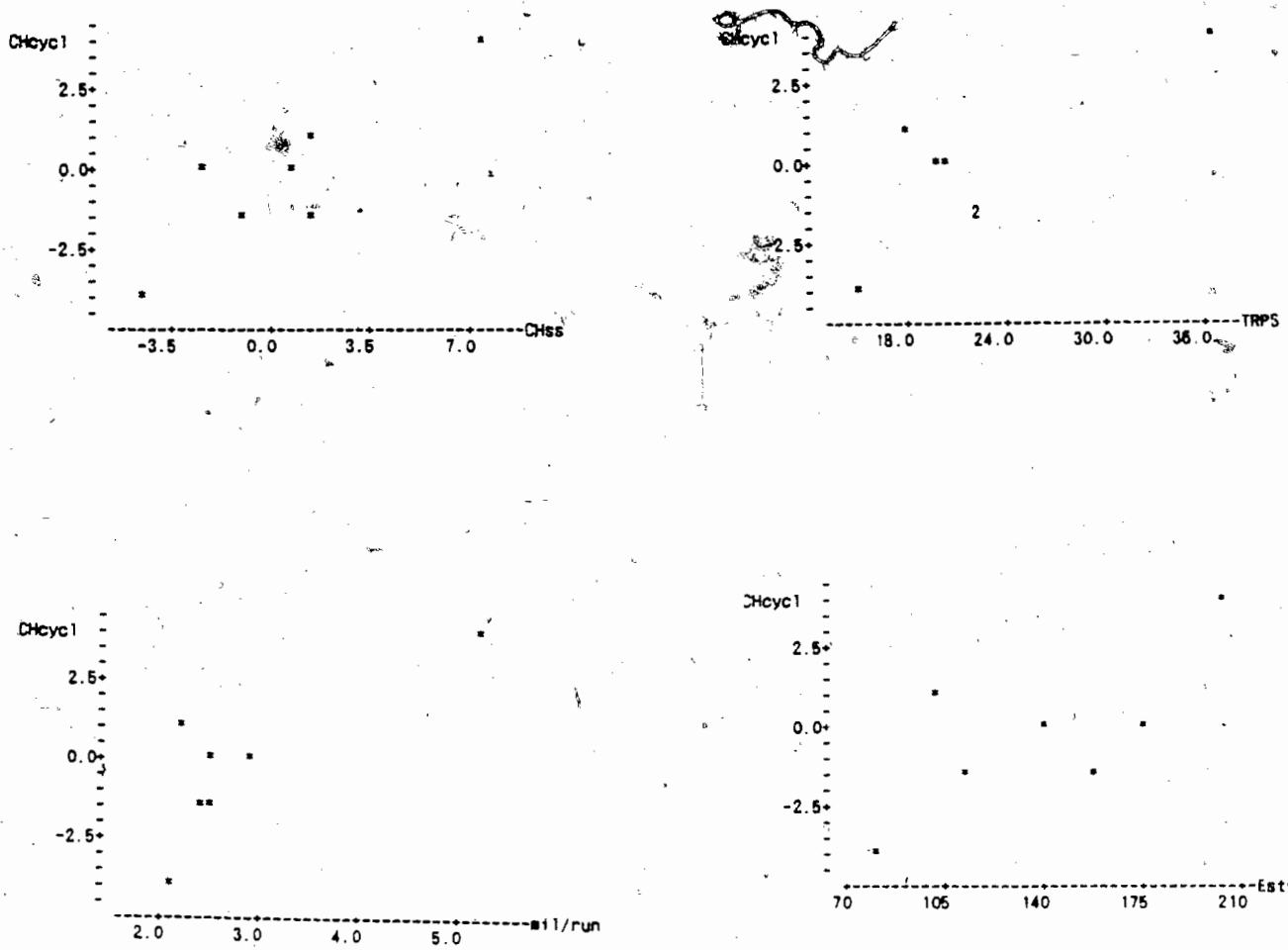


Figure 3.2d: Scatter Plots of $\Delta FOLL$

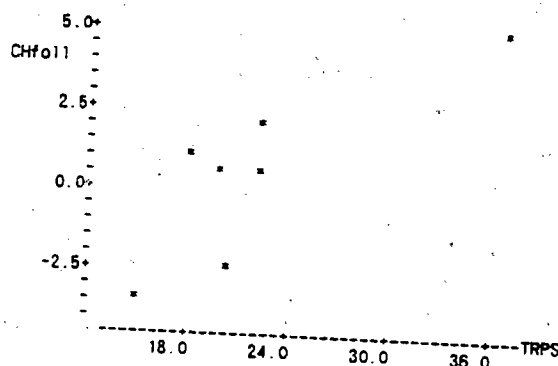
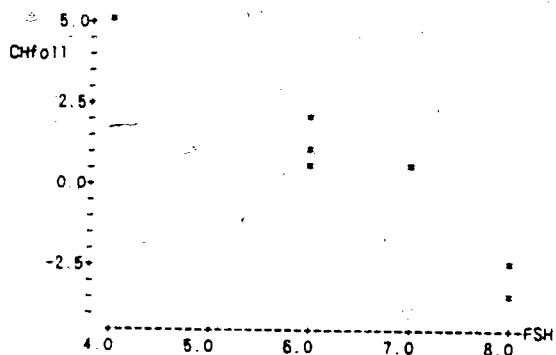
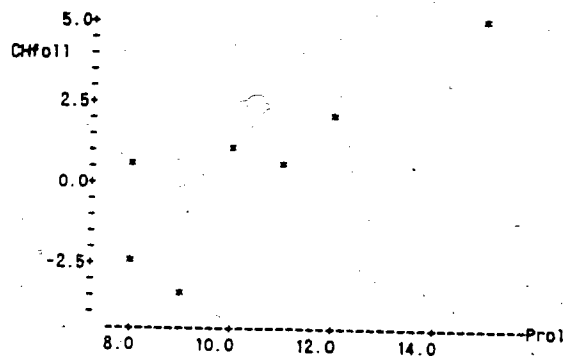
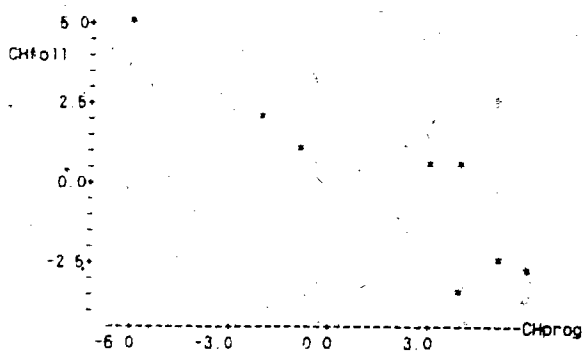


Figure 3.2e: Scatter Plots of $\Delta FOLL$

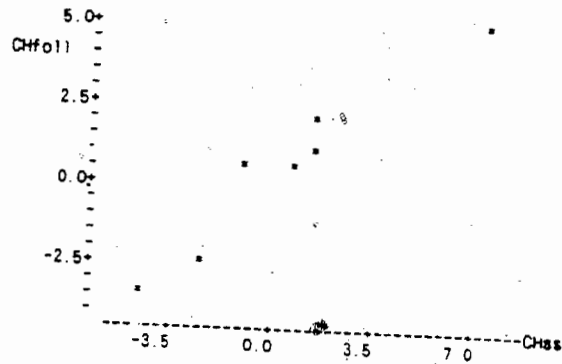
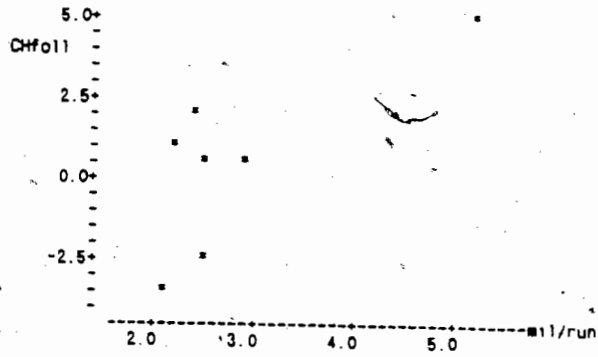


Figure 3.2f: Scatter Plots of $\Delta LUTL$

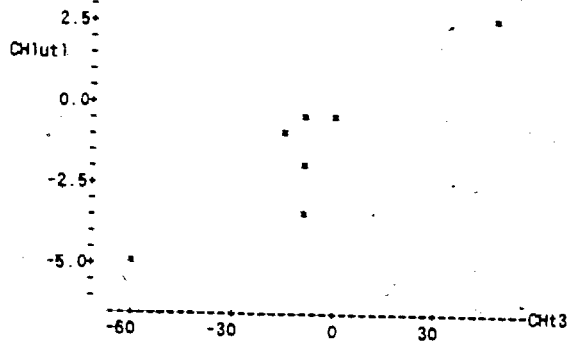
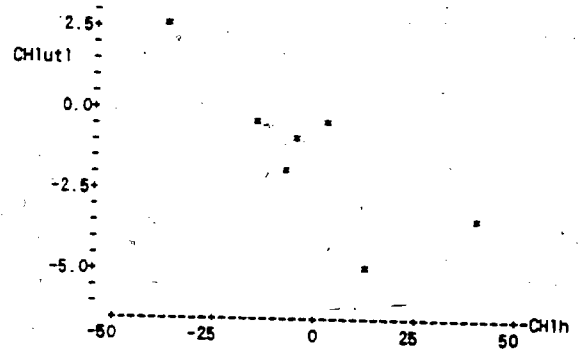
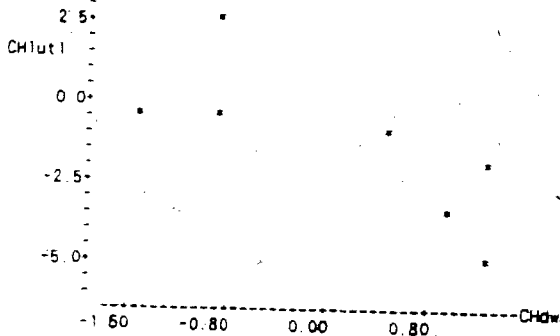
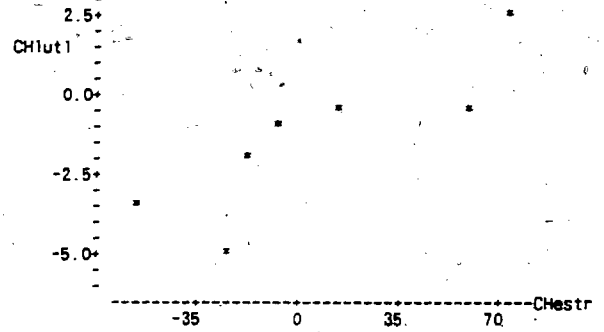
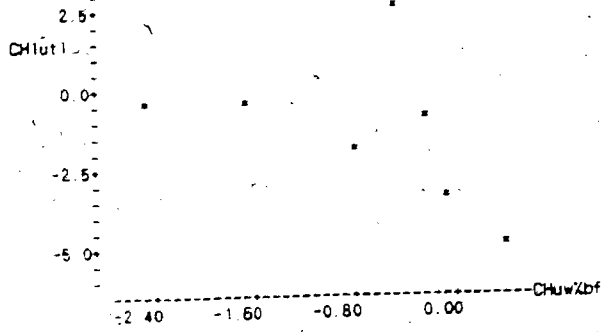
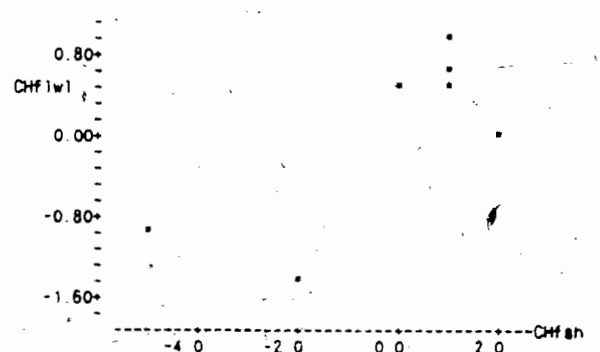
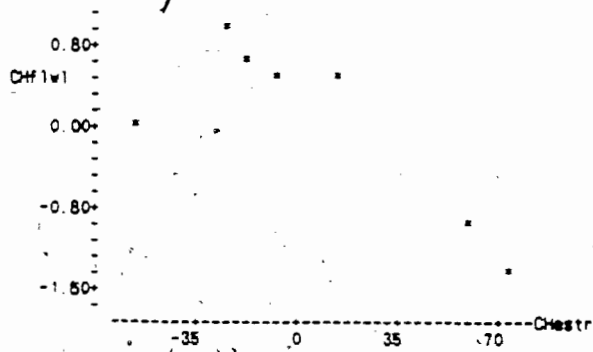
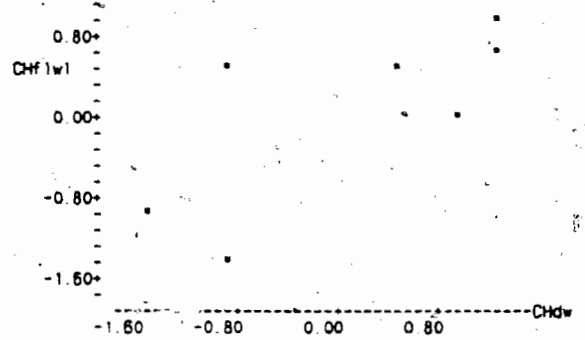
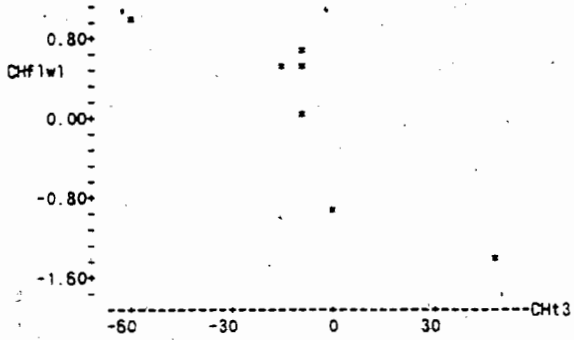


Figure 3.2g: Scatter Plots of $\Delta FLWL$



smallness of sample size, or to the fact that this test does not utilise error-reducing information contained in available independent variables. The results are shown in Table 1 of Appendix A.

As before, first-order regression was employed. Each menstrual variable $\Delta CYCL$, $\Delta FOLL$, $\Delta LUTL$, and $\Delta FLWL$ was regressed on $\Delta morphometric$, $\Delta fitness$, running, and $\Delta hormones$ variables, one variable at a time.

The following table contains all of the relatively significant simple regressions and their significance levels.

Dependent	Explanatory	P-value	RSQ
Δ CYCL	ESTR	0.060	53.0%
"	Δ PROG	0.080	48.0%
"	Δ SS	0.008	77.7%
"	TRPS	0.033	62.9%
"	MIL/RUN	0.027	65.5%
Δ FOLL	Δ PROG	0.008	78.0%
"	FSH	0.000	92.9%
"	PROL	0.010	70.9%
"	MIL/RUN	0.040	57.8%
"	TRPS	0.020	68.5%
"	Δ SS	0.000	91.6%
Δ LUTL	Δ ESTR	0.017	70.7%
"	Δ LH	0.025	66.8%
"	Δ T3	0.005	81.6%
"	Δ %BF	0.035	62.6%
"	Δ DW	0.046	58.0%
"	MIL/CD	0.090	46.7%
Δ FLWL	Δ ESTR	0.037	61.2%
"	Δ FSH	0.056	55.2%
"	Δ T3	0.014	73.5%
"	Δ DW	0.060	53.9%
"	MIL/CD	0.150	36.4%

Next, regressions with two independent variables are

considered. One of the independent variables is one of those above that was found significant by a t-test of regression slope, and the other variable belongs to a different group that is believed a priori to be associated to the corresponding dependent variable. All the different combinations were considered. To test whether the dependent variable is significantly associated with the the two independent variables an overall F-test was performed. A regression F test is reported for those regressions that showed a significant level.

The following table contains the significant regressions. (i.e. Those that have overall $F \leq 0.05$)⁷.

Dependent	Explanatory	t-sig level	RSQ	Signif F
ΔCYCL:	ΔSS	0.002	92.4%	0.005
	ΔLH	0.049		
ΔCYCL:	TRPS	0.005	89.0%	0.010
	T3	0.036		
ΔCYCL:	ΔSS	0.040	83.8%	0.026
	ΔPROG	0.280		

The result indicates that the change in CYCL is highly associated with the variable ΔSS, and ΔLH is less significant in association with ΔCYCL when ΔSS is already in

⁷The search for the significant regressions was based on medicine literature and a priori belief (see sections 1.2 and 1.3), therefore the reported p-levels can not be automatically attributed to a "search" effect

the model. Note that the correlation between ΔSS and ΔLH is 0.206 which indicates that collinearity is not a problem here.

For the regression of $\Delta CYCL$ on ΔSS and ΔLH :

$$\Delta CYCL = -0.62 + 0.626 * \Delta SS - 0.04 * \Delta LH$$

the fitted values and their standard errors are presented in the following table. Working-Hotelling confidence band for the regression plane is used to find the confidence regions.

Working-Hotelling 95% confidence
region for the regression surface

Individual	Fitted	Estimated SE	Lower bound	Upper bound
1	-3.613	0.574	-6.167	-1.060
2	-0.987	0.351	-2.549	0.576
3	4.278	0.732	1.021	7.535
4	-1.300	0.669	-4.278	1.679
5	0.488	0.382	-1.213	2.190
6	0.550	0.616	-3.289	2.189
7	-0.316	0.376	-1.991	1.359

The confidence coefficient (0.95) indicates the percent of time the estimating procedure will yield a confidence region in $(\Delta SS, \Delta LH, \Delta CYCL)$ space which covers the entire true regression plane, in a long series of samples in which the ΔSS and ΔLH observations are kept at the same levels as in the sample actually taken.

The following table contains the multiple regressions of $\Delta FOLL$ with overall $F \leq 0.05$.

Dependent	Explanatory	P-level	RSQ	Signif F
ΔFOLL:	ΔSS	0.000	96.9%	0.000
	ΔESTR	0.080		
ΔFOLL:	TRPS	0.014	86.3%	0.018
	MIL/W	0.084		
ΔFOLL:	MIL/RN	0.004	93.5%	0.009
	Δ%BF	0.009		
ΔFOLL:	ΔSS	0.040	93.1%	0.004
	ΔPROG	0.850		
ΔFOLL:	ΔSS	0.001	94.6%	0.004
	ΔFSH	0.340		
ΔFOLL:	TRPS	0.240	85.0%	0.020
	ΔPROG	0.100		

The result indicates that the change in FOLL is highly associated with Δ%BF and MIL/RN, and none of the hormone variables ΔESTR, ΔPROG, . . . , seems to be significant when ΔSS is already in the model.

The following table contains the fitted values and their standard errors for the regression of ΔFOLL on Δ%BF and MIL/RN:

$$\Delta FOLL = -4.84 + 2.22 * \Delta \%BF + 1.93 * MIL/RN$$

and also Working-Hotelling 95% confidence band for the regression plane.

Working-Hotelling 95% confidence
region for the regression surface

<u>Individual</u>	<u>Fitted</u>	<u>Estimated SE</u>	<u>Lower bound</u>	<u>Upper bound</u>
1	-3.326	0.634	-6.145	0.506
2	-0.903	0.379	-2.590	0.784
3	4.974	0.859	1.151	8.800
4	1.568	0.548	-0.871	4.007
5	1.105	0.356	-0.480	2.690
6	-1.888	0.490	-4.068	0.293
7	1.404	0.605	-1.287	4.095

The confidence coefficient (0.95) indicates the percent of the time the estimating procedure will yield a confidence region in ($\Delta\%BF$, MIL/RN, $\Delta FOLL$) which covers the entire true regression plane, in a long series of samples in which the $\Delta\%BF$ and MIL/RN observations are kept at the same levels as in the sample actually taken.

The following table contains the multiple regressions of $\Delta LUTL$ with overall $F \leq 0.05$.

Dependent	Explanatory	P-level	RSQ	Signif F
$\Delta LUTL$:	ΔDW	0.040	82.8%	0.029
	MIL/CD	0.070		
$\Delta LUTL$:	$\Delta \%BF$	0.020	83.1%	0.020
	MIL/CY	0.090		
$\Delta LUTE$:	$\Delta \%BF$	0.100	85.8%	0.020
	$\Delta ESTR$	0.060		
$\Delta LUTL$:	$\Delta \%BF$	0.020	84.0%	0.020
	ΔFSH	0.080		
$\Delta LUTL$:	$\Delta ESTR$	0.020	86.0%	0.019
	MIL/CD	0.100		

The results indicate that $\Delta LUTL$ is significantly associated with $\Delta ESTR$, and that running and fitness variables are not significant when $\Delta ESTR$ is already in the model.

The following table contains the fitted values and their standard errors for the regression of $\Delta LUTL$ on $\Delta ESTR$:

$$\Delta LUTL = -1.7 + 0.04 * \Delta ESTR$$

and also Working-Hotelling 95% confidence band for the regression line.

Working-Hotelling 95% confidence
band for the regression line

Individual	Fitted	Estimated SE	Lower bound	Upper bound
1	-1.095	0.548	-2.960	0.767
2	-2.434	0.612	-4.516	-0.352
3	-1.960	0.561	-3.865	-0.053
4	-4.162	0.956	-7.410	-0.915
5	0.935	0.869	-2.019	3.890
6	1.453	0.990	-1.910	4.822
7	-2.737	0.658	-4.970	-0.499

The following table contains the multiple regressions of $\Delta FLWL$ with overall $F \leq 0.05$.

Dependent	Explanatory	P-level	RSQ	Signif F
$\Delta FLWL$:	ΔDW	0.280	80.8%	0.030
	$\Delta T3$	0.070		
$\Delta FLWL$:	$\Delta T3$	0.010	83.9%	0.025
	$\Delta \%BF$	0.018		

$\Delta FLWL$ is significantly associated with $\Delta T3$ and $\Delta \%BF$. That is $\Delta \%BF$ has an extra association with $\Delta FLWL$ even when $\Delta T3$ is already in the model. Collinearity could be a problem since $r = -0.62$, which may result in the estimated regression coefficients having large sampling variability. Multicollinearity is usually not a problem when the purpose of the regression analysis is to make inferences on the response function or predictions of new observations,

provided that these inferences are made within the range of observations.

The following table contains the fitted values and their standard errors for the regression of ΔFLWL on ΔBF and ΔT3 :

$$\Delta\text{FLWL} = -0.25 - 0.5 \cdot \Delta\text{BF} - 0.03 \cdot \Delta\text{T3}$$

and also Working-Hotelling 95% confidence region for the regression PLANE.

Working-Hotelling 95% confidence
region for the regression region

<u>Individual</u>	<u>Fitted</u>	<u>Estimated SE</u>	<u>Lower bound</u>	<u>Upper bound</u>
1	-0.549	0.360	-1.054	2.152
2	0.203	0.199	-0.682	1.088
3	0.276	0.181	-0.527	1.080
4	-0.389	0.312	-1.779	0.999
5	-0.377	0.212	-1.322	0.570
6	-1.400	0.363	-3.016	0.215
7	1.236	0.355	-0.344	2.816

3.3 Regression Analysis from Phase A to C

3.3.1 Morphometric and fitness parameters

The same steps as A to B have been taken for this phase. Scatter plots of (ΔDW , ΔSS , ..., and TRPS.) vs. (MIL/CY, MIL/CD,) were studied carefully; a few of these plots are shown in Figures 3.3a.

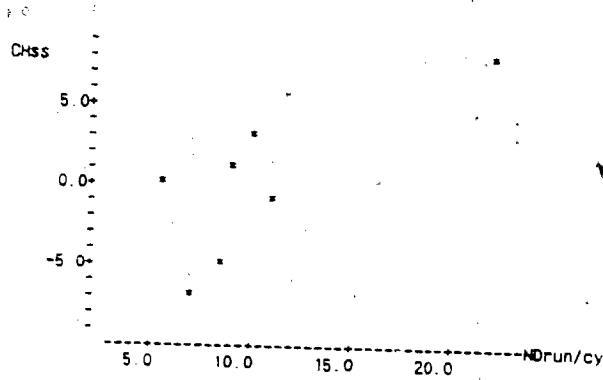
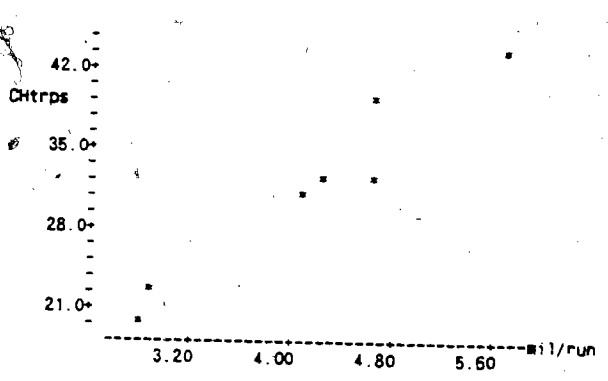
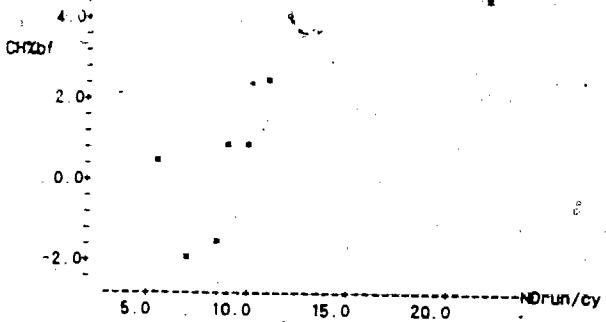
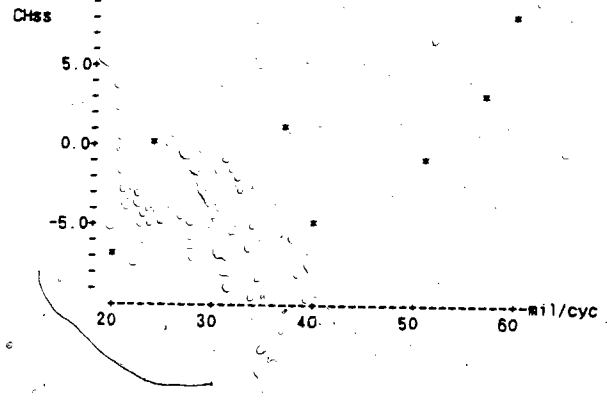
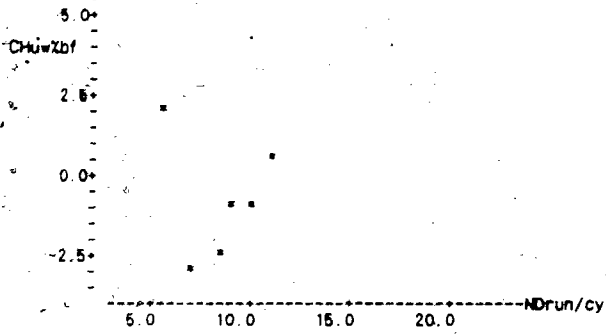
There seems to be no strong suggestion of any trend which could not be reasonably approximated by a first-order model. Many of the plots shown on Page 45 seem to depend strongly on the influence of just on individual (individual 4).⁸

T-tests on averages for ΔDW , ΔSS , $\Delta \%BF$, UWW, and $UW \%BF$, i.e., without any independent variables, except for $\Delta TRPS$, fail to reveal significant differences, the results are shown in Table 2 of Appendix A.

First-order regression was employed to formally quantify the extent to which the data reveals an association between the change in morphometric, fitness variable and the running variables. Each dependent variable (ΔDW , ΔSS , $\Delta \%BF$, ΔUWW , $\Delta UW \%BF$, TRPS) was regressed on running variables (MIL/CY, ML/CD, MIL/RN, MIL/W, NDRUN/CY) one variable at a time. To test whether the dependent variable is significantly associated with the corresponding independent variable, the

⁸for more see section 3.4

Figure 3.3a: Δ Morphometric and Fitness variables vs. Running



T-test for the slope coefficient (which is equivalent to the regression F-test) was utilised.

The following table contains significant regressions and their significance levels.

Dependent	Explanatory	P-value	RSQ
Δ SS	MIL/CY	0.05	54.3%
"	NDRUN/CY	0.04	59.4%
Δ %BF	NDRUN/CY	0.02	65.2%
Δ UW%BF	NDRUN/CY	0.05	56.1%
TRPS	MIL/RN	0.00	93.2%

It seems that there is a strong association between the change (increase) in TRPS from phase A to C and MIL/RN, and also Δ %BF and Δ SS are significantly associated with NDRUN/CY.

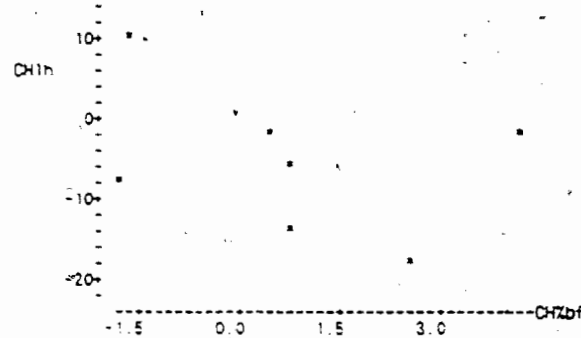
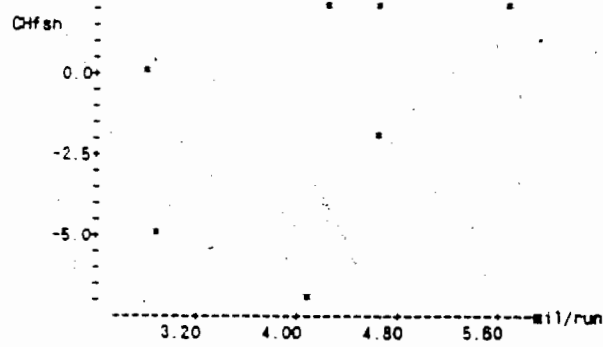
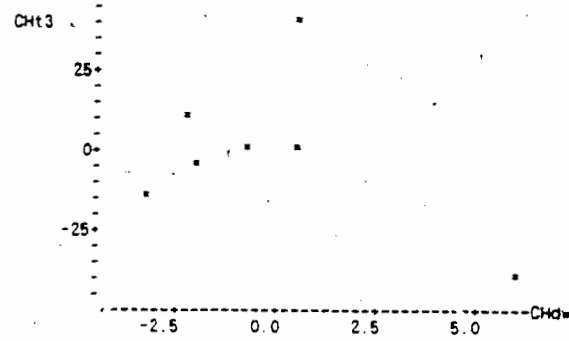
3.3.2 Hormones

Scatter plots were again used to see whether the data reveals any association of hormone changes (Δ ESTR, Δ PROG,) vs. change in the running and fitness variables.

Figure 3.3b displays these plots. These do not reveal any strong association between Δ ESTR and Δ PROG and the rest of the variables, except for an apparently strong association between Δ PROG and MIL/RN.

The result of the t-test on Δ ESTR, Δ PROG, ... are shown in Table 2 of Appendix A. It can be seen that there is

Figure 3.3b: Scatter Plots of Δ Hormones



insufficient evidence to reject the null hypothesis (except for TSH).

For further investigation, simple regressions of Δ PROG, Δ ESTR, Δ FSH, Δ LH, and Δ T3 on running variables and the change in morphometric and fitness variables were examined. For each of the hormone variables regressions with the lowest p-value are given in the following table.

Dependent	Explanatory	P-value	RSQ
Δ ESTR	Δ DW	0.16	34.7%
Δ PROG	Δ DW	0.29	21.8%
Δ FSH	Δ MIL/RN	0.33	19.3%
Δ T3	TRPS	0.02	68.9%
Δ LH	Δ %BF	0.42	13.1%
Δ TSH	TRPS	0.26	23.8%

No associations between hormones and the other relevant variables were detected except for Δ T3 which is significantly associated with TRPS. In spite of the above results, regressions with two independent variables are considered, where Δ PROG, Δ ESTR,... are the dependent and Δ DW, Δ ASS,..., and MIL/CY, MIL/CD,... are the independent variables. Each dependent variable is regressed on two independent variables, consisting of morphometric (including TRPS) variables, and a running variable. An overall F test is performed for all of the regressions, and for those with a small p-value (≤ 0.05), an improvement F test is used to test if the first independent variable is significantly different than zero given that the second independent variable is already in the model. Another improvement F test is done for the second independent variable to find its significance level given that the first independent is already in the model. ⁹

⁹It can be shown that $F_{1,y} = (T_y)^2$. Therefore significance levels are obtained from a T table. In this particular case the improvement F test statistic has one degree of freedom on the numerator and four degree of freedom on the denominator, which is equal to $(T_4)^2$.

The following table shows the multiple regressions of hormones with the lowest overall F.

<u>Dependent</u>	<u>Explanatory</u>	<u>P-level</u>	<u>RSQ</u>	<u>Signif F</u>
Δ ESTR:	Δ DW	0.30	37.9%	0.38
	MIL/CD	0.66		
Δ PROG:	Δ DW	0.16	43.9%	0.32
	NDRUN/CY	0.28		
Δ FSH	Δ DW	0.18	51.5%	0.18
	MIL/RN	0.15		
Δ LH:	Δ %BF	0.17	41.8%	0.33
	NDRUN/CY	0.23		
Δ T3:	TRPS	0.04	83.8%	0.02
	MIL/RN	0.12		
Δ PROL:	TRPS	0.05	93.4%	0.004
	MIL/RN	0.01		

It seems that there is no significant association of Δ PROG, Δ ESTR, Δ LH, and Δ FSH with any such pairs of independent variables. The change in Δ T3 seems to be associated with TRPS, and Δ PROL is significantly associated with TRPS and MIL/RN.

3.3.3 Menstrual Cycle

Scatter plots of $\Delta CYCL$, $\Delta FOLL$, $\Delta LUTL$, and $\Delta FLWL$ vs $\Delta ESTR$, $\Delta PROG$, ..., ΔDW , ΔSS , ..., and MIL/CYC , MIL/CYD , ..., were studied carefully. Some of these plots are shown in Figures 3.3c through 3.3f.

Studies of these plots reveal that there is a strong association between $\Delta CYCL$ and MIL/CD , and also between $\Delta FOLL$ and ΔTSH and $\Delta LUTL$ and ΔTSH . $\Delta FLWL$ and MIL/W seems to be associated linearly as well. For the rest of the scatter plots there seems to be no strong suggestion of any trend.

As before t-tests on averages were performed, i.e. without any independent variable. The results are illustrated in Table 2 of Appendix A. For further analysis, linear regression was employed. Each menstrual variable $\Delta CYCL$, $\Delta FOLL$, $\Delta LUTL$, and $\Delta FLWL$ is regressed on $\Delta morphometric$, $\Delta fitness$, running and the $\Delta hormones$ variables, one variable at a time. For each of the menstrual variables the following table contains the regressions with the $p\text{-value} \leq 0.05$ for the slope coefficient.

<u>Dependent</u>	<u>Explanatory</u>	<u>P-value</u>	<u>RSQ</u>
$\Delta CYCL$	MIL/CD	0.005	81.9%
$\Delta FOLL$	ΔTSH	0.030	63.7%
$\Delta LUTL$	ΔTSH	0.01	79.4%
$\Delta FLWL$	MIL/W	0.02	67.9%

The results indicate that there is a significant change in

Figure 3.3c: Scatter Plots of $\Delta CYCL$

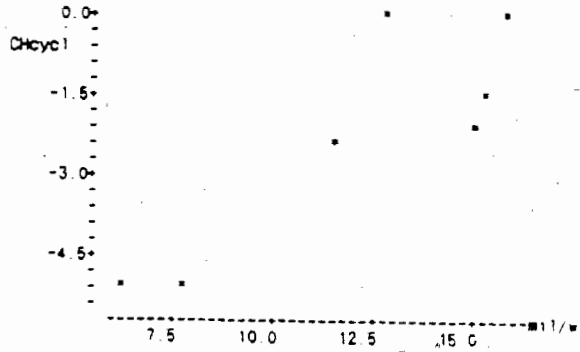
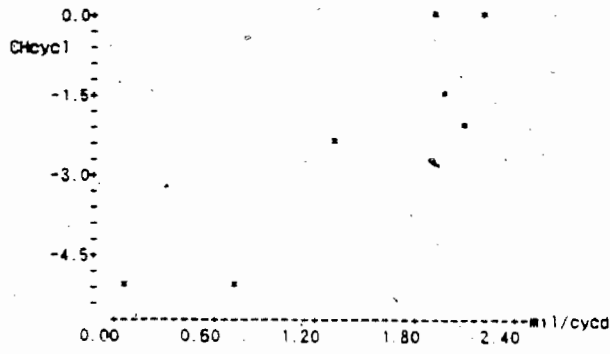


Figure 3.3d: Scatter Plots of $\Delta FOLL$

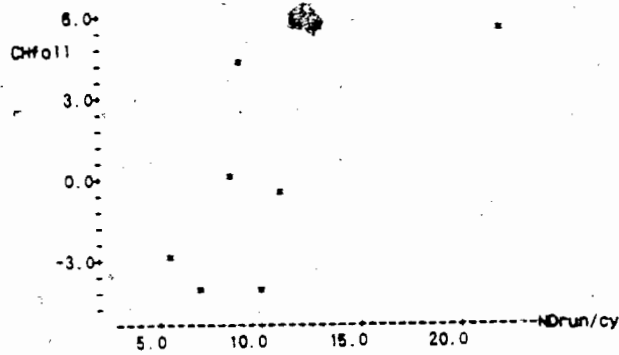
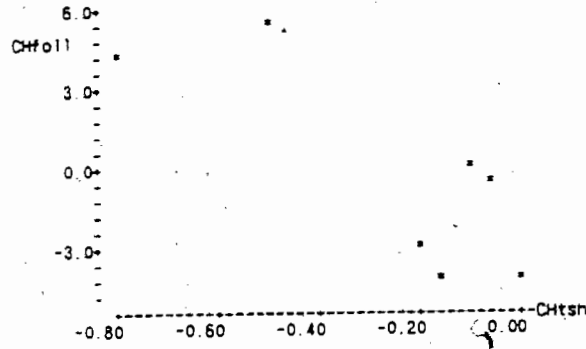


Figure 3.3e: Scatter Plots of ALUTH

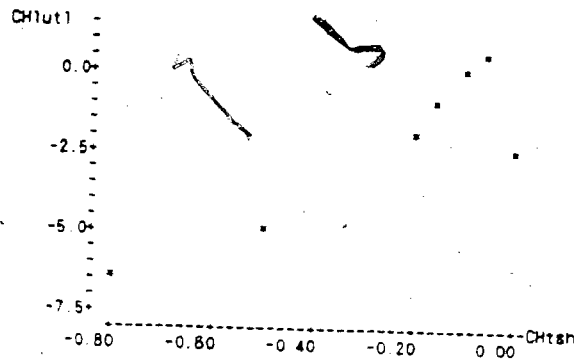
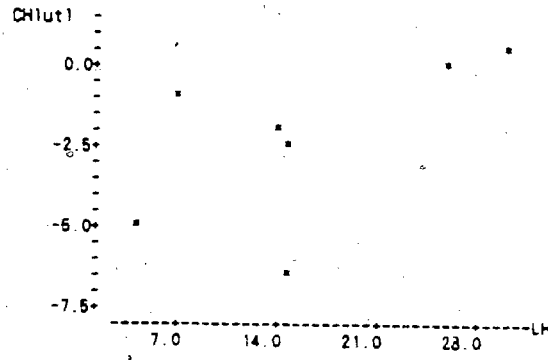
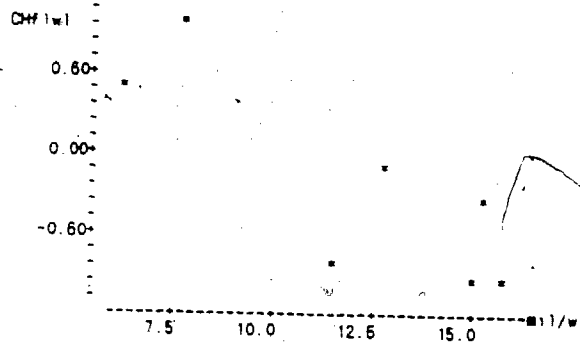
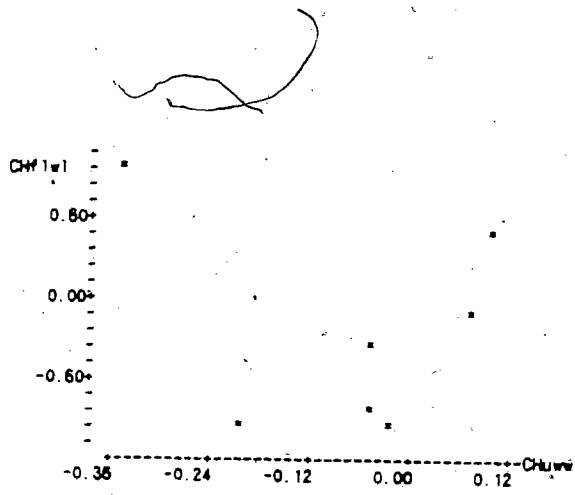


Figure 3.3f: Scatter Plots of $\Delta FLWL$



CYCL and it is associated with MIL/CD, and also $\Delta FOLL$ and $\Delta LUTL$ are both highly associated with ΔTSH , and $\Delta FLWL$ is associated with MIL/W. It seems that the change in menstrual cycle variables are not associated with the morphometric, fitness, and other hormone variables this time span.

Next, regressions with two independent variables are considered. Here, one of the independent variables has been found significant by a t-test on the slope coefficient, and the other variable belongs to a different group believed to be associated with the corresponding dependent variable. All of the different combinations were considered. To test whether the change in the dependent variable is significantly associated with the two independent variables an overall F-test was performed. Improvement F tests were utilized for those regressions that show a significant F statistics.

The following table contains the multiple regressions for the menstrual cycle variables with an overall $F \leq 0.05$.

Dependent	Explanatory	P-level	RSQ	Signif F
$\Delta CYCL$:	MIL/CD	0.00	98.7%	0.000
	LH	0.00		
$\Delta CYCL$:	MIL/W	0.00	94.7%	0.002
	ΔSS	0.01		
$\Delta CYCL$:	MIL/CD	0.00	94.3%	0.003

	T3	0.04		
ΔCYCL:	MIL/CD	0.00	93.9%	0.003
	FSH	0.04		

The results indicate that the change in CYCL is strongly associated with MIL/CD and the level of the hormone LH at time C (the correlation between MIL/CD and LH is 0.34) rather than with ΔLH. It can be seen from the table on page 45 that there is no significant change in LH regarding fitness and running variables. But from the above table it can be seen that the level of the hormones at time C together with running variables are important in explaining the change in CYCL over this time span.

The following table contains the fitted values and their standard errors for the regression of ΔCYCL on MIL/CD and LH:

$$\Delta CYCL = -6.7 + 0.1 * LH + 1.94 * MIL/CD$$

Working-Hotelling 95% confidence region for the regression line is also presented.

Working-Hotelling 95% confidence
region for the regression surface

Individual	Fitted	Estimated SE	Lower bound	Upper bound
1	-4.566	0.173	-5.337	-3.780
2	-1.365	0.138	-1.980	-0.751
3	0.090	0.180	-0.713	0.893
4	-2.240	0.237	-3.295	-1.180
5	-2.630	0.110	-3.122	-2.130
6	-0.007	0.210	-0.940	0.926
7	-5.230	0.240	-6.294	-4.157

The following table contains the multiple regressions of $\Delta FOLL$ with overall F significance level ≤ 0.05 .

Dependent	Explanatory	P-level	RSQ	Signif F
$\Delta FOLL$:	TSH	0.02	78.8%	0.04
	MIL/CY	0.02		
$\Delta FOLL$:	ΔTSH	0.01	86.5%	0.01
	MIL/CD	0.06		
$\Delta FOLL$:	ΔTSH	0.03	85.4%	0.02
	NDRUN/CY	0.07		

The results indicate that the change in FOLL is associated with MIL/CY and TSH level at time C. The other two fitted models indicate that the change in FOLL is significantly associated with ΔTSH , and the running and fitness variables are not significant when ΔTSH is already in the model.

The following table contains the fitted values and their standard errors for the regression of $\Delta FOLL$ on MIL/CY and TSH:

$$\Delta FOLL = 2.48 - 14.9 * TSH + 0.236 * MIL / CY$$

Working-Hotelling 95% confidence region for the regression surface is also presented.

Working-Hotelling 95% confidence
region for the regression surface

Individual	Fitted	Estimated SE	Lower bound	Upper bound
1	-3.930	1.460	-10.43	2.570
2	-3.440	1.800	-11.46	4.587
3	2.940	1.290	-2.780	8.670
4	3.230	1.389	-2.960	9.420
5	2.200	1.213	-3.190	7.970
6	0.396	0.963	-3.890	4.680
7	-3.880	1.350	-9.890	2.133

The following table contains the multiple regressions of $\Delta LUTL$ with overall F significance level ≤ 0.05 .

<u>Dependent</u>	<u>Explanatory</u>	<u>P-level</u>	<u>RSQ</u>	<u>Signif F</u>
$\Delta LUTL$:	ΔTSH	0.01	88.4%	0.01
	ΔSS	0.15		
$\Delta LUTL$:	ΔTSH	0.01	82,5%	0.03
	MIL/CY	0.44		

It seems that $\Delta LUTL$ is significantly associated with ΔTSH and the other variables (fitness and running variables) are not significant when ΔTSH is already in the model.

The following table contains the fitted values and their standard errors of $\Delta LUTL$ on ΔTSH :

$$\Delta LUTL = -0.313 + 7.81 * \Delta TSH$$

Working-Hotelling 95% confidence band for the regression line is also presented.

Working-Hotelling 95% confidence
band for the regression line

<u>Individual</u>	<u>Fitted</u>	<u>Estimated SE</u>	<u>Lower bound</u>	<u>Upper bound</u>
1	-1.490	0.513	-3.230	0.260
2	-0.313	0.660	-2.560	1.933
3	-1.090	0.550	-2.970	0.784
4	-4.218	0.640	-6.410	-2.030
5	-6.560	1.070	-10.22	-2.898
6	-0.704	0.602	-2.750	1.345
7	-1.875	0.487	-3.532	-0.218

The following table contains the multiple regression of $\Delta FLWL$ with overall $F \leq 0.05$.

Dependent	Explanatory	P-level	RSQ	Signif F
$\Delta FLWL$:	$\Delta \% BF$	0.15	79.7%	0.04
	MIL/CD	0.05		
$\Delta FLWL$:	ΔLH	0.047	87.7%	0.015
	MIL/CD	0.008		
$\Delta FLWL$:	ΔFSH	0.005	96.3%	0.001
	MIL/W	0.000		

$\Delta FLWL$ is significantly associated with ΔFSH and MIL/W ($r=0.29$). That is ΔFSH has an extra effect on $\Delta FLWL$ when MIL/W is already in the model.

The following table contains the fitted values and their standard errors for the regression of $\Delta FLWL$ on ΔFSH and MIL/W:

$$\Delta FLWL = 2.27 + 0.12 \Delta FSH - 0.2 \text{MIL/W}$$

Working Hotelling 95% confidence region for the regression plane is also shown.

Working-Hotelling 95% confidence
region for the regression surface

<u>Individual</u>	<u>Fitted</u>	<u>Estimated SE</u>	<u>Lower bound</u>	<u>Upper bound</u>
1	0.440	0.140	-0.188	1.068
2	-0.550	0.105	-1.013	-0.082
3	-0.058	0.094	-0.474	0.358
4	-0.730	0.090	-1.132	-0.328
5	-0.866	0.139	-1.486	-0.245
6	-1.090	0.106	-1.570	-0.618
7	0.962	0.143	0.325	1.598

3.4 Statistical Critique

This was an exercise in data modelling. It produced regression coefficients, F-ratios, significance levels, etc. Any value these summary statistics might have for predicting outcomes (for example: menopausal cycle changes) in subjects in general, depends upon what "subjects in general" means, and upon whether the data analysed can be considered as representative or typical of subjects in general, and upon general knowledge or opinion about the detected patterns, which were already held prior to this data analysis.

In social sciences, the relationships between two variables are usually observational. Association does not mean causation. If the experimenter can control independent variables then association can suggest a causation (Ref 12). It should be emphasized that searching among many

independent variables may tend to fit a well-fitting model by chance, somewhat obscuring the scientific meaning of significance levels (see discussion in BMDP manual program P9R). On the other hand "knowledgable" search does not necessarily entail this danger. It is the investigator's task to strike a subjective balance.

For future experiments, it is recommended that fewer variables should be studied, that is those that have the same nature (MIL/CY, MIL/W, MIL/CD,....) should be combined. And also it would be a good idea for a statistician to be consulted before the sampling procedure, so that the sample can be as representative as possible.

It is also recommended that if possible, more observations should be taken, so that more detailed statistical analyses like regression models with interactions could be studied.

It should be noted that individual 3's response to (Δ SS, TRPS, Δ CYCL, and Δ FOLL) from phase A to B, and individual 4's response to (Δ SS, Δ %BF, and Δ UW%BF) from phase A to C were extremely different than the others. Their extreme response could be due to many factors, for example it could be due to the fact that both subjects had the highest MIL/CY compared to the others (at phase B for individual 3 and at phase C for individual 4). The inclusion of these two subjects has a definite influence on some of the reported

p-values (e.g. from phase A to B no significant regressions of morphometric and fitness variables on running were found, when subject 3 was removed and also from phase A to C no significant regressions of morphometric variables on running were found, when subject 4 was removed). Since there were only 7 subjects, it did not seem reasonable to remove these subjects from the list of data. However further investigation regarding the nature of the extreme responses of these two subjects is recommended.

3.5 Scientific Conclusion

The most compelling associations for each time period is as follows:

Phase A to B:

It seems that $\Delta CYCL$ is associated with ΔSS and ΔLH (see page 37), where ΔSS is significantly associated with MIL/RN (see page 23), no significant change in LH with regard to morphometric, fitness, and running variables was found (see page 26). $\Delta FOLL$ is associated with $\Delta \%BF$ and MIL/RN (see page 39), no significant change in $\%BF$ with regard to running variables was found (see page 23). $\Delta LUTL$ is associated with $\Delta ESTR$ (see page 41), and $\Delta ESTR$ is associated with ΔDW (see page 28), no significant change in DW with regard to running variables was found (see page 23). $\Delta FLWL$ is associated with $\Delta T3$ and $\Delta \%BF$ (see page 42), where $\Delta T3$ is associated with ΔSS and MIL/CD (see page 28).

Phase A to C:

It seems that $\Delta CYCL$ is associated with LH and MIL/CD (see page 56); $\Delta FOLL$ is associated with TSH and MIL/CY (see page 58), $\Delta LUTL$ is associated with ΔTSH (see page 60), and $\Delta FLWL$ is associated with FSH and MIL/W (see page 61).

It looks like that the change in the menstrual cycle variables from time A to B is associated with change in morphometric and hormone variables, where the change from phase A to C is associated with the level of hormones at time C and running variables.

The implications of Dr. J. Prior's work are:
This study explores complex and interrelated variables which subsequently affect menstrual cycle characteristics. The running variable as primary acts through changes in morphometric (nutrition) and fitness (see pages 23 and 46) and directly to effect changes in hormones (see pages 28 and 50). The hormone changes then alter intervals, phase lengths and flow characteristics (see sections 3.2.3 and 3.3.3).

The luteal phase shortening confirms the previously reported changes. This change is of biological and medical significance. The association with $\Delta ESTR$ and ΔTSH may be helpful in other investigations (see tables on page 42 and 60 and also Ref. 16)

APPENDIX A

T tests on average change for fitness, hormones and menstrual cycle variables

Phase A to B:

<u>Variable Name</u>	<u>Average</u>	<u>T statistics</u>	<u>P-value</u>
ΔDW	0.11	0.24	0.81
ΔSS	0.44	0.30	0.77
Δ%BF	-0.07	-0.24	0.81
ΔUWW	0.07	2.08	0.08
ΔUW%BF	-0.76	-2.00	0.09
TRPS	22.02	8.46	0.00

<u>Variable Name</u>	<u>Average</u>	<u>T statistics</u>	<u>P-value</u>
ΔESTR	6.30	0.35	0.73
ΔPROG	1.00	0.64	0.54
ΔFSH	-0.29	0.31	0.76
ΔLH	-1.40	0.15	0.88
ΔT3	-7.10	-0.58	0.58

<u>Variable Name</u>	<u>Average</u>	<u>T statistics</u>	<u>p-value</u>
ΔCYCL	-0.29	-0.30	0.77
ΔFOLL	0.43	0.40	0.70
ΔLUTL	-1.43	-1.57	0.16
ΔFLWL	0.01	0.04	0.96

Phase A to C:

<u>Variable Name</u>	<u>Average</u>	<u>T statistics</u>	<u>P-value</u>
Δ DW	-0.17	-0.15	0.88
Δ SS	-0.11	-0.05	0.96
Δ %BF	0.76	0.95	0.37
Δ UW	-0.07	-1.20	0.27
Δ UW%BF	0.04	0.03	0.97
TRPS	31.63	10.07	0.00

<u>Variable Name</u>	<u>Average</u>	<u>T statistics</u>	<u>P-value</u>
Δ ESTR	-8.00	-0.19	0.85
Δ PROG	-2.57	-1.00	0.34
Δ FSH	-1.14	-0.82	0.44
Δ LH	-5.86	-1.50	0.16
Δ T3	-1.00	-0.10	0.92
Δ TSH	-0.26	-2.35	0.05

<u>Variable Name</u>	<u>Average</u>	<u>T statistics</u>	<u>p-value</u>
Δ CYCL	-2.29	-2.89	0.02
Δ FOLL	-0.33	-0.23	0.82
Δ LUTL	-2.32	-2.40	0.05
Δ FLWL	-0.26	-0.91	0.39

APPENDIX B

Method of Least Squares

To find "good" estimators of the regression parameters β_0 and β_1 , method of least squares is employed. For each sample observation (X_i, Y_i) , the method of least squares considers the deviation of Y_i from its expected value:

$$Y_i - (\beta_0 + \beta_1 X_i) = \epsilon_i$$

In particular, the method of least squares requires that we consider the sum of the n squared deviations, denoted by Q :

$$Q = \sum_{i=1}^n (Y_i - \beta_0 - \beta_1 X_i)^2$$

According to the method of least squares, the estimators of β_0 and β_1 are those values b_0 and b_1 respectively which minimize Q .¹

¹ For more on the mathematical operations and b_0 and b_1 formulas please see (Ref. 5 Page 38).

APPENDIX C

Figure 4: Scatterplot Source File from Phase A to B

```
EMPTY ZZ-TOP OK
EMPTY -T OK
EMPTY -P OK
RUN *MIDAS
READ INT FI=DATS:HYPCONMID V=ALL
WRITE FI=-T V=304-308,330-339 C=16-21 FO=(15F10.4)
WRITE FI=-P V=361-368,161-168 C=16-21 FO=(16F10.4)
MTS
RUN *MINITAB SPRINT=ZZ-TOP
NOECHO
OUTPUT WIDTH IS 80 HEIGHT IS 0
READ -T C1-C16
READ -P C16
*****plotend*****
NAME C1 'Chdw' C2 'Chs' C3 'Chzbf' C4 'Chuw'
NAME C5 'Chwzbf' C6 'TRPS' C7 'Chcyc1' C8 'Chfol1'
NAME C9 'Chlut1' C10 'Chfiw1' C11 'Chsantp' C12 'ml/cyc'
NAME C13 'ml/cycd' C14 'ml/run' C15 'ml/w' C16 'Chtest'
NAME C17 'Chestr' C18 'Chprog' C19 'Chfsh' C20 'Chlh'
NAME C21 'Chsh' C22 'Ch13' C23 'Chpro1' C24 'Test'
NAME C25 'Estr' C26 'Prog' C27 'FSH' C28 'LH' C29 'TSH'
NAME C30 'T3' C31 'Prol'
#Scatter plots of weight change vs. running parameters
PLOT C1 C12
PLOT C1 C13
PLOT C1 C14
PLOT C1 C16
PLOT C2 C12
PLOT C2 C13
PLOT C2 C14
PLOT C2 C16
PLOT C3 C12
PLOT C3 C13
PLOT C3 C14
PLOT C3 C16
PLOT C4 C12
PLOT C4 C13
PLOT C4 C14
PLOT C4 C16
PLOT C5 C12
PLOT C5 C13
PLOT C5 C14
PLOT C5 C16
PLOT C6 C12
PLOT C6 C13
PLOT C6 C14
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PLOT C7 C12
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PLOT C7 C16
PLOT C8 C12
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PLOT C9 C14
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PLOT C12 C16
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PLOT C13 C16
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PLOT C14 C5
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PLOT C14 C7
PLOT C14 C8
PLOT C14 C9
PLOT C14 C10
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Figure 7, continued.

Regressions of: change in foll length vs. change in all vars

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Regressions of: weight change vs. running parameters

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Regressions of: change in hormones vs. change in weight & running

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