Caffeine versus Placebo for Psychomotor Vigilance Lapses under Sleep Deprivation

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1 Introduction

1.1 General Background

This report analyzes the relationship between caffeine and psychomotor vigilance lapses under sleep deprivation. H.P.A. Van Dongen shows the data, E. Olofson, D.F. Dinges, G. Maislin (2004)[1] which posted in the data set of University of Florida(https://users.stat.ufl.edu/~winner/data/caffeine_mixed.dat). The data set contains the experiment results comparing the effects of low-dose caffeine to placebo on the number of psychomotor vigilance lapses, which measured four days of total sleep deprivation with 13 subjects in each group. We use 1 to represent the caffeine group and 2 to represent the placebo group. Moreover, we have extra four columns to record the number of psychomotor vigilance lapses in four days.

2 Objectives and Raised Questions

The following question is building a regression model for mean psychomotor vigilance lapses with baseline (Day 0) and the placebo group (group 2). The main objective of this data set is to determine whether the patterns of change over time differ in the two treatment groups. Then we can construct a time plot that displays the mean psychomotor vigilance lapses versus time (in days) for the two groups. We also can build a plot of the estimated mean psychomotor vigilance lapses versus time (in days) for the two treatment groups. We also can create a test of whether the rate of increase differs in the two groups. The secondary objective is to find the covariance that adequately fits the data..

3 Approach

3.1 Model and Method

The original data set is a multivariate (wide) format, as shown in the following figure. We need to convert it into a univariate (long) format. (Due to the limit of the pages, we show a part of the long format figure).

Obs	id	group	d1	d2	d3	d4
1	1	1	0.4	2.0	23.0	31.3
2	2	1	1.0	5.7	19.1	21.9
3	3	1	0.6	7.4	9.9	25.9
4	4	1	4.7	11.3	18.0	11.7
5	5	1	2.6	5.9	13.6	23.7
6	6	1	1.6	4.0	19.9	24.4
7	7	1	3.3	5.7	11.4	15.4
8	8	1	4.4	4.7	19.6	13.3
9	9	1	0.0	10.1	20.3	12.4
10	10	1	2.6	10.9	8.0	13.7
11	11	1	0.3	3.3	9.7	13.6
12	12	1	3.0	9.3	5.7	13.4
13	13	1	2.7	3.9	12.0	12.0
14	14	2	5.0	9.3	31.9	21.7
15	15	2	5.1	15.6	23.6	43.9
16	16	2	1.0	4.9	18.3	23.0
17	17	2	16.6	35.1	31.7	30.1
18	18	2	15.1	22.0	28.7	32.3
19	19	2	0.0	0.0	2.4	0.0
20	20	2	0.3	1.4	9.1	10.6
21	21	2	1.3	8.1	13.3	22.3
22	22	2	11.6	23.9	16.9	15.9
23	23	2	7.1	32.1	27.0	21.9
24	24	2	12.7	22.0	18.6	20.0
25	25	2	2.6	11.9	25.7	21.3
26	26	2	20.7	21.4	19.7	34.1

Figure 1: Multivariate (wide) format

Obs	id	group	d	time
1	1	1	0.4	0
2	1	1	2.0	1
3	1	1	23.0	2
4	1	1	31.3	3
5	2	1	1.0	0
6	2	1	5.7	1
7	2	1	19.1	2
8	2	1	21.9	3
9	3	1	0.6	0
10	3	1	7.4	1
11	3	1	9.9	2
12	3	1	25.9	3
13	4	1	4.7	0
14	4	1	11.3	1
15	4	1	18.0	2
16	4	1	11.7	3
17	5	1	2.6	0
18	5	1	5.9	1
19	5	1	13.6	2
20	5	1	23.7	3
21	6	1	1.6	0
22	6	1	4.0	1
23	6	1	19.9	2
24	6	1	24.4	3
25	7	1	3.3	0
26	7	1	5.7	1
27	7	1	11.4	2
28	7	1	15.4	3
29	8	1	4.4	0
30	8	1	4.7	1

Figure 2: Partial univariate (long) format

To better understand our data set, we calculate the sample means, standard deviations, and variances of the psychomotor vigilance lapses on each occasion for each treatment group.

The MEANS Procedure

Analysis Variable : d					
group	time	N Obs	Mean	Std Dev	Variance
1	0	13	2.0923077	1.5654933	2.4507692
	1	13	6.4769231	3.0602706	9.3652564
	2	13	14.7076923	5.4609922	29.8224359
	3	13	17.9000000	6.6001263	43.5616667
2	0	13	7.6230769	6.9727032	48.6185897
	1	13	15.9769231	11.1960673	125.3519231
	2	13	20.5307692	8.8175379	77.7489744
	3	13	22.8538462	10.9738033	120.4243590

Figure 3: Sample Means, Standard Deviations, and Variances

Then we use the result shown in figure 3 to construct a time plot that displays the mean psychomotor vigilance lapses versus time (in days) for the two treatment groups.

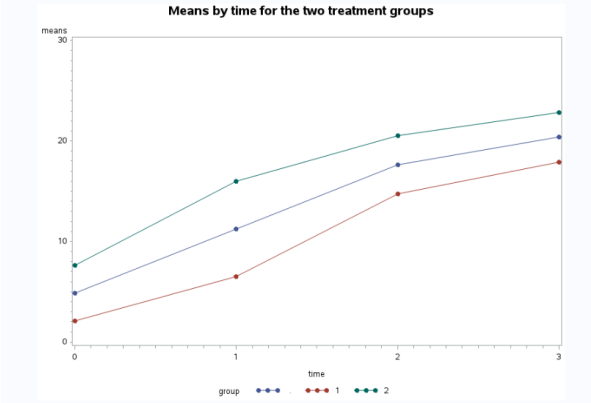
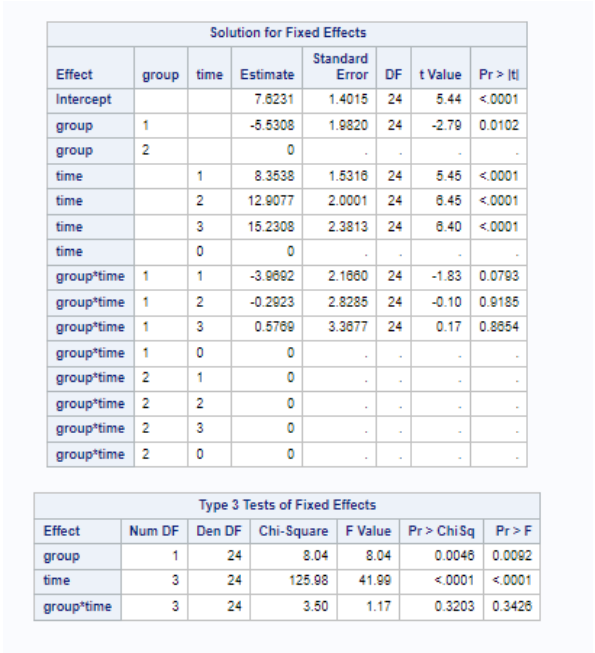


Figure 4: Means by time for the two treatment groups

Figure 4 shows that the number of psychomotor vigilance lapses increases with the increase of time. There is a positive relationship between time and the number of psychomotor vigilance lapses in the two treatment groups. Then we would like to use an unstructured covariance matrix to determine whether the patterns of change over time differ in the two treatment groups.



Solution for Fixed Effects

Effect	group	time	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept			7.6231	1.4015	24	5.44	<.0001
group	1		-5.5308	1.9820	24	-2.79	0.0102
group	2		0	.	.	.	.
time		1	8.3538	1.5316	24	5.45	<.0001
time		2	12.9077	2.0001	24	6.45	<.0001
time		3	15.2308	2.3813	24	6.40	<.0001
time		0	0	.	.	.	.
group*time	1	1	-3.9692	2.1660	24	-1.83	0.0793
group*time	1	2	-0.2923	2.8285	24	-0.10	0.9185
group*time	1	3	0.5769	3.3677	24	0.17	0.8654
group*time	1	0	0	.	.	.	.
group*time	2	1	0	.	.	.	.
group*time	2	2	0	.	.	.	.
group*time	2	3	0	.	.	.	.
group*time	2	0	0	.	.	.	.

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	Chi-Square	F Value	Pr > ChiSq	Pr > F
group	1	24	8.04	8.04	0.0046	0.0092
time	3	24	125.98	41.99	<.0001	<.0001
group*time	3	24	3.50	1.17	0.3203	0.3426

Figure 5: The result of using an unstructured covariance matrix

Then we can use the result of figure 5 to build a linear regression model for the mean psychomotor vigilance lapses.

$$Y_i = X_i\beta + e_i$$

$$\beta = (7.6231, -5.5308, 8.3538, 12.9077, 15.2308, -3.9692, -0.2923, 0.5769)$$

β_1 shows the estimated mean of the placebo group at the baseline. β_2 shows the group effect at baseline. β_3 shows the difference between baseline and day 1 for the Placebo group. β_4 shows the difference between baseline and day 2 for the Placebo group. β_5 shows the difference between baseline and day 3 for the Placebo group. $\beta_6 + \beta_3$ shows t the difference between baseline and day 1 for the caffeine group. $\beta_7 + \beta_4$ shows t the difference between baseline and day 2 for the caffeine group. $\beta_8 + \beta_5$ shows t the difference between baseline and day 3 for the caffeine group.
Moreover, we have two design matrices shown as follows.

Placebo

$$\begin{matrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \end{matrix}$$

Caffeine

$$\begin{matrix} 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & 1 & 0 & 0 & 1 & 0 & 0 \\ 1 & 1 & 0 & 1 & 0 & 0 & 1 & 0 \\ 1 & 1 & 0 & 0 & 1 & 0 & 0 & 1 \end{matrix}$$

Then we can fit a model which includes the effects of a linear trend in groups, time, and their interaction effect. We can use the result of figure 6 to compare the result of figure 5, which does not include the effects of a linear trend.

Solution for Fixed Effects					
Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	-1.4143	2.8498	24	-0.50	0.6242
group	4.3458	1.8024	24	2.41	0.0239
time	4.6919	1.5888	24	2.95	0.0069
group*time	0.5726	1.0048	24	0.57	0.5741

Type 3 Tests of Fixed Effects						
Effect	Num DF	Den DF	Chi-Square	F Value	Pr > ChiSq	Pr > F
group	1	24	5.81	5.81	0.0159	0.0239
time	1	24	8.72	8.72	0.0031	0.0069
group*time	1	24	0.32	0.32	0.5688	0.5741

Figure 6: The result of include the effects of a linear trend

Moreover, we can fit models for the unstructured, compound symmetry, heterogeneous compound symmetry, autoregressive, and heterogeneous autoregressive to find the covariance that adequately fits the data.

Fit Statistics	
-2 Res Log Likelihood	635.4
AIC (Smaller is Better)	655.4
AICC (Smaller is Better)	658.0
BIC (Smaller is Better)	668.0

Figure 7: unstructured

Fit Statistics	
-2 Res Log Likelihood	658.6
AIC (Smaller is Better)	662.6
AICC (Smaller is Better)	662.8
BIC (Smaller is Better)	665.2

Figure 8: compound symmetry

Fit Statistics	
-2 Res Log Likelihood	647.1
AIC (Smaller is Better)	657.1
AICC (Smaller is Better)	657.7
BIC (Smaller is Better)	663.3

Figure 9: heterogeneous compound symmetry

Fit Statistics	
-2 Res Log Likelihood	663.6
AIC (Smaller is Better)	667.6
AICC (Smaller is Better)	667.8
BIC (Smaller is Better)	670.2

Figure 10: autoregressive

Fit Statistics	
-2 Res Log Likelihood	654.2
AIC (Smaller is Better)	664.2
AICC (Smaller is Better)	664.9
BIC (Smaller is Better)	670.5

Figure 11: heterogeneous autoregressive

We can use AIC to find the covariance that adequately fits the data. Then we can construct a time plot (estimated mean versus time) for the caffeine group and placebo group.

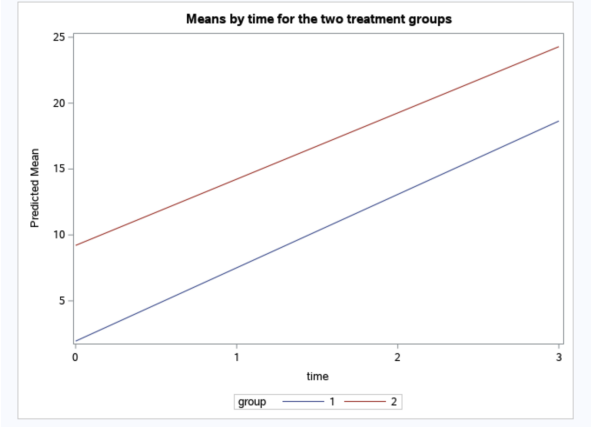


Figure 12: estimated mean versus time

Figure 12 is consistent with figure 4. When we increase the time, the number of psychomotor vigilance lapses will also increase.

Then we would like to use the generalized estimating equations (GEE) and calculate the Wald statistics for type 3 GEE analysis.

Analysis Of GEE Parameter Estimates

Empirical Standard Error Estimates

Parameter			Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept			7.6231	1.8580	3.9814	11.2647	4.10	<.0001
time	1		8.3538	1.9212	4.5883	12.1194	4.35	<.0001
time	2		12.9077	2.2200	8.5565	17.2589	5.81	<.0001
time	3		15.2308	2.5488	10.2352	20.2263	5.98	<.0001
time	0		0.0000	0.0000	0.0000	0.0000	.	.
group	1		-5.5308	1.9043	-9.2631	-1.7985	-2.90	0.0037
group	2		0.0000	0.0000	0.0000	0.0000	.	.
group*time	1	1	-3.9692	2.0810	-8.0479	0.1094	-1.91	0.0565
group*time	1	2	-0.2923	2.7176	-5.6186	5.0340	-0.11	0.9143
group*time	1	3	0.5769	3.2356	-5.7648	6.9186	0.18	0.8585
group*time	1	0	0.0000	0.0000	0.0000	0.0000	.	.
group*time	2	1	0.0000	0.0000	0.0000	0.0000	.	.
group*time	2	2	0.0000	0.0000	0.0000	0.0000	.	.
group*time	2	3	0.0000	0.0000	0.0000	0.0000	.	.
group*time	2	0	0.0000	0.0000	0.0000	0.0000	.	.

Wald Statistics For Type 3 GEE Analysis

Source	DF	Chi-Square	Pr > ChiSq
time	3	136.48	<.0001
group	1	8.71	0.0032
group*time	3	3.80	0.2844

Figure 13: The result of GEE

Figure 13 shows that the p-value of time is < 0.0001 and the p-value of the group is 0.0032. Therefore, the time effect and group effect are statistically significant in this model.

3.2 Results Interpretation

According to the result of figure 5, the p-value of the group effect is 0.0239, the p-value of the time effect is 0.0069, and the p-value of the interaction effect $group \times time$ is 0.5741. Therefore, we conclude the group effect and time effect are statistically significant, and the interaction effect $group \times time$ is not statistically significant. Then we include the effect of a linear trend in groups, time, and their interaction effect. The result is shown in figure 6. We find that the result of figure 5 is consistent with figure 6. Thus, we know the group effect and time effect will influence the number of psychomotor vigilance lapses for each subject. In addition, we also use generalized estimating equations (GEE) to fit our data. The result is shown in figure 13, which is consistent with figure 6. Moreover, we would like to fit models for different kinds of covariance. Based on the result shown in figures 7,8,9,10, and 11, we know compound symmetry has the minimum AIC, which indicates it adequately fits the data.

4 Conclusion and Discussion

This report aims to analyze the effects of low-dose caffeine on the number of psychomotor vigilance lapses under sleep deprivation. Then we build a time plot for the mean psychomotor vigilance lapses versus time. We find out that if we increase the time effect, the number of psychomotor vigilance lapses will also increase. Based on the result given in the approach section, we find out the p-value of the group effect is 0.0239, the p-value of the time effect is 0.0069, and the p-value of the interaction effect $group \times time$ is 0.5741. If we set the statistically significant level as 0.05, the group effect and time effect are statistically significant, and the interaction effect between $group \times time$ is not statistically significant. Thus, we conclude that there is no interaction effect between group and time. After applying different kinds of covariance to our model, we find out the compound symmetry has the minimum AIC, indicating it adequately fits the data.

5 Appendix

```
data caffeine;
inflie "/home/u60740473/Mycontent/caffeine_mixed.txt";
input id group d1 d2 d3 d4;
run;

proc print data=caffeine;
run;

data long_caffeine;
inflie "/home/u60740473/Mycontent/caffeine_mixed.txt";
input id group d1 d2 d3 d4;
d = d1; time = 0;output;
d = d2; time = 1;output;
d = d3; time = 2;output;
d = d4; time = 3;output;
drop d1 d2 d3 d4;

proc print data=long_caffeine;
run;

data long_caffeine;
set long_caffeine;
t=time;
run;

proc means data=long_caffeine mean std var;
class group time;
var d;
output out=meansbytime mean=means;
run;

title1 "Means by time for the two treatment groups";
symbol1 interpol=join value=dot;
proc gplot data=meansbytime;
plot means*time = group;
run;
/*Unstructured*/
proc mixed data =long_caffeine ;
class id group time (ref=FIRST);
model d=group time group*time /s chisq;
repeated time /subject=id type=un  r rcorr;
run;

/*includes the effects of a linear trend*/
proc mixed data =long_caffeine ;
class id t (ref=FIRST);
model d=group time group*time /s chisq;
repeated t /subject=id type=un  r rcorr;
run;

/*More covariance*/
proc mixed data =long_caffeine ;
class id group time (ref=FIRST);
model d=group time group*time /s chisq;
```

```
repeated time /subject=id type=cs  r rcorr;
run;


proc mixed data =long_caffeine ;
class id group time (ref=FIRST);
model d=group time group*time /s chisq;
repeated time /subject=id type=csh  r rcorr;
run;

proc mixed data =long_caffeine ;
class id group time (ref=FIRST);
model d=group time group*time /s chisq;
repeated time /subject=id type=AR(1)  r rcorr;
run;

proc mixed data =long_caffeine ;
class id group time (ref=FIRST);
model d=group time group*time /s chisq;
repeated time /subject=id type=ARH(1)  r rcorr;
run;

proc mixed data=long_caffeine;
class id group t;
model d = group time group*time/s chisq solution
outp = output1 outpm = output2;
repeated t /type =cs subject=id r;
run;


proc print data = output2;
run;
proc sgplot data = output2;
vline time / response = pred stat = MEAN group = group;
format group ;
run;

proc genmod data=long_caffeine;
class id group time (ref=FIRST);
model d=time group time*group/ type1 type3 wald;
repeated subject=id/ type=un corrw;
run;
```