

Chapter 10

Repeated Measures Analysis of Variance Plus Predictors (10 Patients)

1 General Purpose

Repeated-measures-analysis of variance (ANOVA) (Chap. 9) allows for more than two continuous outcome variables, but does not include predictor variables. In this chapter repeated-measures ANOVA with predictor variables is reviewed. In addition to testing differences between the paired observations, it can simultaneously test the effects of the predictors on the outcome variables.

2 Schematic Overview of Type of Data File

Outcome 1	outcome 2	outcome 3	predictor
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.	.	.	.
.	.	.	.
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.	.	.	.
.	.	.	.
.	.	.	.
.	.	.	.

3 Primary Scientific Question

Do three different pills produce significantly different clinical outcome effects. Does the predictor have a significant effect on the outcomes.

4 Data Example

In a crossover study of three different sleeping pills the significance of difference between hours of sleep between the different treatments was assessed.

Hours of sleep after sleeping pill			age (years)
a	b	c	
6,10	6,80	6,20	55,00
7,00	7,00	7,90	65,00
8,20	9,00	6,90	84,00
7,60	7,80	6,70	56,00
6,50	6,60	6,30	44,00
8,40	8,00	6,40	85,00
6,90	7,30	6,20	53,00
6,70	7,00	6,10	65,00
7,40	7,50	6,80	66,00
5,80	5,80	6,30	63,00
6,20	6,70	6,10	55,00
6,90	6,00	7,80	65,00
8,10	8,90	6,80	83,00
7,50	7,80	6,80	56,00
6,40	6,50	6,20	44,00
8,40	7,90	6,30	86,00
6,90	7,40	6,20	53,00
6,60	7,10	6,20	65,00
7,30	6,90	6,90	65,00
5,90	5,90	6,40	62,00

5 Analysis, Repeated Measures ANOVA

The data file is in extras.springer.com, and is entitled “chapter10repeatedmeasuresanova+predictor”. Open the data file in SPSS. For analysis the statistical model Repeated Measures in the module General Linear Model is required. Command:

Analyze....General Linear Model....Repeated Measures....Repeated Measures Define Factors....Within-subject Factor name: treat....Number of Levels: 3.... click Add....click Define: Within-Subjects Variables (treat): enter treatmenta, treatmentb, treatmentc....Between-Subjects Factors: enter "age"....click OK.

The output sheets show the underneath tables.

Mauchly's test of sphericity^a

Measure:MEASURE_1

Within subjects effect	Mauchly's W	Approx Chi-Square	df	Sig.	Epsilon ^b		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
treat	,297	8,502	2	,014	,587	1,000	,500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix

^aDesign: Intercept + age. Within subjects design: treat

^bMaybe used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the tests of within-subjects effects table

Tests of within-subjects effects

Measure:MEASURE_1

Source		Type III sum of squares	df	Mean square	F	Sig.
treat	Sphericity assumed	6,070	2	3,035	15,981	,000
	Greenhouse-Geisser	6,070	1,174	5,169	15,981	,002
	Huynh-Feldt	6,070	2,000	3,035	15,981	,000
	Lower-bound	6,070	1,000	6,070	15,981	,004
treat*age	Sphericity assumed	8,797	22	,400	2,105	,065
	Greenhouse-Geisser	8,797	12,917	,681	2,105	,129
	Huynh-Feldt	8,797	22,000	,400	2,105	,065
	Lower-bound	8,797	11,000	,800	2,105	,150
Error (treat)	Sphericity assumed	3,039	16	,190		
	Greenhouse-Geisser	3,039	9,394	,323		
	Huynh-Feldt	3,039	16,000	,190		
	Lower-bound	3,039	8,000	,380		

Tests of within-subjects contrasts

Measure:MEASURE_1

Source	treat	Type III sum of squares	df	Mean square	F	Sig.
treat	Linear	3,409	1	3,409	23,633	,001
	Quadratic	2,661	1	2,661	11,296	,010
treat*age	Linear	5,349	11	,486	3,371	,048
	Quadratic	3,448	11	,313	1,331	,350
Error(treat)	Linear	1,154	8	,144		
	Quadratic	1,885	8	,236		

Tests of between-subjects effects

Measure:MEASURE_1

Transformed Variable:Average

Source	Type III sum of squares	df	Mean square	F	Sig.
Intercept	2312,388	1	2312,388	17885,053	,000
age	19,245	11	1,750	13,532	,001
Error	1,034	8	,129		

The repeated-measures ANOVA tests whether a significant difference exists between three treatments. An important criterion for validity of the test is the presence of sphericity in the data, meaning that all data come from Gaussian distributions. It appears from the above upper table that this is not true, because based on this table we are unable to reject the null-hypothesis of non-sphericity. This means that an ANOVA test corrected for non-sphericity has to be performed. There are three possibilities: the Greenhouse, Huynh, and Lower-bound methods.

All of them produce virtually the same p-values, between 0,000 and 0,004. This means that there is a very significant different between the magnitudes of the three outcomes. The same table also shows that there is a tendency to interaction between the three treatments and age ($p = 0,065-0,150$). The tests of within-subjects contrasts confirms the appropriateness of the linear model: the linear regressions produce better p-values than did the quadratic regressions. The tests of between-subjects table shows, that age is a very significant predictor of the outcomes a $p = 0,001$. The elderly sleep better on the pills a and b, in the younger there is no difference between the hours of sleep between the three pills.

Like with the repeated-measures without predictors (Chap. 9), Bonferroni-adjusted post-hoc tests have to be performed in order to find out which of the treatments performs the best, and what is the precise effect of age on separate outcomes (more information about the adjustments for multiple testing including the Bonferroni procedure is given in the textbook “Statistics applied to clinical trials”, 5th edition, the Chaps. 8 and 9, 2012, Springer Heidelberg Germany, from the same authors).

6 Conclusion

In a crossover study of multiple different treatment modalities plus predictor variables the significance of difference between the outcomes of the different treatments can be tested simultaneously with the overall effects of the predictor variables. The test results are overall results, and post-hoc tests must be performed in order to find out, if differences exist between treatment 1 and 2, 2 and 3, or 1 and 3, and what effects the predictors have on the separate outcome measures. This rapidly gets rather complex, and some would prefer to skip the overall assessments, and start with Bonferroni adjusted one by one tests right away.

7 Note

More background, theoretical and mathematical information of repeated measures ANOVA is given in *Statistics applied to clinical studies* 5th edition, Chap. 2, Springer Heidelberg Germany, 2012, from the same authors.