Code for myokines

```
# Fit the model and calculate residuals
model <- lmer(Variable ~ Group * Time + Age + Sex + (1 | ID), data = DATA_Germen)
res <- residuals(model)
abs_res <- abs(res)
# Determine outlier threshold (mean + 2*SD)
threshold <- mean(abs_res) + 2 * sd(abs_res)
# Identify outlier observations
all_outliers <- which(abs_res > threshold)
# Create dataset excluding outliers
DATA_no_outliers <- DATA_Germen[-all_outliers, ]
# Fit the model without outliers
model_no_outliers <- lmer(Variable ~ Group * Time + Age + Sex + (1 | ID), data = DATA_no_outliers)
# Display model summary
summary(model_no_outliers)
```

Code for cognitive outcomes

```
# Fit the model and calculate residuals
model <- lmer(Variable ~ Group * Time + Age + Sex + Education + (1 | ID), data = DATA_Germen)
res <- residuals(model)
abs_res <- abs(res)
# Determine outlier threshold (mean + 2*SD)
threshold <- mean(abs_res) + 2 * sd(abs_res)
# Identify outlier observations
all_outliers <- which(abs_res > threshold)
# Create dataset excluding outliers
DATA_no_outliers <- DATA_Germen[-all_outliers, ]
# Fit the model without outliers
model_no_outliers <- lmer(Variable ~ Group * Time + Age + Sex + Education + (1 | ID), data = DATA_no_outliers)
# Display model summary
summary(model_no_outliers)
```

1. **Results Summary for BDNF**

LMEM (Including Outliers):
Model formula: BDNF ~ Group * Time + Age + Sex + (1 | ID)
Sample size: 74 observations, 47 subjects
Significant effect: *Group2:Time2 interaction* (Estimate = 4120.44, p = 0.0208)
Model fit (REML): 1263.1

Outlier Detection: outliers by residuals: observations #10, 26, 30, 43

LMEM (Excluding Outliers):

Sample size: 71 observations, 46 subjects
Significant effect: *Group2:Time2 interaction* remains (Estimate = 3599.0, p = 0.04)
Estimates and SEs slightly changed but results are consistent
model fit (REML): 1203.5

Conclusion: Removing outliers does not substantially affect the main findings for BDNF. Considering the physiological relevance of these outliers and the limited sample size, they were retained in the final analysis.

2. **Results Summary for CTSB**

LMEM (Including Outliers):
Model formula: CTSB ~ Group * Time + Age + Sex + (1 | ID)
Sample size: 78 observations, 47 subjects
No significant fixed effects observed (all p > 0.14)
Model fit (REML): 1213.4

Outlier Detection: outliers by residuals: observations #18, 20, 29, 45

LMEM (Excluding Outliers):
Sample size: 74 observations, 47 subjects
No significant fixed effects (all p > 0.3)
Estimates and SEs slightly changed but overall consistent results
model fit (REML): 1147.2

Conclusion: Excluding outliers did not affect the results for CTSB. No significant Group, Time, or interaction effects were found either with or without outliers. Given the physiological relevance of outliers and the limited sample size, they were retained in the final analysis

3. **Results for Simon Effect**

LMEM (Including Outliers):
Sample size: 78 observations, 47 subjects
Significant fixed effects: Time2 (p < 0.001), Sex1 (p = 0.0086)
Model fit (REML): 654.7 (approximate, if you want I can check exact)

Outlier Detection: outliers by residuals: observations #22, 30, 50

LMEM (Excluding Outliers):
Sample size: 75 observations, 47 subjects
Significant fixed effects: Time2 (p < 0.001), Sex1 (p = 0.0086)
Estimates and SEs slightly changed but overall consistent results
Model fit (REML): 647.4

Conclusion: Excluding outliers did not substantially affect the results for Simon Effect. Significant effects of Time2 and Sex1 remained stable. Given the physiological relevance of outliers and the limited sample size, they were retained in the final analysis.

4. **Results for Conflict Effect**

LMEM (Including Outliers):
Sample size: 78 observations, 47 subjects
Significant fixed effects: Intercept (p = 0.0075), Group1 (p = 0.0266), Group2 (p = 0.0239), Age (p = 0.0043), Sex1 (p = 0.0256)
Model fit: 457.1

Outlier Detection: outliers by residuals: observations #39, 57, 58

LMEM (Excluding Outliers):
Sample size: 75 observations, 45 subjects
Significant fixed effects: Intercept (p = 0.0083), Group1 (p = 0.025), Group2 (p = 0.024), Age (p = 0.0047), Sex1 (p = 0.037)
Estimates and SEs slightly changed but overall consistent results
Model fit (REML): 440.4

Conclusion: Excluding outliers did not change the main findings. The significant effects of Group, Age, and Sex on Conflict Effect remain consistent. Given the physiological relevance of outliers and the limited sample size, retaining them in the analysis is reasonable.

5. **N-back accuracy**

LMEM (Including Outliers):
Sample size: 76 observations, 46 subjects
Significant fixed effects: Time2 (p = 0.037); Age (p = 0.022)
No significant effects for Group, Sex, Education, or interactions
Model fit (REML): 564.3

Outlier Detection: outliers by residuals: observations #30, 41, 42, 44, 51

LMEM (Excluding Outliers):
Sample size: 73 observations, 45 subjects
Significant fixed effects: Time2 (p = 0.041); Age (p = 0.026)
No significant effects for Group, Sex, Education, or interactions
Estimates and SEs slightly changed but overall consistent results
Model fit (REML): 543

Conclusion: Excluding outliers did not substantially affect the results for accuracy. Significant effects of Time2 and Age remained stable. Given the physiological relevance of outliers and the limited sample size, they were retained in the final analysis.

6. **N-back Reaction times**

LMEM (Including Outliers):
Sample size: 76 observations, 46 subjects
No significant fixed effects observed (all $p > 0.20$)
Model fit (REML): 887

Outlier Detection: outliers by residuals: observations #13, 21, 23, 24, 63, 64

LMEM (Excluding Outliers):
Sample size: 70 observations, 43 subjects
No significant fixed effects observed (all $p > 0.26$)
Estimates and SEs slightly changed but overall consistent results
Model fit (REML): 811.5

Conclusion: Excluding outliers did not substantially affect the results for reaction times No significant effects of Group, Time, or their interaction were found either with or without outliers. Given the physiological relevance of outliers and limited sample size, they were retained in the final analysis.