

## Supplemental Digital Content 2. Results of Mixed Effects Model from 4.5 to 6.5 Hours

| Outcome               | Parameter                   | Coefficient | 95% CI           | <i>P</i> Value† |
|-----------------------|-----------------------------|-------------|------------------|-----------------|
| NRS                   | Intercept                   | 11.148      | 10.174 to 12.121 |                 |
|                       | Dose, low                   | 0.825       | 0.632 to 1.019   | <0.001          |
|                       | Time, per minute after 4.5h | -0.020      | -0.023 to -0.018 | <0.001          |
|                       | Session, 2 <sup>nd</sup>    | -0.394      | -0.587 to -0.200 | <0.001          |
|                       | Order, low 1 <sup>st</sup>  | 0.082       | -0.660 to 0.824  | 0.821           |
| Log Hyperalgesia Area | Intercept                   | 3.866       | 3.065 to 4.666   |                 |
|                       | Dose, low                   | -0.305      | -0.444 to -0.166 | <0.001          |
|                       | Time, per minute after 4.5h | -0.001      | -0.003 to 0.001  | 0.432           |
|                       | Session, 2 <sup>nd</sup>    | -0.427      | -0.566 to -0.288 | <0.001          |
|                       | Order, low 1 <sup>st</sup>  | 0.169       | -0.345 to 0.683  | 0.502           |
| Log Allodynia Area    | Intercept                   | 3.097       | 1.950 to 4.243   |                 |
|                       | Dose, low                   | -0.040      | -0.235 to 0.154  | 0.682           |
|                       | Time, per minute after 4.5h | -0.004      | -0.007 to -0.001 | 0.010           |
|                       | Session, 2 <sup>nd</sup>    | -0.310      | -0.505 to -0.116 | 0.002           |
|                       | Order, low 1 <sup>st</sup>  | 0.513       | -0.282 to 1.307  | 0.194           |
| Log CPP Threshold     | Intercept                   | 3.412       | 2.518 to 4.306   |                 |
|                       | Dose, low                   | -0.430      | -0.563 to -0.297 | <0.001          |
|                       | Time, per minute after 4.5h | 0.000       | -0.001 to 0.001  | 0.876           |
|                       | Session, 2 <sup>nd</sup>    | 0.366       | 0.233 to 0.498   | <0.001          |
|                       | Order, low 1 <sup>st</sup>  | -0.110      | -0.976 to 0.756  | 0.795           |
| Log CPP Tolerance     | Intercept                   | 4.687       | 3.887 to 5.488   |                 |
|                       | Dose, low                   | -0.325      | -0.434 to -0.217 | <0.001          |
|                       | Time, per minute after 4.5h | -0.001      | -0.002 to 0.001  | 0.283           |
|                       | Session, 2 <sup>nd</sup>    | 0.161       | 0.053 to 0.270   | 0.004           |
|                       | Order, low 1 <sup>st</sup>  | -0.208      | -1.051 to 0.635  | 0.614           |

† *P* values have been a topic of debate in mixed effects models. While we recommend using the 95% CI as the sole assessment, for those who would like *P* values, these have been included by ANOVA using a likelihood ratio test comparing a model with vs. without the examined parameter.

CI = confidence interval, CPP = cold pressor pain; NRS = numerical rating scale.