02b - Longitudinal Analysis of Cannabis-related Temperatures (IP Administration)

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IP Administration Model - July

Chronic effects of cannabis

For this analysis, I compared the temperature at during the 'predose' window across dosage groups using time in days as a continuous covariate. Data from dosing days and non-dosing days were included since we are only looking at the predose window.

Two-Way ANOVA Results

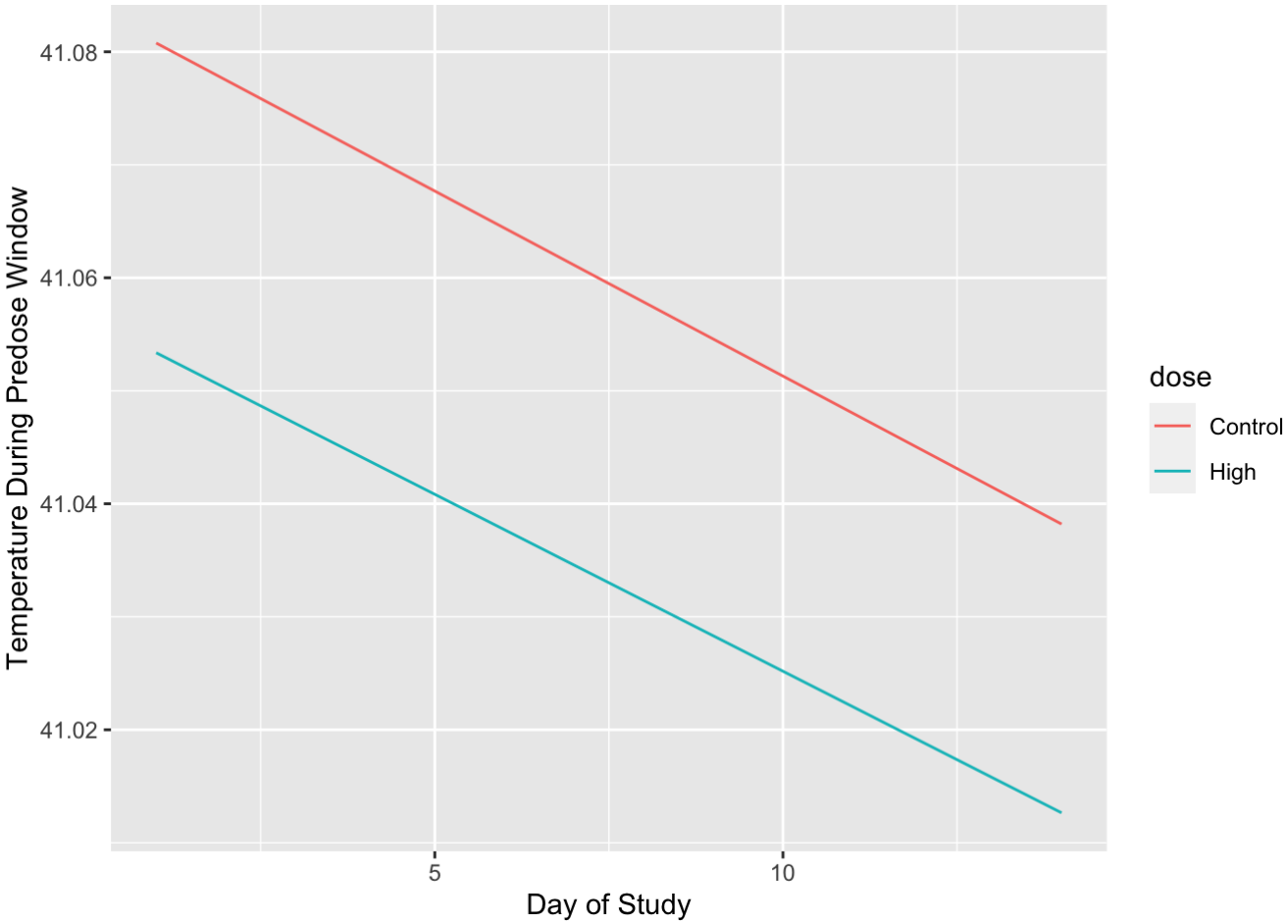
	Sum Sq	Mean Sq	NumDF	DenDF	F value	Pr(>F)
dose	0.0003292	0.0003292	1	1.418617	2.7894944	0.2844948
study_day	0.0062251	0.0062251	1	37.000000	52.7557048	0.0000000
dose:study_day	0.0000031	0.0000031	1	37.000000	0.0262312	0.8722182

Comparing Slopes, i.e., study day trends, across dosage groups

dose	study_day.trend	SE	df	lower.CL	upper.CL
Control	-0.0032747	0.0007202	37	-0.0047340	-0.0018155
High	-0.0031319	0.0005093	37	-0.0041637	-0.0021000

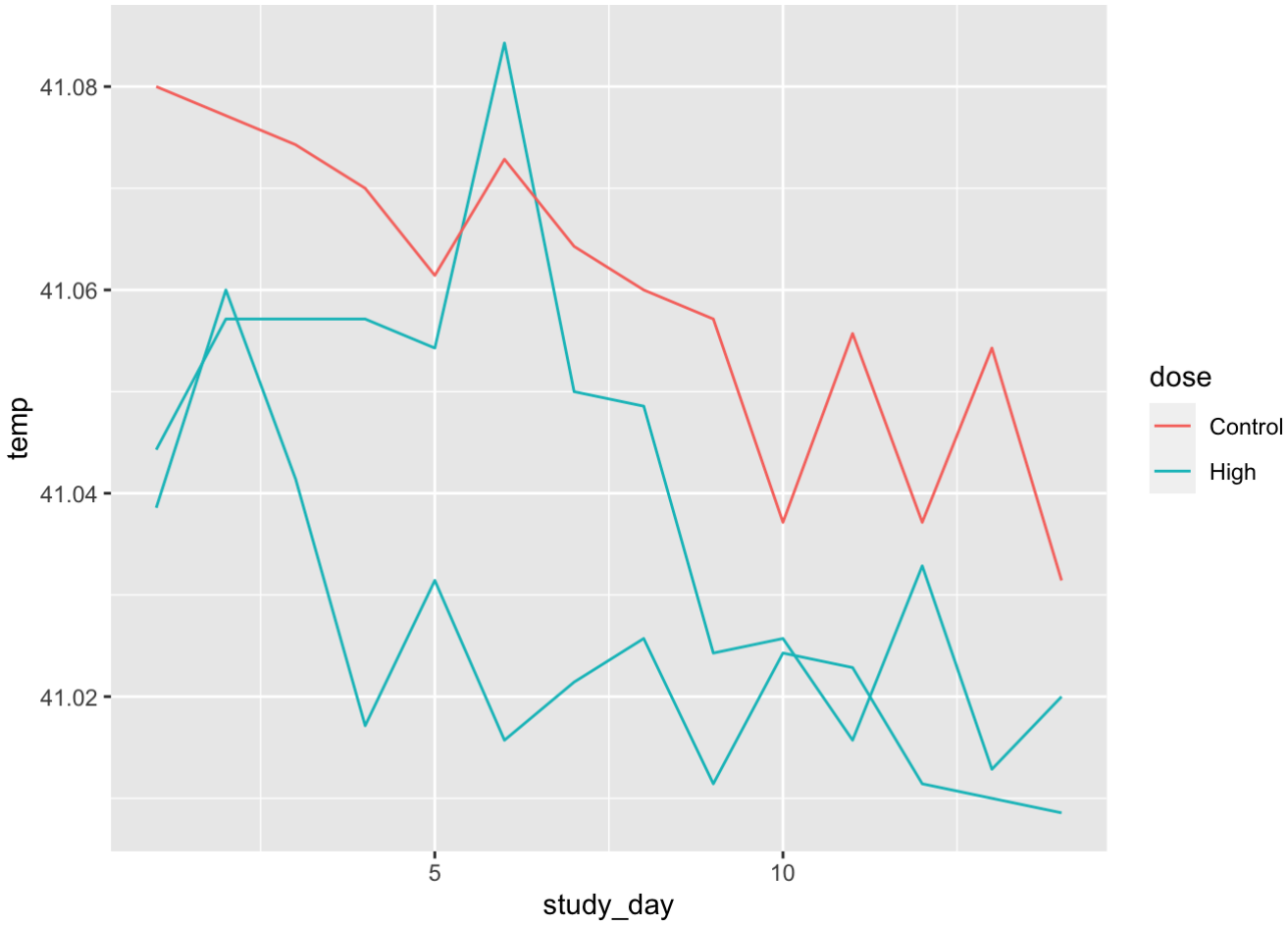
contrast	estimate	SE	df	t.ratio	p.value
Control - High	-0.0001429	0.000882	37	-0.1619605	0.8722182

Model-based dose group estimates



Observed data

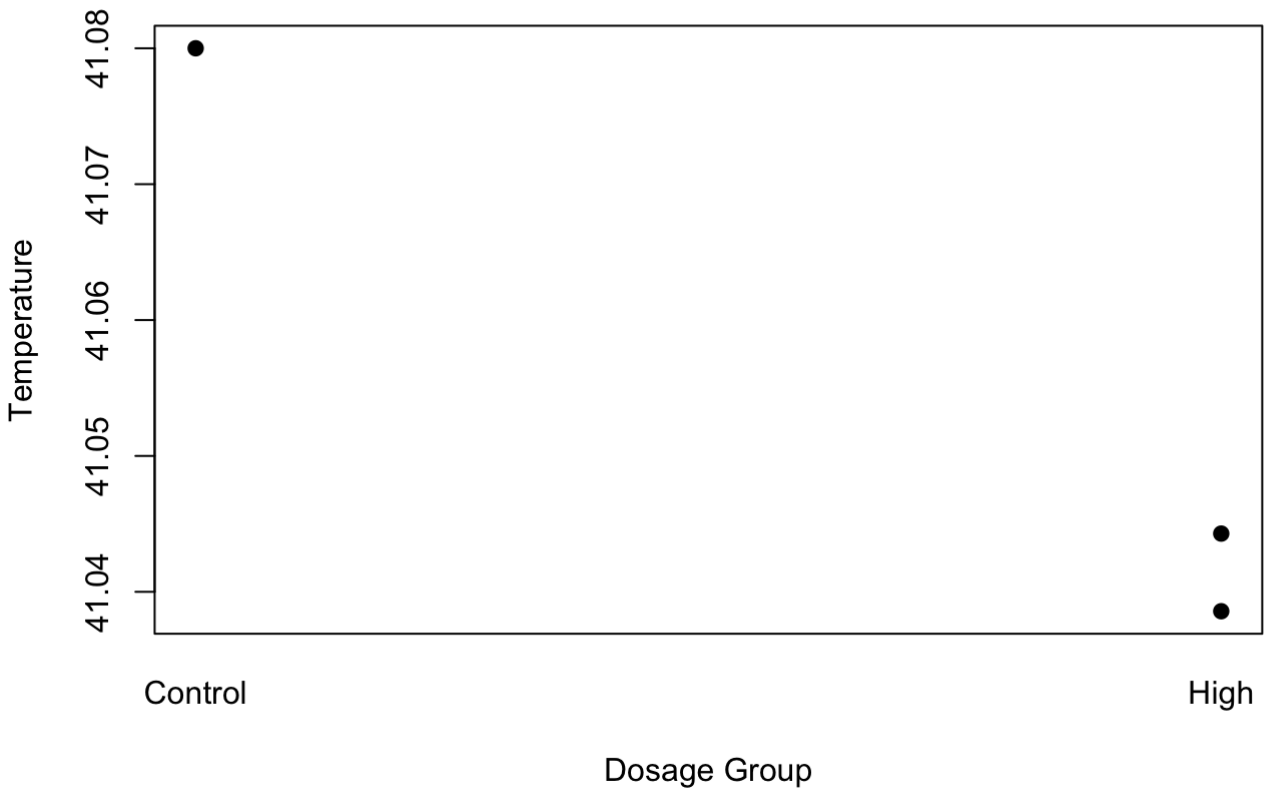
Each line represents an individual mice.



Based on my understanding of the study design, the 2 dosage groups should not differ in temperature at day 1 during the predose window because none of the animals would have received any cannabis prior to that time point.

Since this graphic made it look like the dosage groups differed at day 1, I tested that directly.

Omnibus p-value for dosage effect: 0.081



contrast	estimate	SE	df	t.ratio	p.value
Control - High	0.0385714	0.0049487	1	7.794237	0.0812345

Acute Effects of Cannabis on Temperature

To examine the acute effects (i.e., within a treatment day) of cannabis, data points were limited to those collected during a ‘dose’ day.

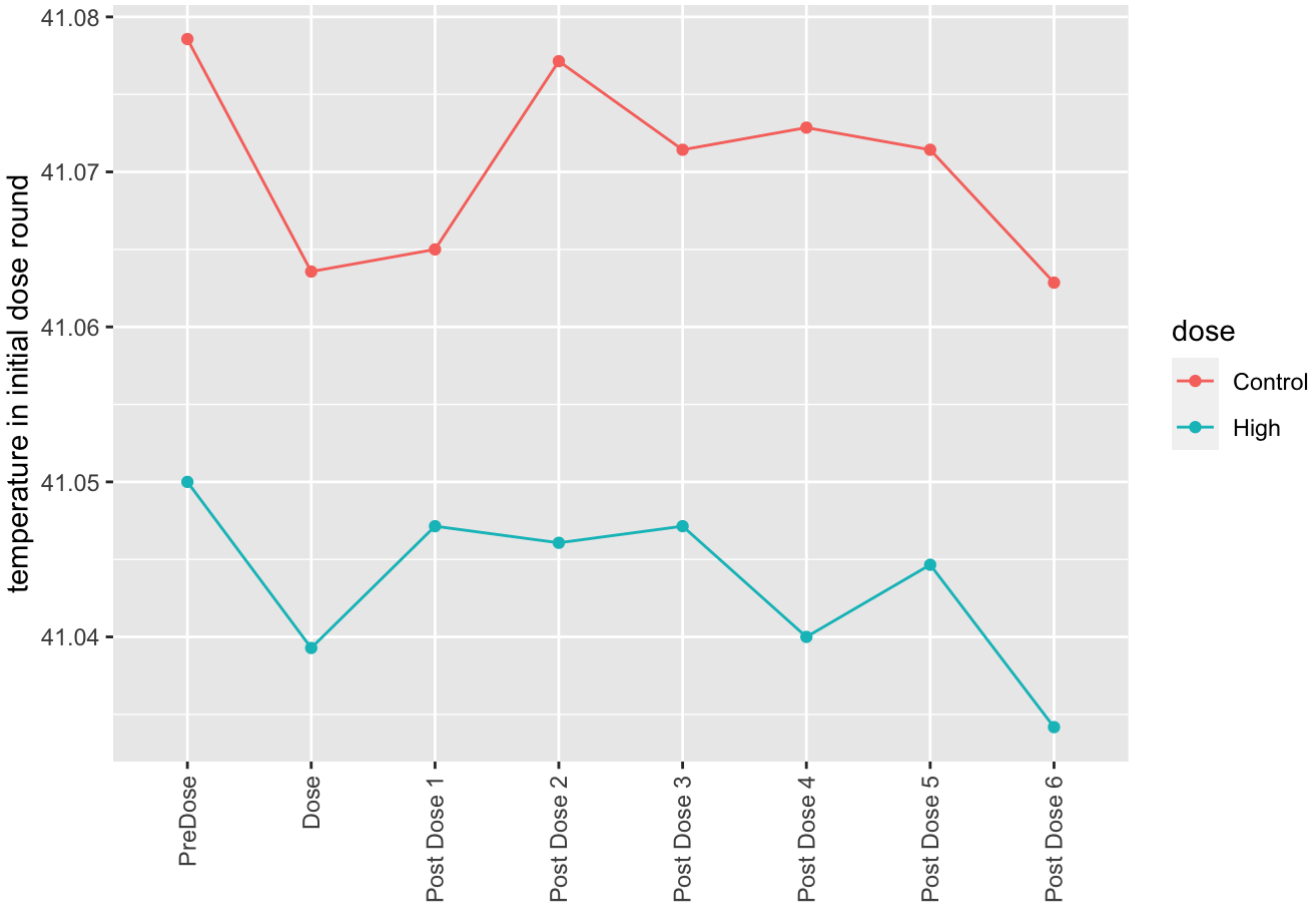
Initial Acute Effect of Cannabis on Temperature

First, the initial acute effects of cannabis were assessed by only focusing on changes in temperature across different windows of time on the first study day that mice were exposed to cannabis

Two-Way ANOVA Results

	Sum Sq	Mean Sq	NumDF	DenDF	F value	Pr(>F)
dose	0.0017403	0.0017403	1	0.972474	13.7286328	0.1733375
time_window	0.0009455	0.0001351	7	29.013771	1.0655797	0.4098024
dose:time_window	0.0002051	0.0000293	7	29.013771	0.2311722	0.9742878

There were no significant differences based on time window.



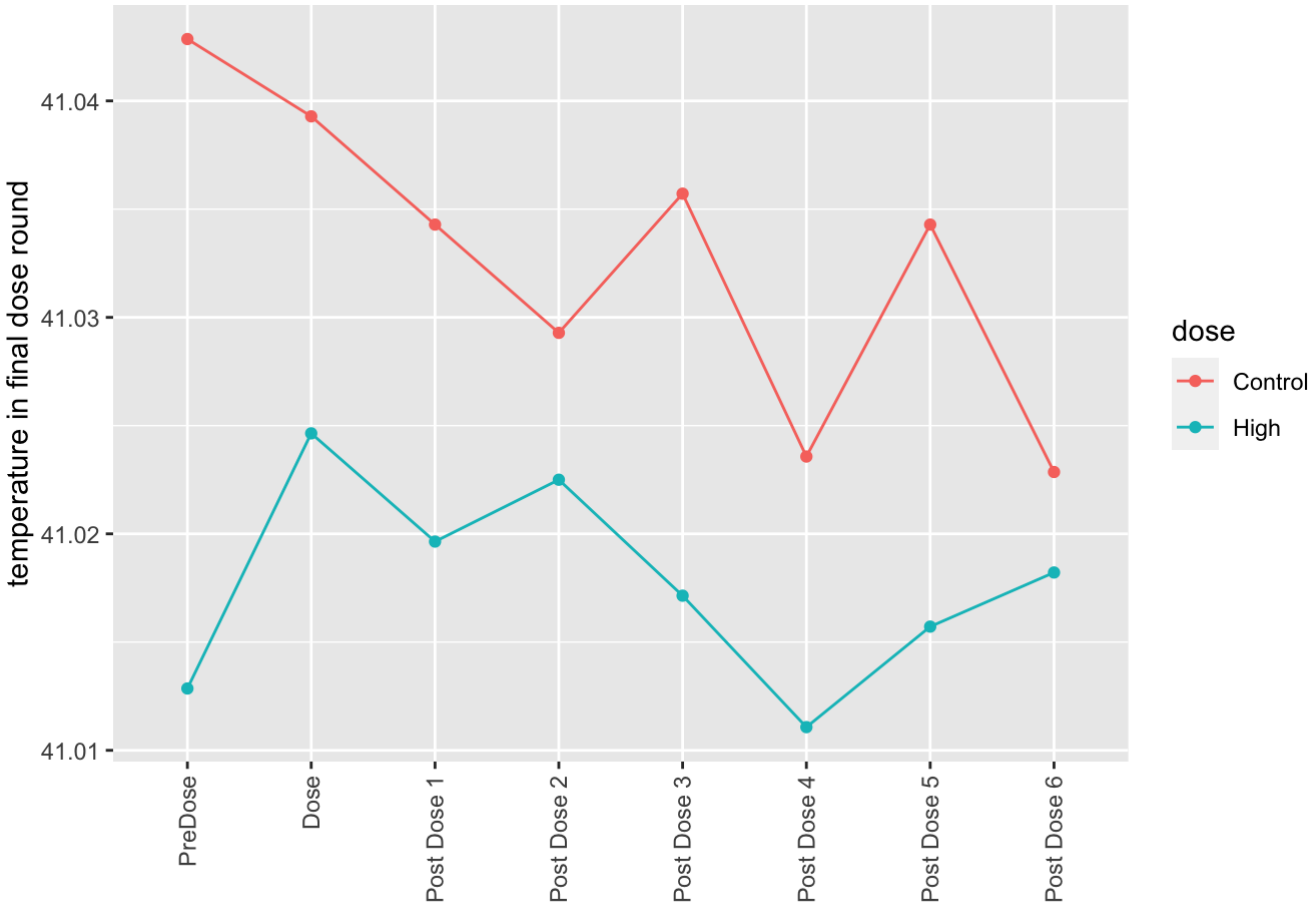
Acute Effect of Cannabis on Temperature After Chronic Exposure to Cannabis

Two-Way ANOVA Results

	Sum Sq	Mean Sq	NumDF	DenDF	F value	Pr(>F)
dose	0.0006973	0.0006973	1	0.9999998	5.2396303	0.2622106
time_window	0.0007561	0.0001080	7	31.0000001	0.8116573	0.5844739
dose:time_window	0.0005757	0.0000822	7	31.0000001	0.6179564	0.7369058

There were no significant differences based on time window.

Time Window Effect in Last Round of Dose Stratified by Dose



IP Administration Model - January

Please note that there are no control mice for IP administration in the January experiment.

Chronic effects of cannabis

For this analysis, I compared the temperature at during the 'predose' window across dosage groups using time in days as a continuous covariate. Data from dosing days and non-dosing days were included since we are only looking at the predose window.

Two-Way ANOVA Results

	Sum Sq	Mean Sq	NumDF	DenDF	F value	Pr(>F)
dose	1.268425	0.6342123	2	12.50017	5.449289	0.0198723
study_day	4.553008	4.5530083	1	52.00000	39.120432	0.0000001
dose:study_day	1.252931	0.6264653	2	52.00000	5.382726	0.0075050

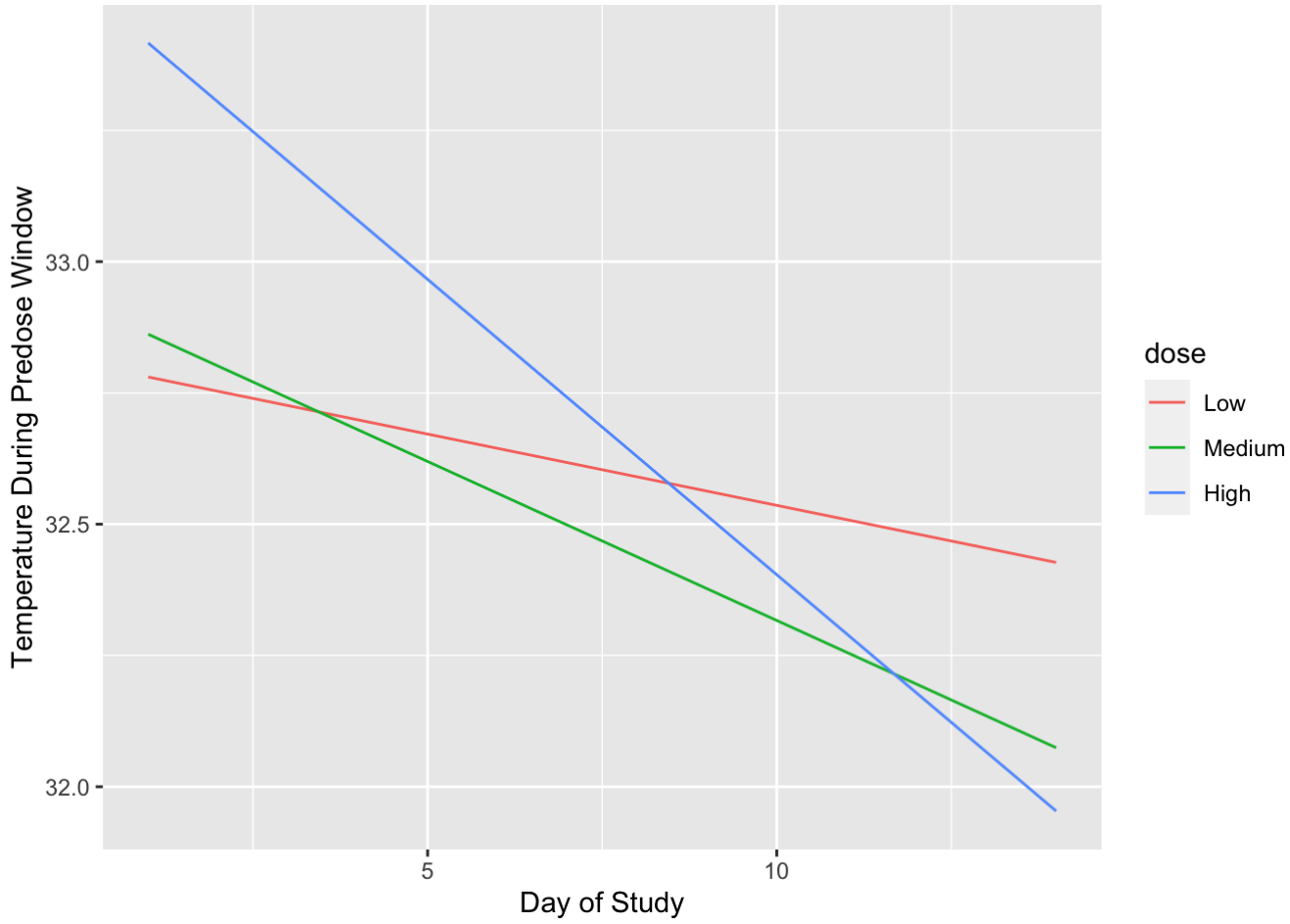
Comparing Slopes, i.e., study day trends, across dosage groups

dose	study_day.trend	SE	df	lower.CL	upper.CL
Low	-0.0271743	0.022643	52	-0.0726109	0.0182622

dose	study_day.trend	SE	df	lower.CL	upper.CL
Medium	-0.0605821	0.016011	52	-0.0927106	-0.0284536
High	-0.1125299	0.016011	52	-0.1446584	-0.0804014

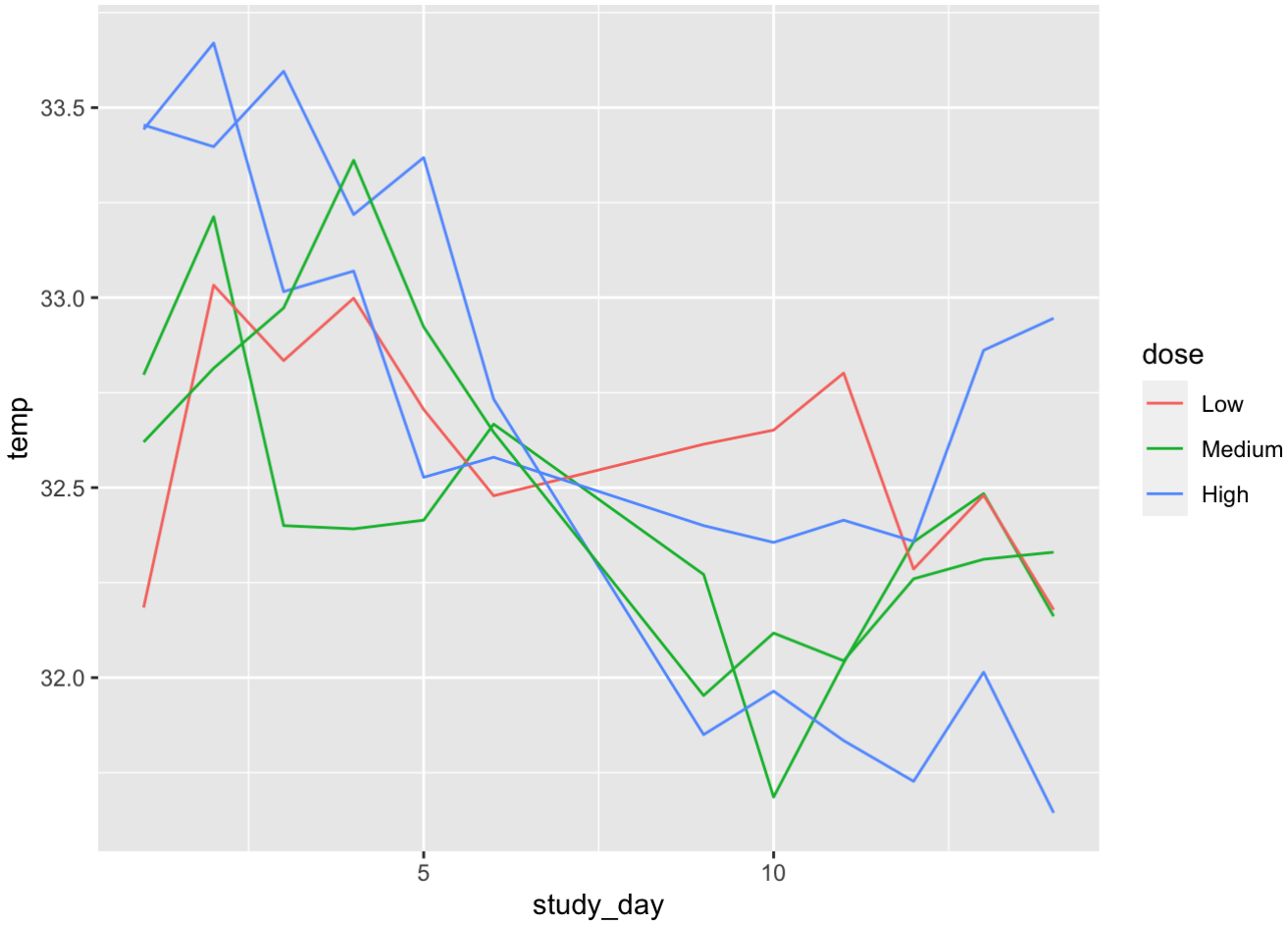
contrast	estimate	SE	df	t.ratio	p.value
Low - Medium	0.0334078	0.0277319	52	1.204669	0.4558066
Low - High	0.0853556	0.0277319	52	3.077881	0.0091674
Medium - High	0.0519478	0.0226430	52	2.294206	0.0655045

Model-based dose group estimates



Observed data

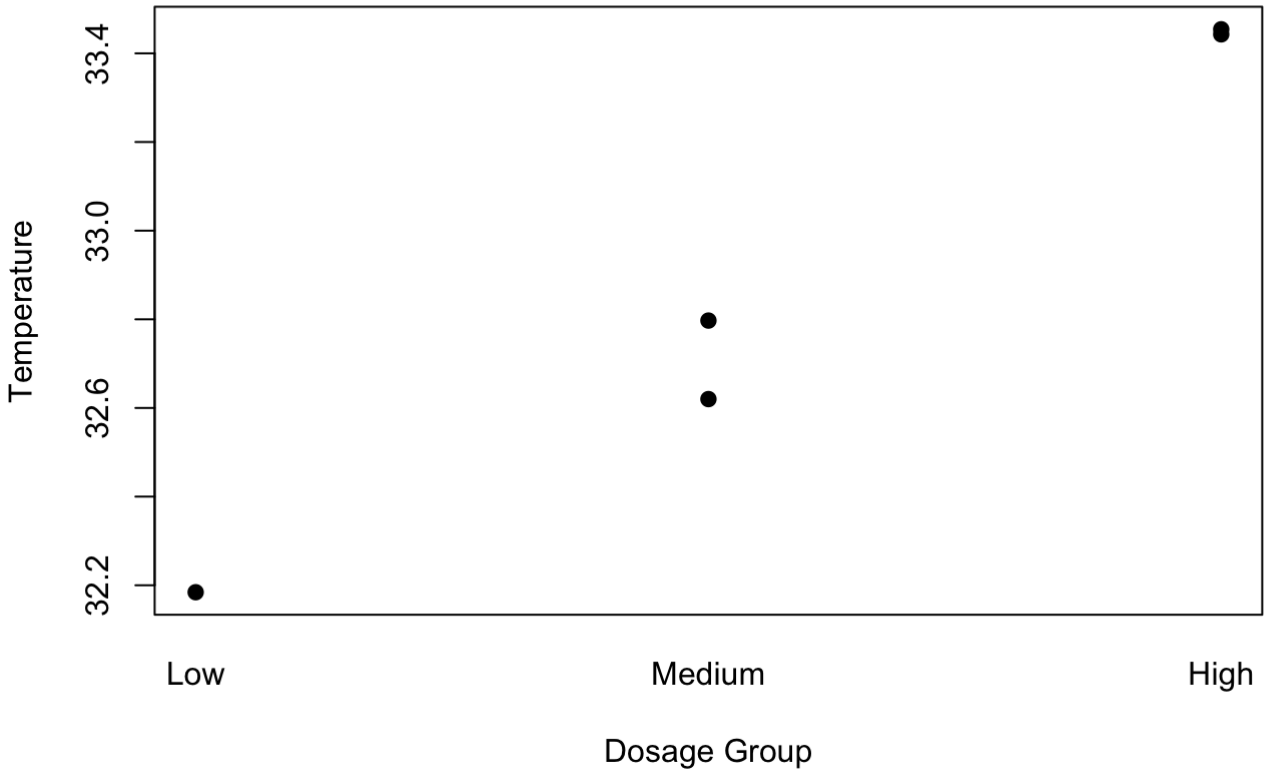
Each line represents an individual mice.



Based on my understanding of the study design, the 3 dosage groups should not differ in temperature at day 1 during the predose window because none of the animals would have received any cannabis prior to that time point.

Since this graphic made it look like the dosage groups differed at day 1, I tested that directly.

Omnibus p-value for dosage effect: 0.013



There are significant differences in starting temperature between the three dose levels.

contrast	estimate	SE	df	t.ratio	p.value
Low - Medium	-0.5242857	0.1087029	2	-4.823106	0.0727858
Low - High	-1.2642857	0.1087029	2	-11.630650	0.0133246
Medium - High	-0.7400000	0.0887556	2	-8.337505	0.0256049

Acute Effects of Cannabis on Temperature

To examine the acute effects (i.e., within a treatment day) of cannabis, data points were limited to those collected during a ‘dose’ day.

Initial Acute Effect of Cannabis on Temperature

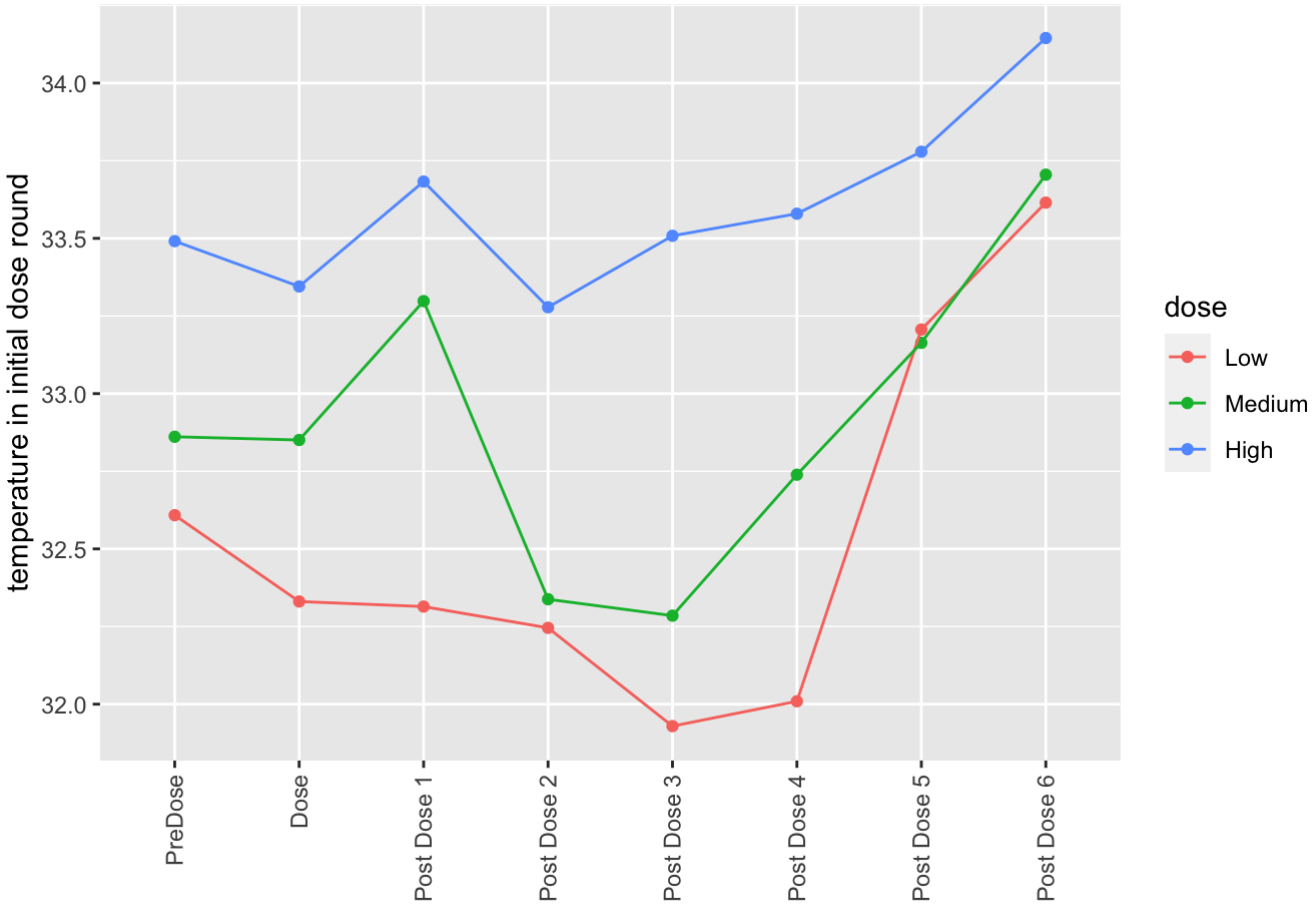
First, the initial acute effects of cannabis were assessed by only focusing on changes in temperature across different windows of time on the first study day that mice were exposed to cannabis

Two-Way ANOVA Results

	Sum Sq	Mean Sq	NumDF	DenDF	F value	Pr(>F)
dose	11.26076	5.6303782	2	2	30.928498	0.0313200

	Sum Sq	Mean Sq	NumDF	DenDF	F value	Pr(>F)
time_window	11.07705	1.5824353	7	54	8.692550	0.0000004
dose:time_window	2.55176	0.1822686	14	54	1.001228	0.4655373

There were significant main effects of both dose and time window, but the interaction effect was not significant.



contrast	dose	estimate	SE	df	t.ratio	p.value
Dose - PreDose	Low	-0.2779464	0.4266673	54	-0.6514360	0.5175280
Post Dose 1 - PreDose	Low	-0.2942857	0.4266673	54	-0.6897311	0.4933169
Post Dose 2 - PreDose	Low	-0.3628571	0.4266673	54	-0.8504451	0.3988329
Post Dose 3 - PreDose	Low	-0.6792857	0.4266673	54	-1.5920735	0.1172058
Post Dose 4 - PreDose	Low	-0.5992857	0.4266673	54	-1.4045738	0.1658742
Post Dose 5 - PreDose	Low	0.5978571	0.4266673	54	1.4012256	0.1668678
Post Dose 6 - PreDose	Low	1.0064286	0.4266673	54	2.3588134	0.0219817

contrast	dose	estimate	SE	df	t.ratio	p.value
Dose - PreDose	Medium	-0.0104018	0.3016993	54	-0.0344773	0.9726237
Post Dose 1 - PreDose	Medium	0.4367857	0.3016993	54	1.4477516	0.1534678
Post Dose 2 - PreDose	Medium	-0.5232143	0.3016993	54	-1.7342241	0.0885842
Post Dose 3 - PreDose	Medium	-0.5760714	0.3016993	54	-1.9094222	0.0615265
Post Dose 4 - PreDose	Medium	-0.1221429	0.3016993	54	-0.4048496	0.6871874
Post Dose 5 - PreDose	Medium	0.3025000	0.3016993	54	1.0026538	0.3204998
Post Dose 6 - PreDose	Medium	0.8439286	0.3016993	54	2.7972502	0.0071275

contrast	dose	estimate	SE	df	t.ratio	p.value
Dose - PreDose	High	-0.1459375	0.3016993	54	-0.4837183	0.6305416
Post Dose 1 - PreDose	High	0.1917857	0.3016993	54	0.6356849	0.5276668
Post Dose 2 - PreDose	High	-0.2128571	0.3016993	54	-0.7055274	0.4835146
Post Dose 3 - PreDose	High	0.0171429	0.3016993	54	0.0568210	0.9548975
Post Dose 4 - PreDose	High	0.0882143	0.3016993	54	0.2923914	0.7711079
Post Dose 5 - PreDose	High	0.2878571	0.3016993	54	0.9541192	0.3442750
Post Dose 6 - PreDose	High	0.6539286	0.3016993	54	2.1674842	0.0346259

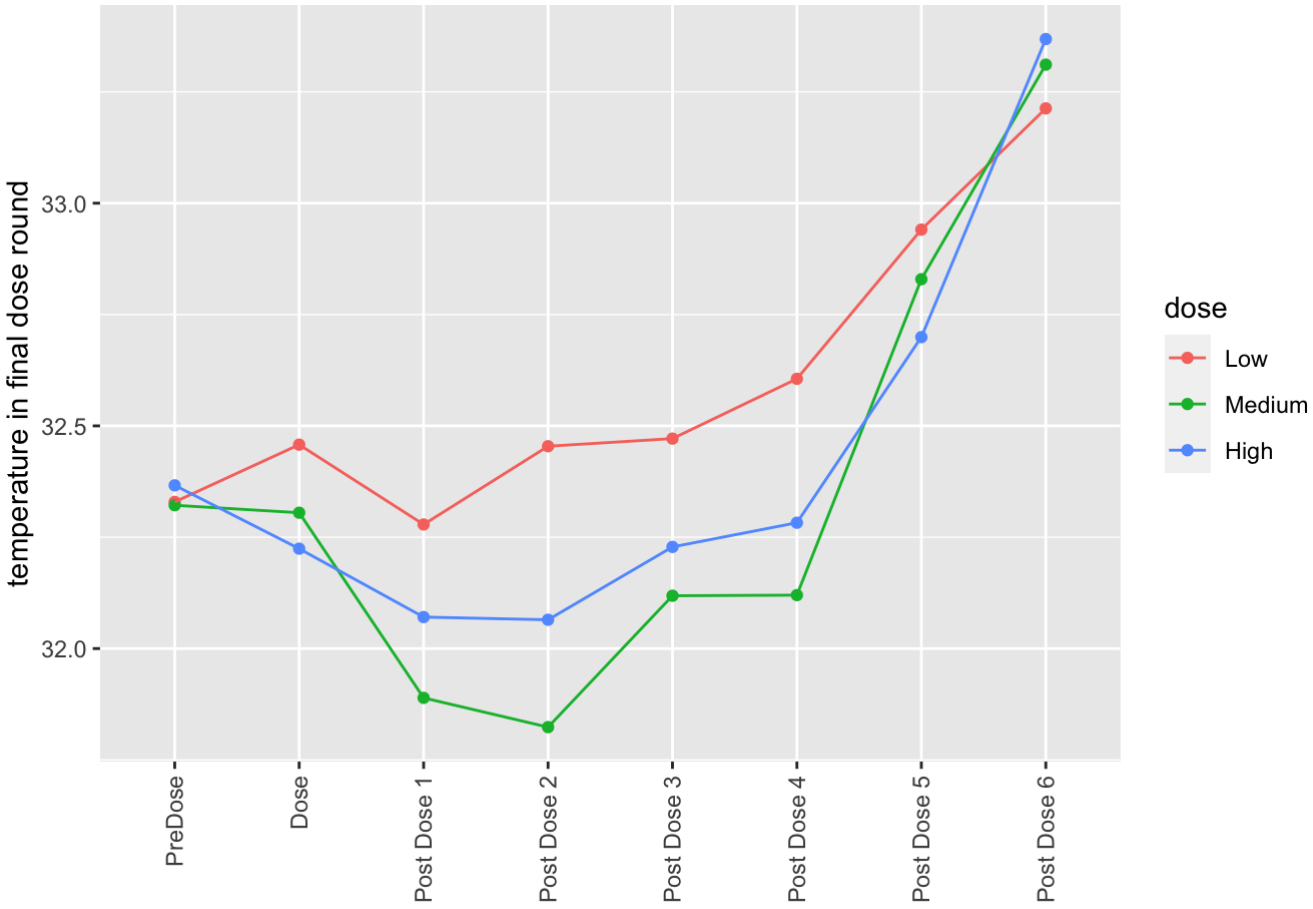
Acute Effect of Cannabis on Temperature After Chronic Exposure to Cannabis

Two-Way ANOVA Results

	Sum Sq	Mean Sq	NumDF	DenDF	F value	Pr(>F)
dose	0.0209838	0.0104919	2	2	0.1066663	0.9036148
time_window	10.6091850	1.5155979	7	54	15.4083961	0.0000000
dose:time_window	0.7242059	0.0517290	14	54	0.5259052	0.9070458

The two-way ANOVA results suggest that there are is a significant difference across time windows and that difference is consistent across dosage group.

Time Window Effect in Last Round of Dose Stratified by Dose



contrast	dose	estimate	SE	df	t.ratio	p.value
Dose - PreDose	Low	0.1285714	0.3136269	54	0.4099503	0.6834643
Post Dose 1 - PreDose	Low	-0.0507143	0.3136269	54	-0.1617026	0.8721436
Post Dose 2 - PreDose	Low	0.1250000	0.3136269	54	0.3985628	0.6917870
Post Dose 3 - PreDose	Low	0.1421429	0.3136269	54	0.4532228	0.6522043
Post Dose 4 - PreDose	Low	0.2764286	0.3136269	54	0.8813931	0.3820114
Post Dose 5 - PreDose	Low	0.6114286	0.3136269	54	1.9495414	0.0564319
Post Dose 6 - PreDose	Low	0.8835714	0.3136269	54	2.8172695	0.0067521

contrast	dose	estimate	SE	df	t.ratio	p.value
Dose - PreDose	Medium	-0.0167857	0.2217677	54	-0.0756905	0.9399450
Post Dose 1 - PreDose	Medium	-0.4325000	0.2217677	54	-1.9502390	0.0563466
Post Dose 2 - PreDose	Medium	-0.4982143	0.2217677	54	-2.2465594	0.0287792
Post Dose 3 - PreDose	Medium	-0.2032143	0.2217677	54	-0.9163385	0.3635636

contrast	dose	estimate	SE	df	t.ratio	p.value
Post Dose 4 - PreDose	Medium	-0.2017857	0.2217677	54	-0.9098968	0.3669205
Post Dose 5 - PreDose	Medium	0.5075000	0.2217677	54	2.2884307	0.0260518
Post Dose 6 - PreDose	Medium	0.9892857	0.2217677	54	4.4609100	0.0000418

contrast	dose	estimate	SE	df	t.ratio	p.value
Dose - PreDose	High	-0.1421429	0.2217677	54	-0.6409539	0.5242636
Post Dose 1 - PreDose	High	-0.2957143	0.2217677	54	-1.3334417	0.1879847
Post Dose 2 - PreDose	High	-0.3017857	0.2217677	54	-1.3608191	0.1792235
Post Dose 3 - PreDose	High	-0.1382143	0.2217677	54	-0.6232390	0.5357510
Post Dose 4 - PreDose	High	-0.0839286	0.2217677	54	-0.3784526	0.7065782
Post Dose 5 - PreDose	High	0.3328571	0.2217677	54	1.5009271	0.1391993
Post Dose 6 - PreDose	High	1.0021429	0.2217677	54	4.5188857	0.0000343