

02c - Longitudinal Analysis of Cannabis-related Temperatures (Gavage Administration)

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IP Administration Model - January

Please note that there are no control mice for gavage 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

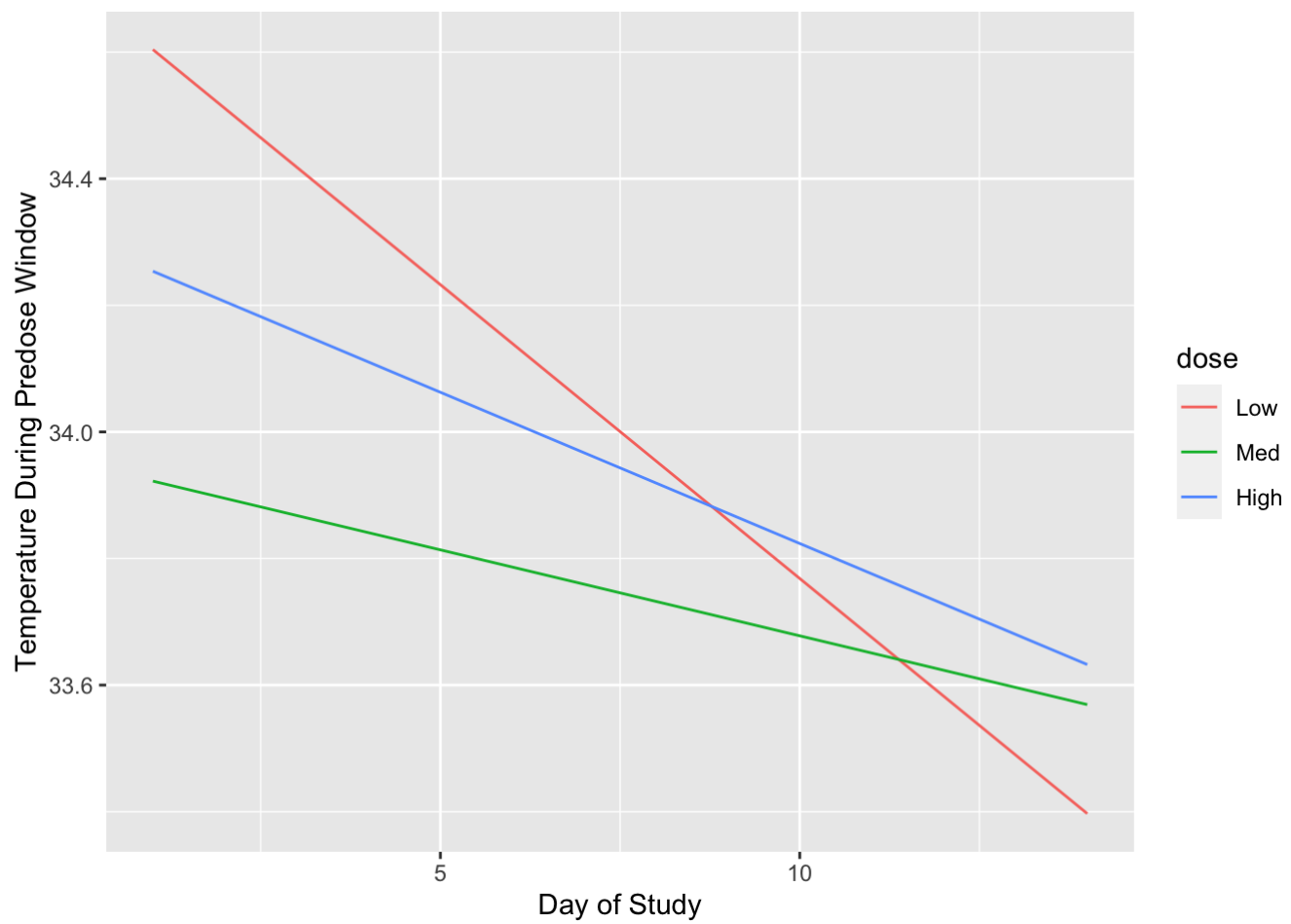
	Sum Sq	Mean Sq	NumDF	DenDF	F value	Pr(>F)
dose	0.0964646	0.0482323	2	3.273454	0.2879752	0.7669998
study_day	4.2620535	4.2620535	1	63.000000	25.4469595	0.0000041
dose:study_day	1.0249445	0.5124722	2	63.000000	3.0597598	0.0539268

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

dose	study_day.trend	SE	df	lower.CL	upper.CL
Low	-0.0928587	0.0192072	63	-0.1312412	-0.0544762
Med	-0.0271586	0.0192072	63	-0.0655411	0.0112239
High	-0.0478021	0.0192072	63	-0.0861846	-0.0094196

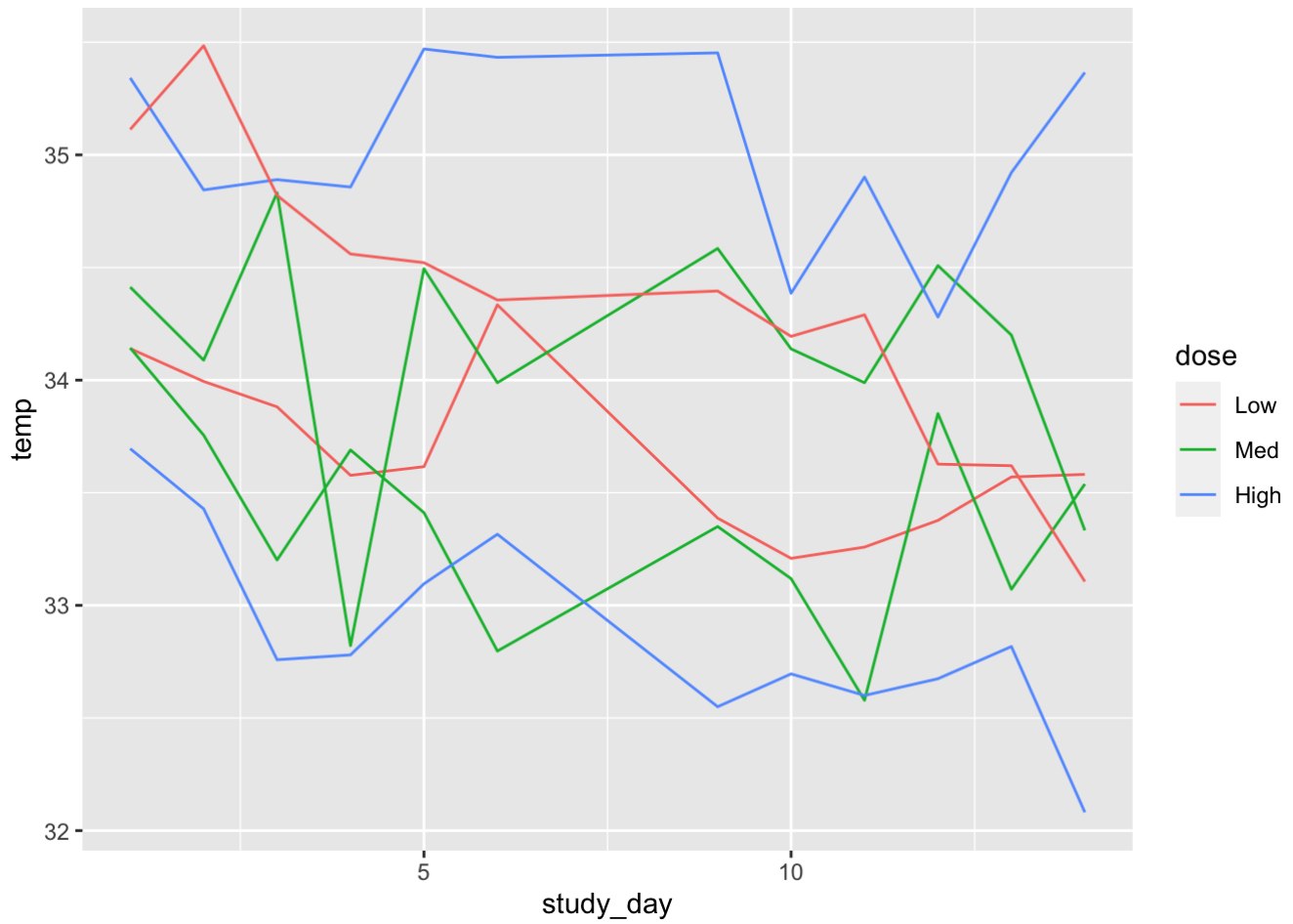
contrast	estimate	SE	df	t.ratio	p.value
Low - Med	-0.0657001	0.0271631	63	-2.4187313	0.0478686
Low - High	-0.0450566	0.0271631	63	-1.6587473	0.2291083
Med - High	0.0206435	0.0271631	63	0.7599841	0.7287348

Model-based dose group estimates



Observed data

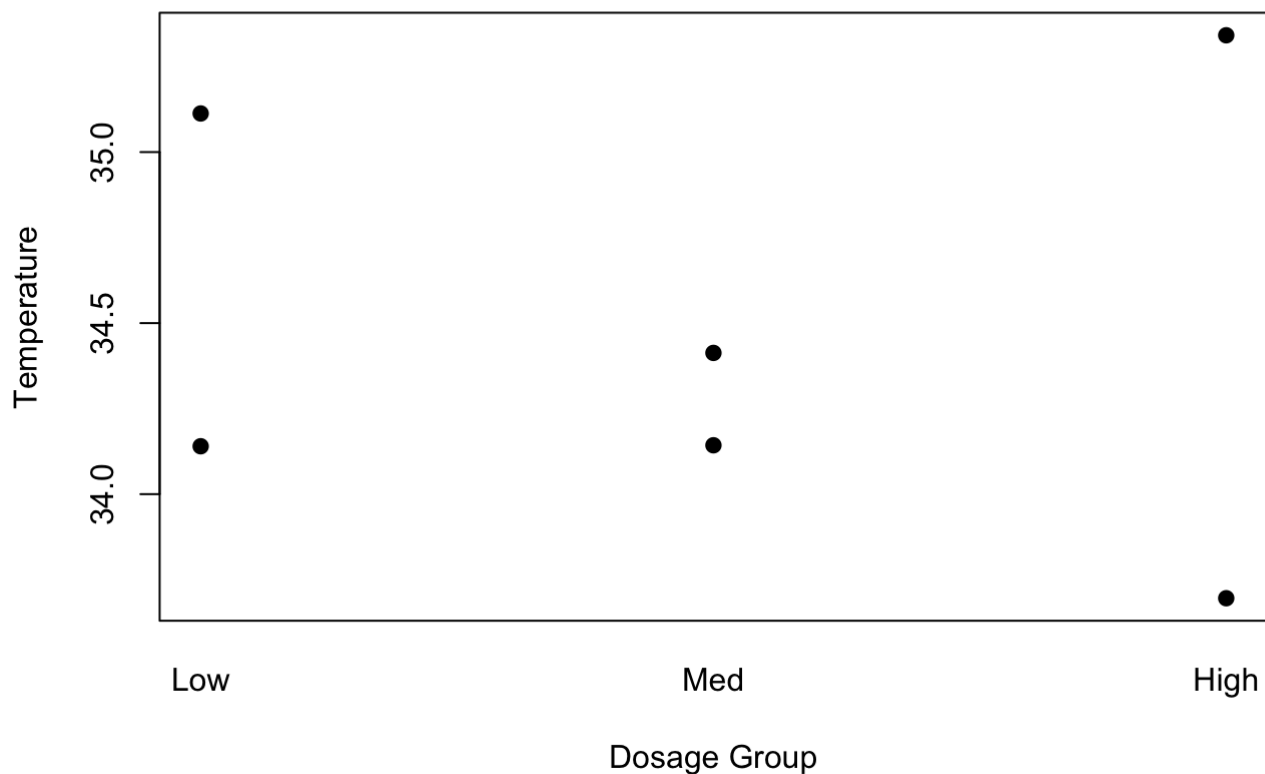
Each line represents an individual mice.



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: 0.906



There are no significant differences in starting temperature between the three dose levels.

contrast	estimate	SE	df	t.ratio	p.value
Low - Med	0.3485714	0.7882181	3	0.4422271	0.9011736
Low - High	0.1078571	0.7882181	3	0.1368367	0.9897655
Med - High	-0.2407143	0.7882181	3	-0.3053905	0.9507146

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

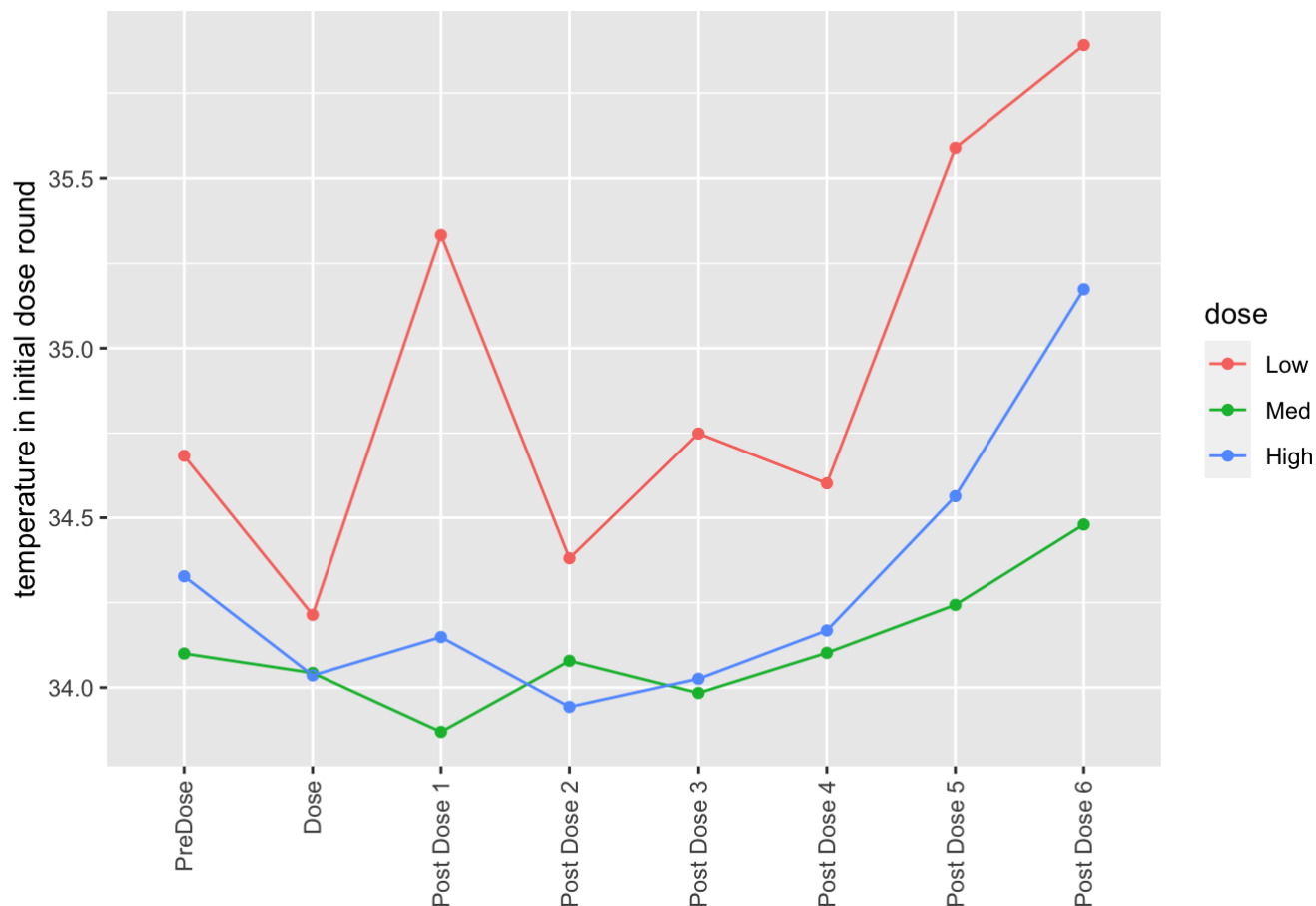
First, the initial acute effects of cannabis were assessed by only focusing on changes in temperature across different windows of time on the first study day that mice were exposed to cannabis

Two-Way ANOVA Results

	Sum Sq	Mean Sq	NumDF	DenDF	F value	Pr(>F)
dose	0.1328044	0.0664022	2	2.999999	0.4503222	0.6744929

	Sum Sq	Mean Sq	NumDF	DenDF	F value	Pr(>F)
time_window	11.4185381	1.6312197	7	69.000000	11.0625024	0.0000000
dose:time_window	4.2532917	0.3038066	14	69.000000	2.0603360	0.0251586

Based on the significant interaction effect, the model suggest that the effect of the within-day time window differs between doses.



contrast	dose	estimate	SE	df	t.ratio	p.value
Dose - PreDose	Low	-0.4689286	0.271528	69	-1.7269992	0.0886423
Post Dose 1 - PreDose	Low	0.6503571	0.271528	69	2.3951757	0.0193312
Post Dose 2 - PreDose	Low	-0.3021429	0.271528	69	-1.1127505	0.2696774
Post Dose 3 - PreDose	Low	0.0657143	0.271528	69	0.2420167	0.8094851
Post Dose 4 - PreDose	Low	-0.0814286	0.271528	69	-0.2998902	0.7651625
Post Dose 5 - PreDose	Low	0.9060714	0.271528	69	3.3369361	0.0013673
Post Dose 6 - PreDose	Low	1.2085714	0.271528	69	4.4510019	0.0000320

contrast	dose	estimate	SE	df	t.ratio	p.value
Dose - PreDose	Med	-0.0569643	0.271528	69	-0.2097916	0.8344485
Post Dose 1 - PreDose	Med	-0.2307143	0.271528	69	-0.8496889	0.3984367
Post Dose 2 - PreDose	Med	-0.0214286	0.271528	69	-0.0789185	0.9373259
Post Dose 3 - PreDose	Med	-0.1160714	0.271528	69	-0.4274751	0.6703645
Post Dose 4 - PreDose	Med	0.0021429	0.271528	69	0.0078918	0.9937261
Post Dose 5 - PreDose	Med	0.1432143	0.271528	69	0.5274385	0.5995811
Post Dose 6 - PreDose	Med	0.3800000	0.271528	69	1.3994876	0.1661466

contrast	dose	estimate	SE	df	t.ratio	p.value
Dose - PreDose	High	-0.2917857	0.271528	69	-1.0746065	0.2862944
Post Dose 1 - PreDose	High	-0.1789286	0.271528	69	-0.6589693	0.5121087
Post Dose 2 - PreDose	High	-0.3846429	0.271528	69	-1.4165866	0.1611029
Post Dose 3 - PreDose	High	-0.3017857	0.271528	69	-1.1114352	0.2702389
Post Dose 4 - PreDose	High	-0.1596429	0.271528	69	-0.5879426	0.5584902
Post Dose 5 - PreDose	High	0.2360714	0.271528	69	0.8694185	0.3876326
Post Dose 6 - PreDose	High	0.8460714	0.271528	69	3.1159644	0.0026715

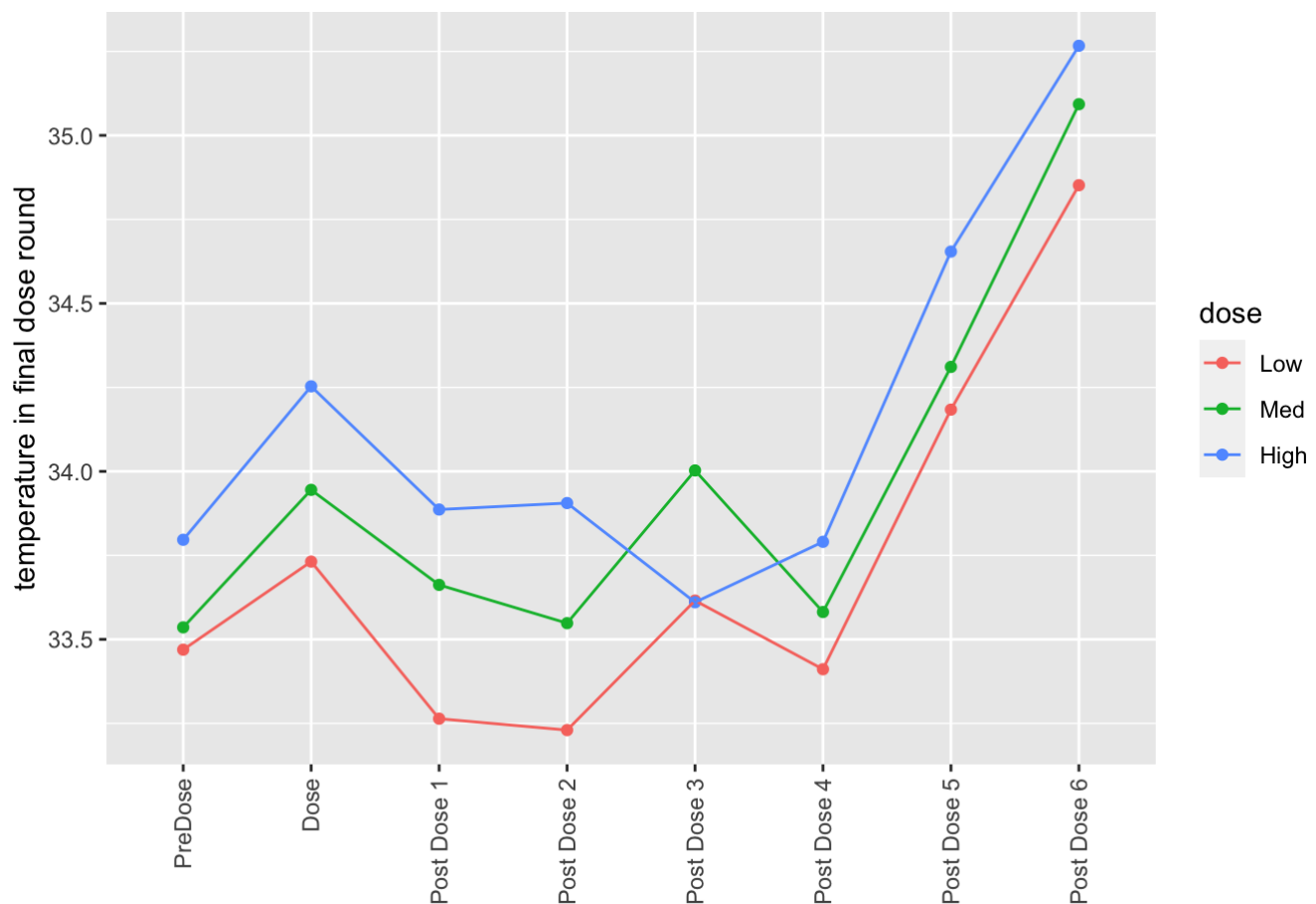
Acute Effect of Cannabis on Temperature After Chronic Exposure to Cannabis

Two-Way ANOVA Results

	Sum Sq	Mean Sq	NumDF	DenDF	F value	Pr(>F)
dose	0.0269399	0.0134699	2	3	0.0555393	0.9469246
time_window	24.0656917	3.4379560	7	69	14.1753985	0.0000000
dose:time_window	1.0969491	0.0783535	14	69	0.3230676	0.9889615

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	0.2621429	0.3482311	69	0.7527842	0.4541403
Post Dose 1 - PreDose	Low	-0.2053571	0.3482311	69	-0.5897152	0.5573078
Post Dose 2 - PreDose	Low	-0.2392857	0.3482311	69	-0.6871464	0.4942936
Post Dose 3 - PreDose	Low	0.1460714	0.3482311	69	0.4194670	0.6761780
Post Dose 4 - PreDose	Low	-0.0582143	0.3482311	69	-0.1671714	0.8677241
Post Dose 5 - PreDose	Low	0.7146429	0.3482311	69	2.0522088	0.0439453
Post Dose 6 - PreDose	Low	1.3825000	0.3482311	69	3.9700650	0.0001738

contrast	dose	estimate	SE	df	t.ratio	p.value
Dose - PreDose	Med	0.4092857	0.3482311	69	1.1753280	0.2439033
Post Dose 1 - PreDose	Med	0.1264286	0.3482311	69	0.3630594	0.7176704
Post Dose 2 - PreDose	Med	0.0125000	0.3482311	69	0.0358957	0.9714692
Post Dose 3 - PreDose	Med	0.4671429	0.3482311	69	1.3414738	0.1841653

contrast	dose	estimate	SE	df	t.ratio	p.value
Post Dose 4 - PreDose	Med	0.0457143	0.3482311	69	0.1312757	0.8959392
Post Dose 5 - PreDose	Med	0.7753571	0.3482311	69	2.2265593	0.0292439
Post Dose 6 - PreDose	Med	1.5571429	0.3482311	69	4.4715793	0.0000297

contrast	dose	estimate	SE	df	t.ratio	p.value
Dose - PreDose	High	0.4567857	0.3482311	69	1.3117316	0.1939584
Post Dose 1 - PreDose	High	0.0900000	0.3482311	69	0.2584491	0.7968297
Post Dose 2 - PreDose	High	0.1092857	0.3482311	69	0.3138310	0.7545962
Post Dose 3 - PreDose	High	-0.1860714	0.3482311	69	-0.5343332	0.5948285
Post Dose 4 - PreDose	High	-0.0060714	0.3482311	69	-0.0174351	0.9861399
Post Dose 5 - PreDose	High	0.8578571	0.3482311	69	2.4634710	0.0162576
Post Dose 6 - PreDose	High	1.4703571	0.3482311	69	4.2223606	0.0000725