UCLA

Statistics 101B

Lifestyle Activities and their Effects on Physical and Mental Flu Recovery

Author
Emily Alendorf
Author
Jieyi Wang

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Abstract

Recent mental health research has shown there is room to understand the connection between mindfullness, mental health, and physical health. We pursued this relationship by studying simulated Island inhabitants as they recovered from the Flu and performed lifestyle activities such as running, petting a dog, or recalling happy memories. We measured their physical recovery through white blood cell count and their happiness or emotional recovery through serotonin and dopamine levels. We found significant effects on white blood cell count depends on whether you consider participants as random effects or fixed effects. We found Sex strongly predicts serotonin levels, and dopamine is significantly related to lifestyle activities, particularly running and happy memories. There was no significant effect of repeated measures for any of the response variables.

Introduction and Research Background

Given the current global health crisis from COVID-19, it has become increasingly interesting to investigate what factors influence the human body's healing process. Specifically, are there non-biological factors–such as lifestyle choices–that can influence the healing process?

Our main inspiration was a 2013 paper by Chidi N. Obasi et al.[1] which found meditation to be more effective at improving quality of life during cold and flu recovery than physical exercise, thus improving the overall recovery process. In this experiment, meditation and physical exercise were both lifestyle choices which stood to improve physical recovery from the flu. While meditation was found to have no effect on physical recovery, mental and emotional metrics were improved by meditation over physical exercise.

In the spirit of Obasi et al.we chose to distinguish between two metric of health during recovery: physical health and mental health. Within the limits of the Island, we chose to measure physical health during the process of recovery through the body's white blood cell count. We chose to measure mental and emotional health through chemicals in the brain which have been associated with happiness: serotonin and dopamine.[2]

In order to understand which types of lifestyle choices are most beneficial to recovery, we have also chosen activities which fit under the categories of physical health and mental health. Our choices of activities–specifically mental health activities– were limited to those available on the island. For example, we have not considered diet because within the constraints of the Island, we are limited in our ability to affect the day-to-day lifestyle choices of our participants. That is why we chose to focus on once-daily actions such as going for a run, or briefly meditating.

Like Obasi et al. we wanted to study a simple physical exercise so we chose running 1 km, as it would not provide excessive strain on the sick participants. To represent mental health activities, we chose thinking happy thoughts for one minutes (the closest island activity to meditation) as well as petting a dog for 15 minutes, as animals have been known to have positive effects on pet owners.[3]

Methods and Procedures

Design

We knew we needed to take multiple measures to understand the progression of recovery, but we also knew subject-to-subject variability of recovery could be high. It wouldn't be feasible to give every subject every treatment as that would effectively require inoculating every person four different times. Repeated Measures was suited to our design because it allowed us to take multiple measures while blocking on potential nuisance factors like sex and age while not giving every person every treatment, but still measuring person-to-person variability.

When we originally calculated our sample size, we were operating under the assumption the Two-Factor Completely Randomized Block design was going to be most appropriate for our experiment and that we should expect an effect size of about .30 (given Chidi N. Obasi et al.). Using GPower with a power of .80 and a confidence of 95%, we estimated a sample size of 128 total participants, with 16 participants in each of the eight groups (assuming we were blocking on sex only). Upon realizing the Repeated Measures design was the most appropriate design for our experiment, we realized the appropriate sample size was about 32 total participants with 4 in each of the eight groups. By that time, however, we had already begun collecting data, so we continued with our sample size of 128 throughout the experiment. This will end up being helpful for estimating the post-hoc power of our effects sizes, as they turned out much smaller than expected.

We also decided after data collection (from the advice of Professor Almohalwas) to include an additional blocking factor of age. As a result, this variable was not considered when calculating the original sample size. Because we did not use randomized strategies to select age ranges, but our subjects were selected randomly, that brings our model to a four factor mixed effects repeated measures design.

Participants and Sampling Method

To achieve a random sampling, the easiest way is to give each village an index and sample one randomly each time. The problem is there are no immediately available indexes; but we can do it in an indirect way. We record the number of villages in each city and calculate the accumulated sum from city 1 to city k for each city. Next we generate a random number from 1 - 276, find the corresponding interval (city) it falls in. Then we minus the accumulated number from it: say the result is k, then go to the k-th village in this city. Finally we pick a house by trying every third house until getting a viable participant in the house

Procedure

Our experiment took place over the course of eight days. This in accordance with Harvard Health which found the average person sees flu symptoms one to four days after exposure and symptoms last five to seven days after that. In order to maximize the earliest effect of the virus we chose to wait four days after exposure. We intended to continue to experiment for the full seven days after, but in the middle of collecting data, we realized through a G Power calculation that we could still expect over 80% power with our overly-large sample size if we only measured four days. So we chose to continue the experiment for a total of eight days.

Day 0:
All participants receive 1 dose of the available flu virus from the island: 50 μg of Influenza W42.

Day 1-3:

We did not interact at all with the subjects during these days while we waited for symptoms to manifest.

Day 4-8:
We initialized the first round of treatments on the fourth day since injection. Participants performed their assigned Activity (either running 1 km, thinking happy memories for 1 minute, petting a dog for 15 minutes, or nothing at all–the control group). In order to take our measurements at the time of peak serotonin and dopamine levels, we had to wait the appropriate amount of time after each activity. Running required a 30 minute break [4], thinking happy memories required 20 minutes [5], and petting a dog required 10 minutes [3].

The entire procedure from day 0 to day eight can be summarized by Figure 1.

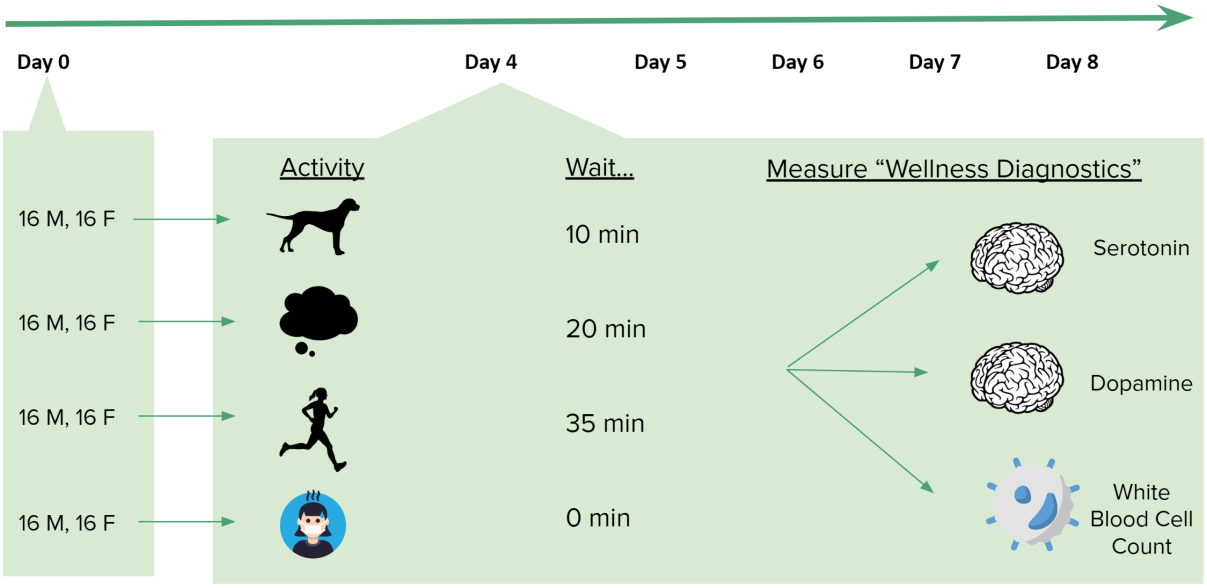


Figure 1: Summary of procedure from day 1 to day 8

Instruments

As mentioned above, we used the Island throughout this experiment as a simulated environment for our participants. Simulating random numbers for sampling was done in R Studio and all of the procedure was performed on simulated participants on the Island. Data was collected from the Island in Excel and then cleaned and analyzed in R. We primarily used the Dplyr library for data cleaning, aov and lmer functions for modelling, and GGplot2 and Kable libraries for visualizations. Some irregularity when collective dopamine data is reflected in the variable `weird_dopamine_record` in our final dataset.

Exploration of Data

Patterns in Figure 2 show white blood cell counts are not consistent over time and there appears to be potential interaction between Age, Activity, and Sex as older females respond better to running (by having a lower count) than younger females. And the same pattern is present for males.

In Figure 3, we again see evidence of interaction between Sex and Activity on dopamine level, but no interaction with Age. Males responded best to happy memories and females responded best to petting a dog.

In Figure 4, we can see the potential effects of Sex on Serotonin as males appear to have lower levels overall. Sex and Age also appear to interact with Activity as younger females responded worse to running than older females who responded best to running. Males fluctuated in their response to running, but by day 8 all responded best to running. All sex and age groups responded differently to control groups as well.

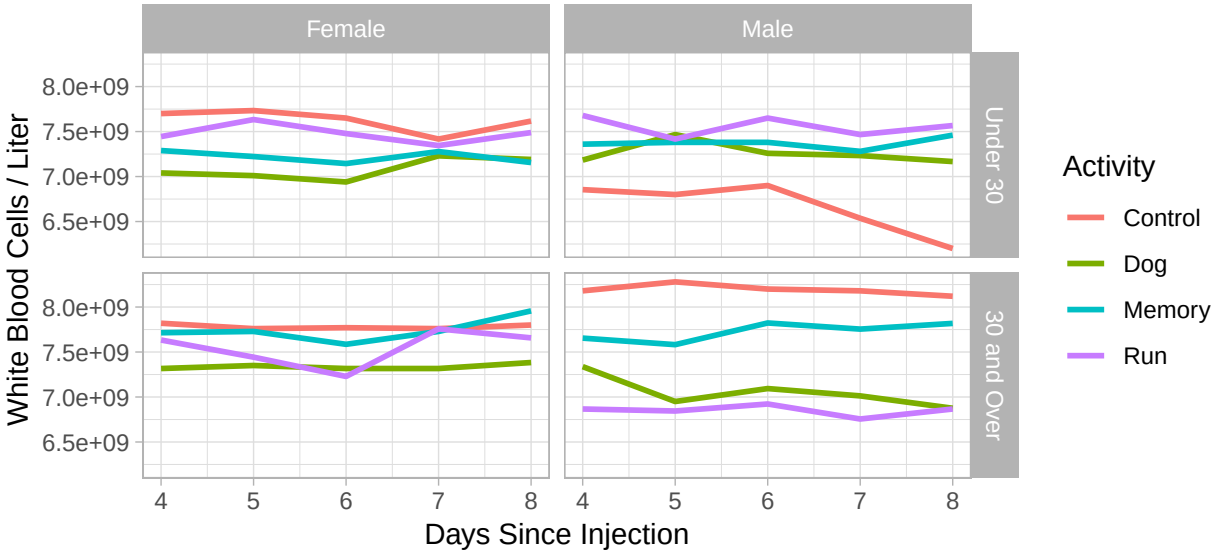


Figure 2: Mean White Blood Cell Count Since Injection by Activty, Age, and Sex

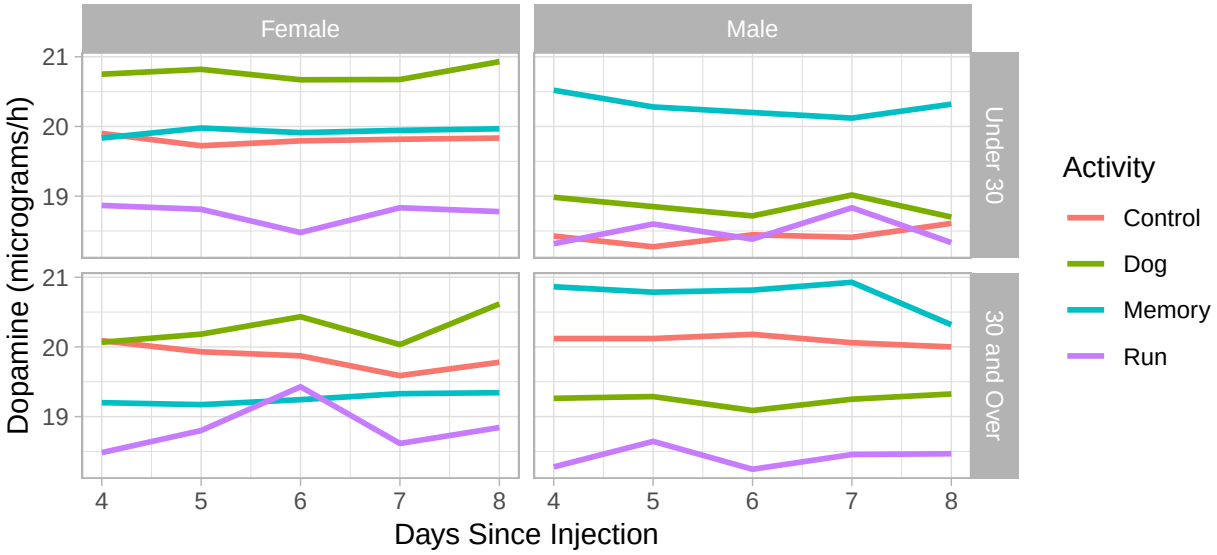


Figure 3: Mean Dopamine Levels Since Injection by Activty, Age, and Sex

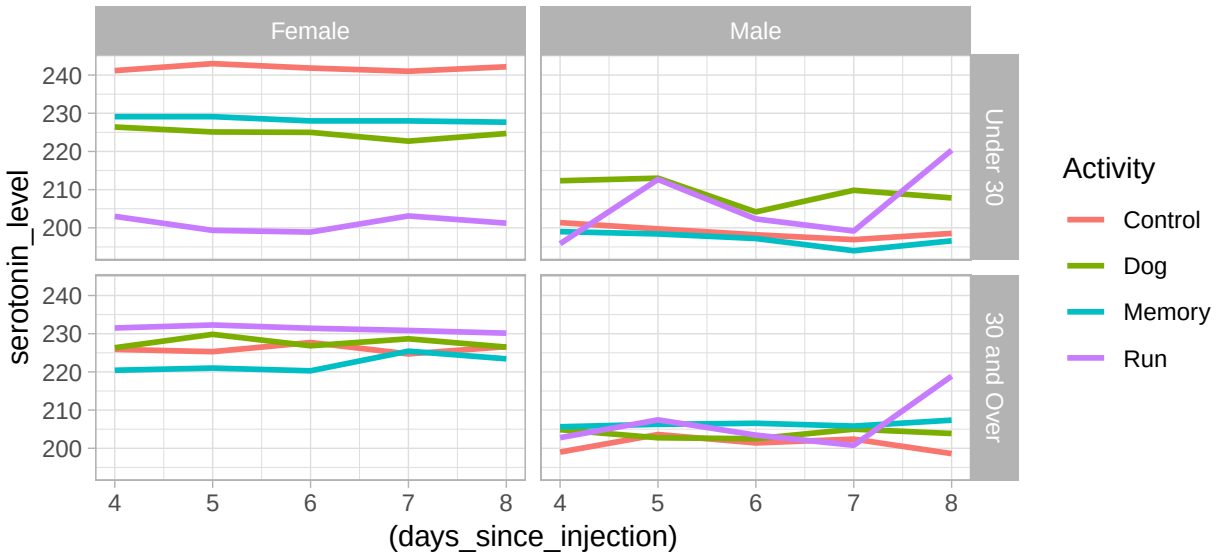


Figure 4: Mean Serotonin Levels Since Injection by Activty, Age, and Sex

Modelling

The models we are investigating are:

$$WhiteBloodCellCount \sim Activity * Sex * Age * DaysSinceInjection + Error(Participant)$$

$$DopamineLevel \sim Activity * Sex * Age * DaysSinceInjection + Error(Participant)$$

$$SerotoninLevel \sim Activity * Sex * Age * DaysSinceInjection + Error(Participant)$$

White Blood Cell Count

Running the full model with all interactions (Figure 5), shows that none of the interactions nor any of the predictors are significant.

Furthermore, running a Chi Squared test between a lmer model and a lm model returns a value of 1, suggesting we should reject the null hypothesis that individual participants have random effects and should be considered in the error of the mode. Therefore, a modified model is

$$WhiteBloodCellCount \sim Activity * Sex * Age * DaysSinceInjection$$

This model determines that Sex, Age, the interaction of Activity and Age, and the interaction of Activity and Sex and Age are all significant in predicting White Blood Cell count. Patterns which we saw in the exploratory graphs are confirmed: age, sex, and activity all interacted to determine white blood cell count. Additionally, females had higher White Blood Cell Counts (7.46×10^9 versus 7.26×10^9 in males) and participants 30 and above had higher counts (7.51×10^9 versus 7.22×10^9 in younger participants). Neither Activity nor days since injection were significant alone in predicting White Blood Cell count.

white blood cell count ANOVA result

Predictor	df_{Num}	df_{Den}	*Epsilon*	SS_{Num}	SS_{Den}	*F*	*p*	η^2_g
(Intercept)	1.00	108.0		3.359E+22	8.167E+20	4441.67	.000	.97
Activity	3.00	108.0		1.110E+19	8.167E+20	0.49	.691	.01
Sex	1.00	108.0		2.978E+18	8.167E+20	0.39	.532	.00
Age_block	1.00	108.0		7.975E+18	8.167E+20	1.05	.307	.01
Activity x Sex	3.00	108.0		3.635E+18	8.167E+20	0.16	.923	.00
Activity x Age_block	3.00	108.0		2.804E+19	8.167E+20	1.24	.300	.03
Sex x Age_block	1.00	108.0		5.361E+15	8.167E+20	0.00	.979	.00
Activity x Sex x Age_block	3.00	108.0		2.338E+19	8.167E+20	1.03	.382	.02
days	2.36	254.8	0.59	3.647E+17	1.017E+20	0.39	.714	.00
Activity x days	7.08	254.8	0.59	1.855E+18	1.017E+20	0.66	.710	.00
Sex x days	2.36	254.8	0.59	1.533E+18	1.017E+20	1.63	.193	.00
Age_block x days	2.36	254.8	0.59	6.319E+17	1.017E+20	0.67	.536	.00
Activity x Sex x days	7.08	254.8	0.59	1.080E+18	1.017E+20	0.38	.914	.00
Activity x Age_block x days	7.08	254.8	0.59	1.516E+18	1.017E+20	0.54	.808	.00
Sex x Age_block x days	2.36	254.8	0.59	5.665E+16	1.017E+20	0.06	.961	.00
Activity x Sex x Age_block x days	7.08	254.8	0.59	2.155E+18	1.017E+20	0.76	.621	.00

Figure 5

Table 1: Summary of modified ANOVA for White Blood Cell Count

Predictors	Df	Sum.Sq	Mean.Sq	F.value	P.value
Activity	3	1.159746e+19	3.865821e+18	2.284	0.078
as.factor(days_since_injection)	4	2.882559e+17	7.206397e+16	0.043	0.997
Sex	1	6.696808e+18	6.696808e+18	3.956	0.047
Age_block	1	1.267257e+19	1.267257e+19	7.486	0.006
Activity:as.factor(days_since_injection)	12	2.084237e+18	1.736865e+17	0.103	1
Activity:Sex	3	9.482986e+18	3.160995e+18	1.867	0.134
as.factor(days_since_injection):Sex	4	1.774444e+18	4.436110e+17	0.262	0.902
Activity:Age_block	3	2.617810e+19	8.726035e+18	5.155	0.002
as.factor(days_since_injection):Age_block	4	8.192452e+17	2.048113e+17	0.121	0.975
Sex:Age_block	1	8.114926e+15	8.114926e+15	0.005	0.945
Activity:as.factor(days_since_injection):Sex	12	1.148949e+18	9.574574e+16	0.057	1
Activity:as.factor(days_since_injection):Age_block	12	1.360895e+18	1.134079e+17	0.067	1
Activity:Sex:Age_block	3	2.464274e+19	8.214246e+18	4.853	0.002
as.factor(days_since_injection):Sex:Age_block	4	2.471380e+16	6.178451e+15	0.004	1
Activity:as.factor(days_since_injection):Sex:Age_block	12	1.980194e+18	1.650161e+17	0.097	1
Residuals	544	9.208655e+20	1.692767e+18		

Figure 6 is an effects table based on a Tukey HSD post hoc analysis of all the interactions between Age, Sex, and Activity. It had been filtered to show only significant interactions. From it we can draw the following conclusions, Male participants who were age 30 and above and pet dogs or thought happy memories or ran all had significantly lower white blood cell counts than the control group of the same demographics. Older women in the control group had higher White Blood Cell counts than younger men. Older women who thought happy memories had higher White Blood Cell counts than younger males in the control group.

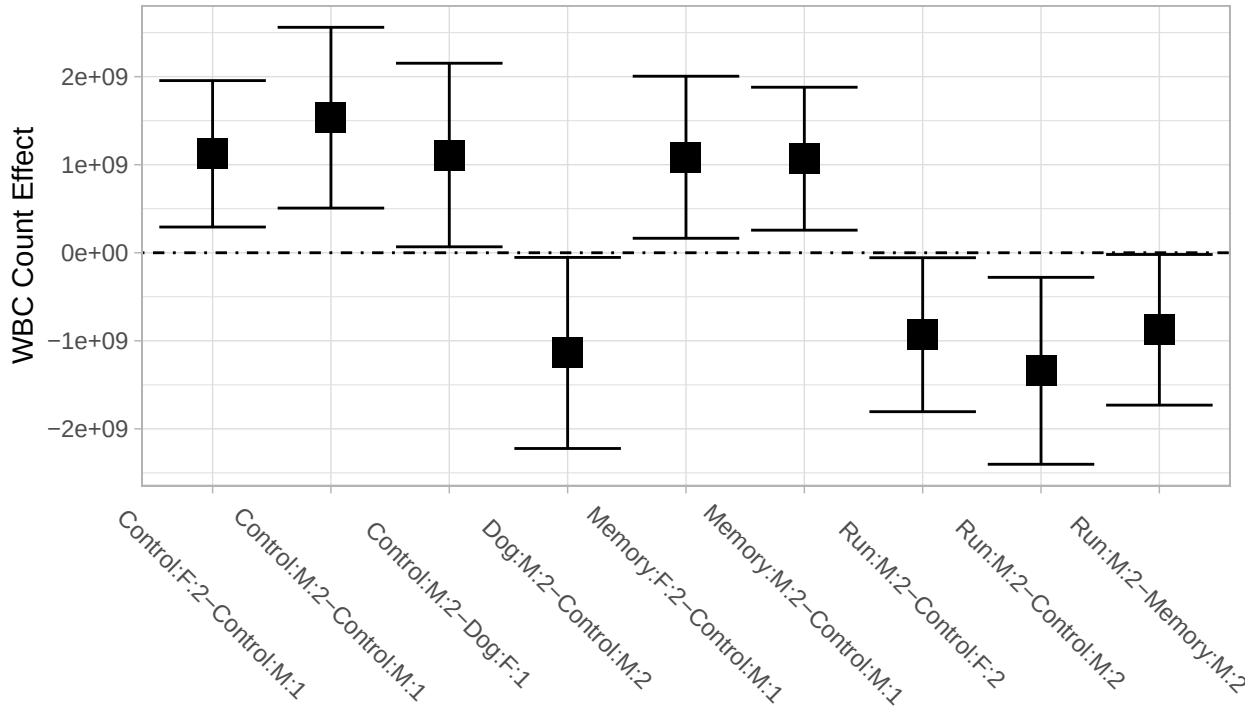


Figure 6: Effects Plot of Significant Interactions on White Blood Cell Count

This model is valid because, even though days since injection is not significant, this model satisfies all diagnostics: homoskedasticity, linearity, normality of errors and no bad leverage points.(See appendix for plots).

Dopamine Levels

Running the full dopamine model with all interactions (Figure 7) shows that the only significant predictor of dopamine is Activity. This cannot be repaired by considering participants as fixed effects because running a Chi Squared test between a lm() and lmer() model returns 0 which tells us there is a significant difference between including participants as random effects and keeping them as fixed effects.

An effects plot from a post hoc Tukey HSD in Figure 8 shows us that running was associated with the lowest dopamine levels and was significantly lower than both the control group and the group that pet dogs. On the other hand, participants who thought happy memories had the highest dopamine levels, but they were only significantly higher than the control group.

dopamine level ANOVA result

Predictor	df_{Num}	df_{Den}	*Epsilon*	SS_{Num}	SS_{Den}	*F*	*p*	η^2_g
(Intercept)	1.00	108.00		235795.30	2254.82	11293.97	.000	.99
Activity	3.00	108.00		201.99	2254.82	3.22	.025	.08
Sex	1.00	108.00		15.68	2254.82	0.75	.388	.01
Age_block	1.00	108.00		2.30	2254.82	0.11	.741	.00
Activity x Sex	3.00	108.00		108.95	2254.82	1.74	.163	.04
Activity x Age_block	3.00	108.00		22.89	2254.82	0.37	.778	.01
Sex x Age_block	1.00	108.00		30.12	2254.82	1.44	.232	.01
Activity x Sex x Age_block	3.00	108.00		12.29	2254.82	0.20	.899	.01
days	2.92	315.42	0.73	0.12	138.52	0.09	.963	.00
Activity x days	8.76	315.42	0.73	2.01	138.52	0.52	.854	.00
Sex x days	2.92	315.42	0.73	1.60	138.52	1.25	.291	.00
Age_block x days	2.92	315.42	0.73	1.31	138.52	1.02	.381	.00
Activity x Sex x days	8.76	315.42	0.73	3.01	138.52	0.78	.629	.00
Activity x Age_block x days	8.76	315.42	0.73	3.04	138.52	0.79	.622	.00
Sex x Age_block x days	2.92	315.42	0.73	0.90	138.52	0.70	.549	.00
Activity x Sex x Age_block x days	8.76	315.42	0.73	2.52	138.52	0.65	.746	.00

Figure 7

Our final model for dopamine will be:

$$DopamineLevel \sim Activity$$

Plotting the diagnostics of this model shows that it satisfies all conditions (see Appendix).

Serotonin Levels

Running the full model with all interactions (Figure 9), shows that Sex is a strong predictor of Serotonin. From our earlier explorations we know that means females have a significantly higher level of serotonin than males. Additionally, days are significant predictors of serotonin. The following interactions are also significant: Activity X Days, Sex X Days, Activity X Days X Sex. We will continue regarding participants as random effects because the Chi Squared test between the lm() and lmer() models returned 0, rejecting the null hypothesis that participants do have fixed effects.

The effects plots in Figure 10 represent effects of different activities based on sex. Females had higher serotonin levels than males among all activities except running. Among females, the most significant activity was running and it's impact on dopamine levels was the most negative. Among just males, non of the activities was significantly different.

These interactions refine our final model for serotonin to:

$$SerotoninLevel \sim Activity * Sex * DaysSinceInjection + Error(Participant)$$

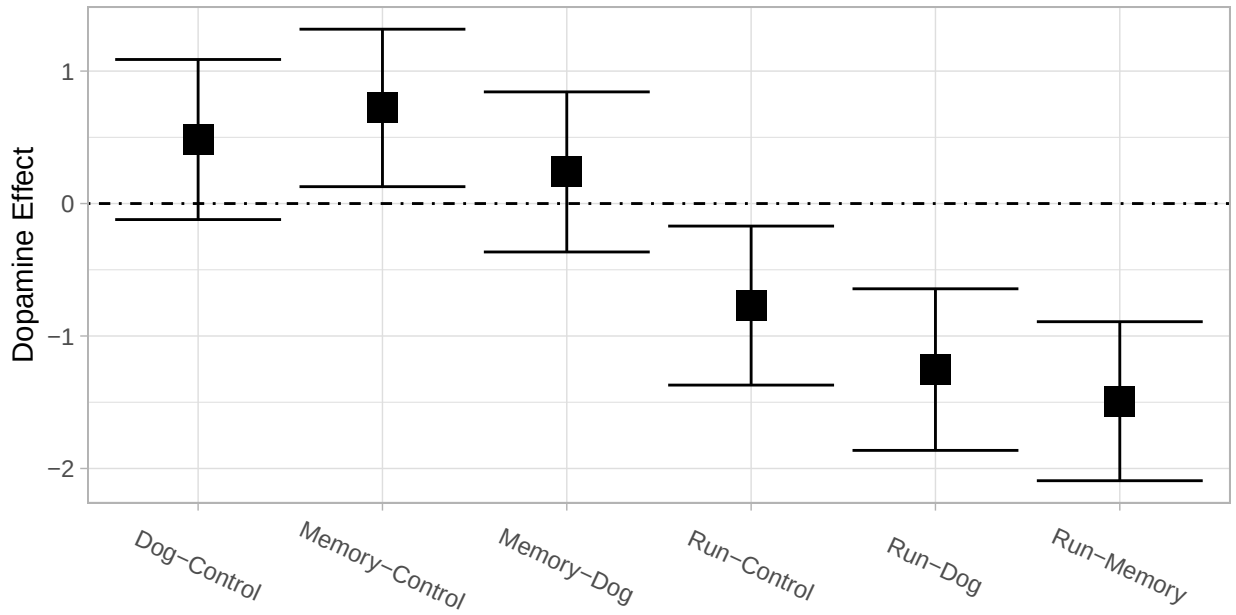


Figure 8: Effects Plot of Activity on Dopamine Level

This model satisfies all conditions, except for some problems with normality (see Appendix).

Conclusion

The global COVID-19 pandemic has reemphasized the importance of understanding what helps humans recover from viral illnesses, like the common cold and influenza. What's more, mental health research has brought to light the potential benefits meditation and mindfulness exercises can have on mental health and wellness. Our goal with this experiment was to explore the relationships between white blood cell count, dopamine level, and serotonin level and various lifestyle activities which can benefit physical and mental health.

For white blood cell counts with random effects, no factors are significant. This means there are no significant differences in white blood cell counts between male and female and across different activity groups; also this shows the counts stay relatively stable over the period of flu. However, if you consider individuals as fixed effects, Sex and Age are both significant in determining count and the interaction of Activity, Sex and Age is significant. Regardless of the effect of individuals, we see white blood cell count staying constant over time. This suggests lifestyle activities were not impactful on the physical health and recovery of participants during our five day time frame.

For dopamine level, activity factor is significant, which means activity has a significant effect on the dopamine level during flu. All other factors are not significant; this means sex, time, age and their interactions are not affecting the dopamine level. This is the purest indication that lifestyle activities can affect happiness, even during sickness. Those who thought happy memories had significantly higher dopamine levels than the control group. However, running had the reverse effect and lowered dopamine levels significantly below the control group. This suggests dopamine responded better to emotional wellness activities and was hindered by

serotonin level ANOVA result

Predictor	df_{Num}	df_{Den}	*Epsilon*	SS_{Num}	SS_{Den}	*F*	*p*	η^2_g
(Intercept)	1.00	108.00		2.85E+07	348305.34	8825.84	.000	.99
Activity	3.00	108.00		3630.0	348305.34	0.38	.771	.01
Sex	1.00	108.00		68414.1	348305.34	21.21	.000	.16
Age_block	1.00	108.00		618.8	348305.34	0.19	.662	.00
Activity x Sex	3.00	108.00		11055.6	348305.34	1.14	.335	.03
Activity x Age_block	3.00	108.00		10310.6	348305.34	1.07	.367	.03
Sex x Age_block	1.00	108.00		58.2	348305.34	0.02	.893	.00
Activity x Sex x Age_block	3.00	108.00		13919.1	348305.34	1.44	.236	.04
days	3.78	407.98	0.94	564.8	11550.61	5.28	.000	.00
Activity x days	11.33	407.98	0.94	1532.9	11550.61	4.78	.000	.00
Sex x days	3.78	407.98	0.94	514.5	11550.61	4.81	.001	.00
Age_block x days	3.78	407.98	0.94	162.5	11550.61	1.52	.199	.00
Activity x Sex x days	11.33	407.98	0.94	2021.1	11550.61	6.30	.000	.01
Activity x Age_block x days	11.33	407.98	0.94	230.1	11550.61	0.72	.727	.00
Sex x Age_block x days	3.78	407.98	0.94	79.9	11550.61	0.75	.553	.00
Activity x Sex x Age_block x days	11.33	407.98	0.94	484.7	11550.61	1.51	.122	.00

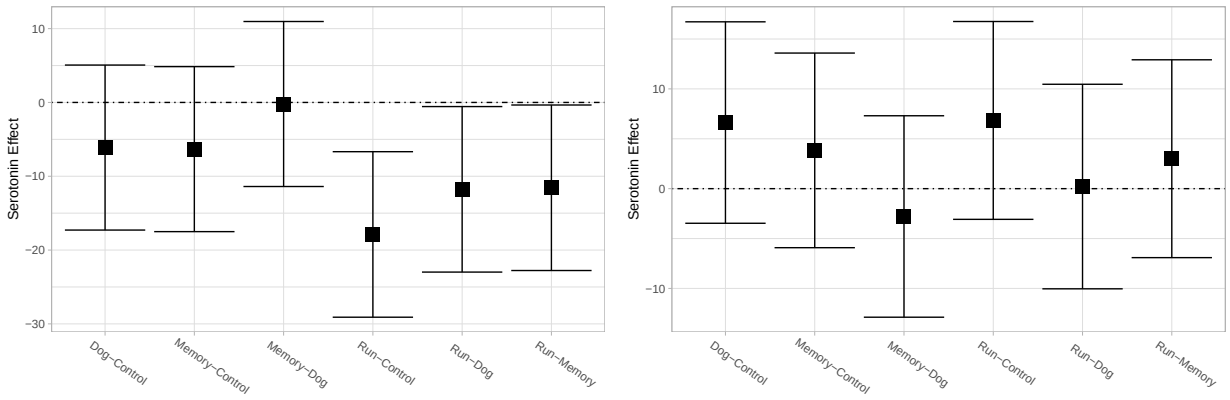
Figure 9

physical exertion.

For serotonin level, sex is a siginificant determinant and female serotonin levels were higher than male levels regardless of age. When considering random effects, we see days since injection are significant, which means the serotonin level varies with time during the recovery of flu. Additionally,the three interactions between activity, days and sex are all found to be significant. One way to interpret this is the effect of sex and different activities are changing over time. Another way can be the time series pattern of serotonin level is significantly different between different sex and activity groups. Nevertheless, different age groups and sexes can expect to see difference effects based on the activities they perform. Females saw significantly lower serotonin levels compared to all other exercises, regardless of age. For males, there were no significant differences between any two activities.

Because the effects size of these conclusions are so much smaller than we initially anticipated (see the η^2 columns in Figures 5, 7 and 8) the resulting power of our effects are also much smaller. Our largest effect size was .16 for the effect of Sex on Serotonin. Because this only involved two groups over 128 participants, this conclusion has a post-hoc power of 99.48%. Our next largest effect was .08 for the effect of Activity on Dopamine. Because this involved four groups over 128 participants, this only had a post-hoc power of 36.24%.

Further experiments of this nature could improve upon our work by increasing sample size to account for small effects sizes. We would also adjust the metrics for measuring happiness to include more subjective measures, like surveys. This allows for a more hollistic understanding of happiness and wellness during recovery. A longer time period of data collection would also allow for a fuller understanding of the progression of flu recovery. Time-series analysis techniques would also benefit this research in understanding day-to-day



(a) Effects Plot of Activity and Sex on Serotonin Level

(b) Effects Plot of Activity and Sex on Serotonin Level

Figure 10: Effects Plot of Activity by Sex

changes.

While lifestyle activities were only found to improve happiness in terms of Dopamine levels, the differences in white blood cell count under some models suggests there are potential physical benefits to wellness lifestyle activities during flu recovery. And even if a person's white blood cell count isn't any higher or lower, perhaps improves happiness and mental health is enough to guarantee a successful recovery.

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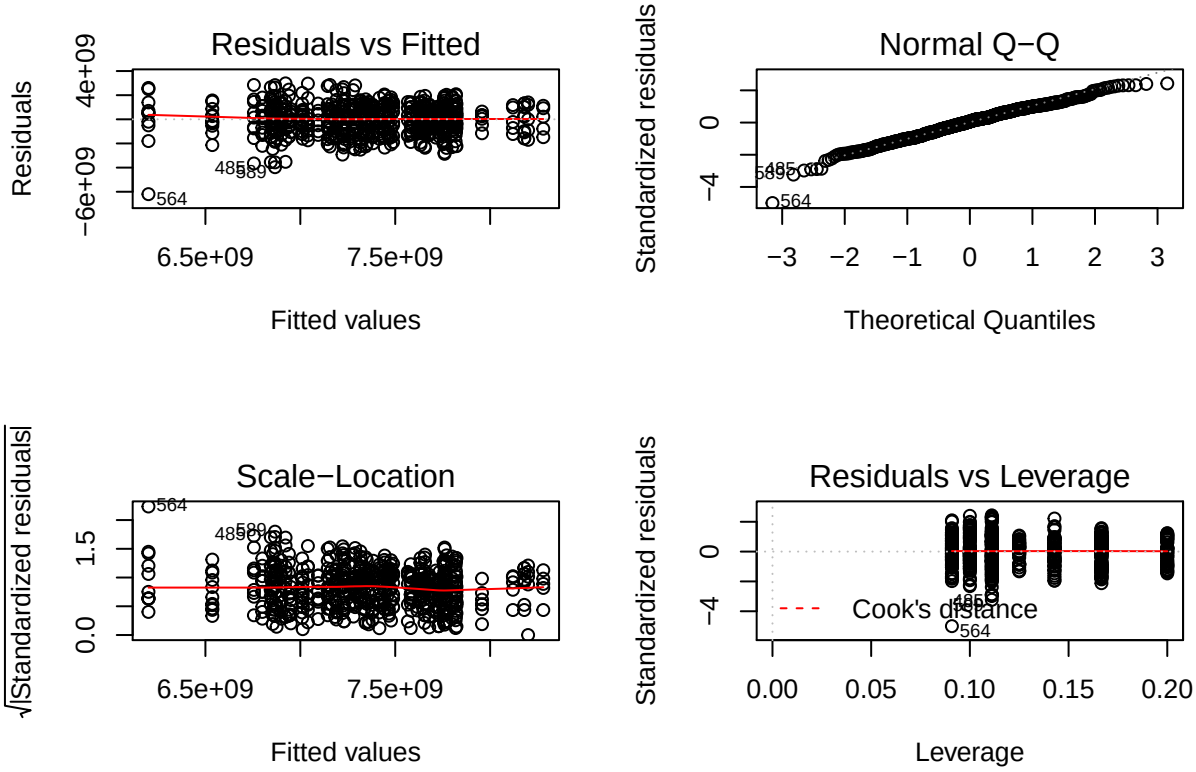
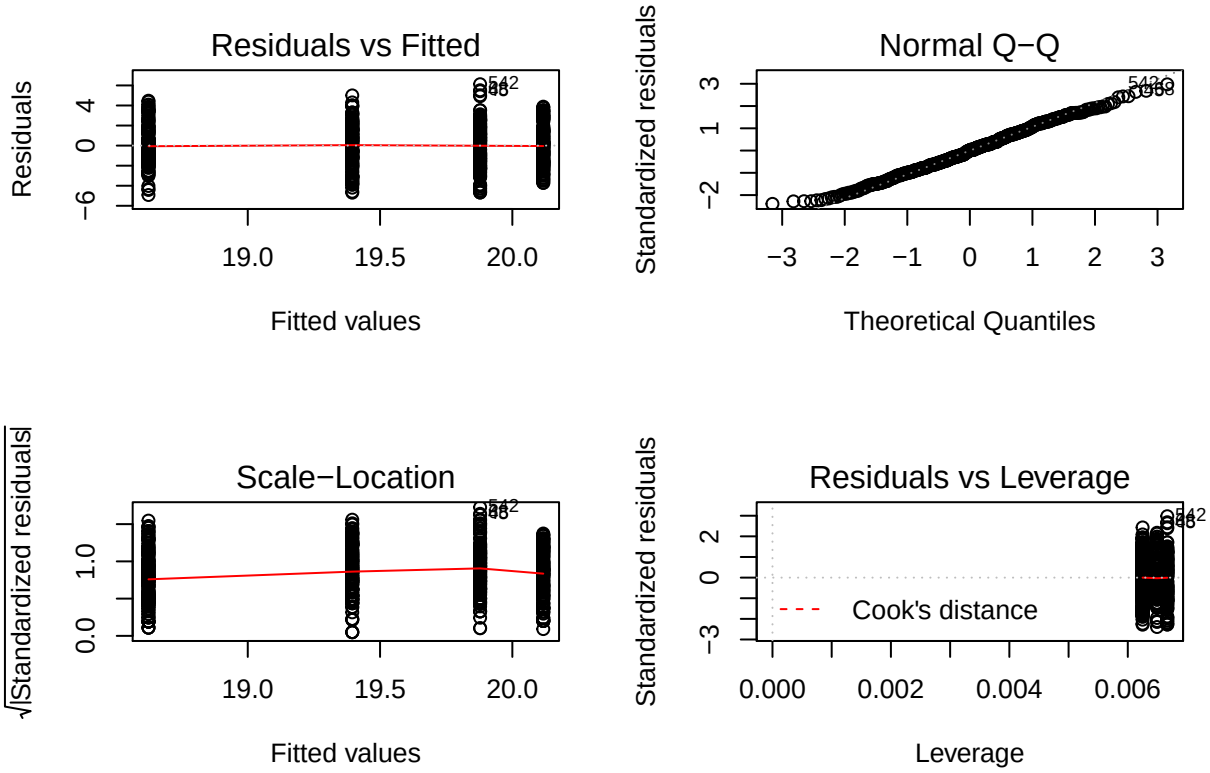
Appendix: Diagnostic Plots

Diagnosic Plots for Final White Blood Cell Model



Diagnosic Plots for Final Dopamine Model



Diagnosic Plots for Final Serotonin Model